

Annex 11

Guidance on the selection of comparator pharmaceutical products for equivalence assessment of interchangeable multisource (generic) products

Introduction

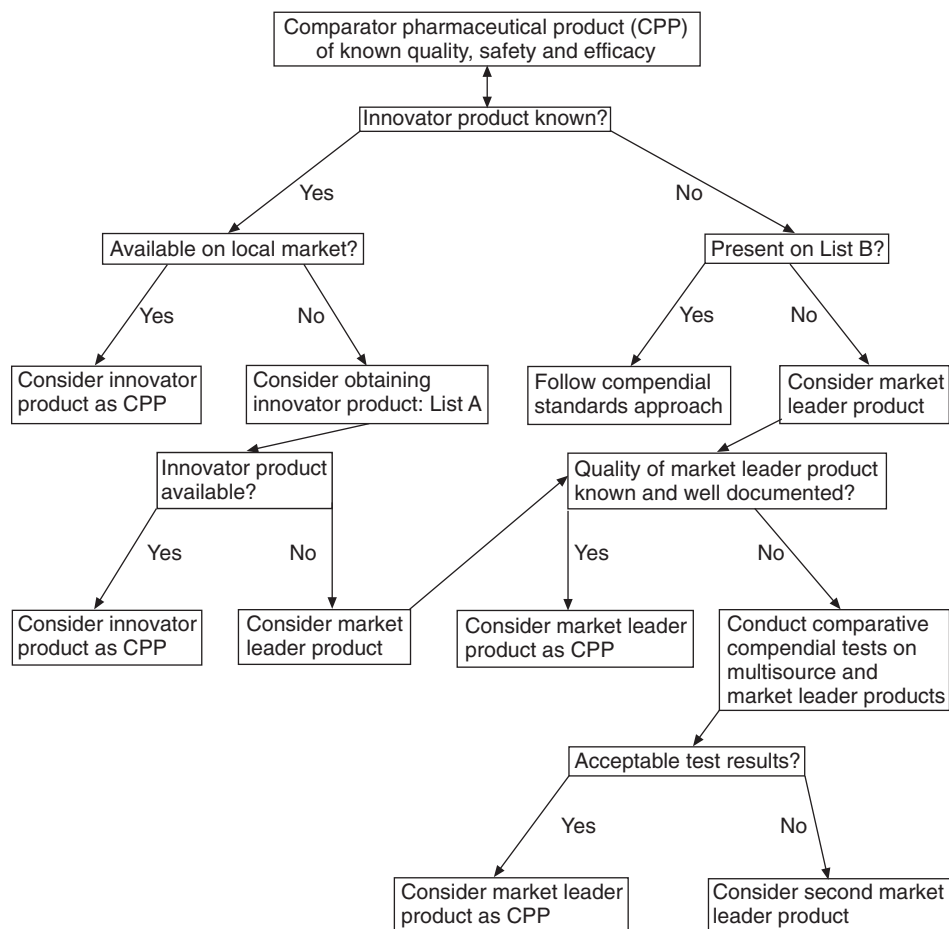
This annex provides a list of comparator products for equivalence assessment of interchangeable multisource (generic) products. The information on comparator pharmaceutical products was collected by the Secretariat from drug regulatory authorities and pharmaceutical companies. The list has been drawn up to assist regulatory authorities and pharmaceutical companies in deciding on appropriate comparator products in the context of multisource (generic) marketing authorization. The information could also be used for drug procurement purposes. Where the comparator pharmaceutical product is not clearly defined, criteria are suggested that are provided in a decision-tree format (see Figure 1). This permits the selection of a comparator pharmaceutical product.

The guidelines on registration requirements to establish interchangeability of multisource (generic) pharmaceutical products published by WHO (*1*) state that multisource products must satisfy the same standards of quality, safety and efficacy as those applicable to the corresponding innovator product. They recommend that quality attributes of a multisource product should be tested against the innovator product for which interchange is intended.

The innovator product is usually the most logical comparator product because its quality, safety and efficacy should have been well assessed in pre- and post-marketing studies and, in addition, the data on its safety and efficacy are usually linked to a pharmaceutical product with defined specifications for quality and performance. Despite acceptance of the general objective, there is no agreement on the criteria for selecting a list of international comparator products, nor does a list of such products exist. The comparator product chosen is either the most widely used “leading” product on the market or the product that was first introduced in that market. For this reason, among others, significant differences may exist between the comparator products used in different countries.

Figure 1

Decision-tree for use in identifying a comparator pharmaceutical product



In the light of the various approaches currently under scientific and regulatory discussion, the feasibility of developing a system of international comparator products was considered. This initiative led to the recommendations given here, which replace those of Part Seven of the previously published WHO guidelines on multisource pharmaceutical products (1).

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

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

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.
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
chtab	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
sbldtab	tablet, sublingual
sctab	scored tablet
sgtab	sugar-coated tablet
sl	solution
sr	sustained-release 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.

Table 1

International comparator products for equivalence assessment of interchangeable multisource (generic) products^a

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products		
			Trademark	Primary market	Manufacturer
List A					
alendazole	6.1.1	chtab, 200mg	Zental	France	SmithKline Beecham
amloride, hydrochloride	16	tab, 5mg	Midamor	United Kingdom	Merck, Sharp & Dohme
aminophylline	25.1	tab, 100mg, 200mg (sr), 125mg	Aminophyllin	Germany	BYK Gulden Lomborg
amitriptyline, hydrochloride	24.2.1	tab, 25mg	Elavil	USA	Zeneca
amoxicillin	6.2.1	cap, 250mg, 500mg pwoSP, 125mg/5ml tab, 250mg, 500mg	Amoxil	United Kingdom	SmithKline Beecham
atenolol	12.1	tab, 50mg, 100mg	Tenormin	United Kingdom	Zeneca
	12.2	tab, 50mg, 100mg			
	12.3	tab, 50mg, 100mg			
atropine, sulfate	21.5	eyd, 0-1%, 0.5%, 1%	Atropin Dispersa	Switzerland	Ciba Vision (Novartis)
benznidazole	6.5.5	tab, 100mg	Radanil	Argentina, Brazil, Switzerland	Roche
biperiden, hydrochloride	9	tab, 2mg	Akineton	Germany	Knoll
captopril	12.3	sctab, 25mg	Capoten	USA	Bristol-Myers Squibb
carbamazepine	5	sctab, 100mg, 200mg (sr)	Tegretol	Switzerland	Novartis
chloramphenicol	6.2.2	cap, 250mg	Chloromycetin	USA	Parke-Davis
chloramphenicol, sodium succinate	6.2.2	oilspinj, 0.5g/2ml	Chloromycetin sodium succinate	USA	Parke-Davis/Parkedale
chloroquine, phosphate	6.5.3	tab, 25mg, 100mg, ^b 150mg, ^{b,c} 500mg	Alaren phosphate	USA	Sanofi Winthrop
chlorphenamine, hydrogen maleate	3	tab, 4mg	Chlorfrimeton	USA	Schering-Plough
ciclosporin	8.1	cap, 25mg	Sandimmun	Switzerland	Novartis

Table 1 (continued)

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products		
			Trademark	Primary market	Manufacturer
cimetidine	17.1	tab, 200mg	Tagamet	France	SmithKline Beecham
ciprofloxacin, hydrochloride	6.2.2	tab, 250mg	Ciprobay	Germany	Bayer
clofazimine	6.2.3	cap, 50 mg, 100mg	Lamprene	Switzerland	Novartis
clomifene, citrate	18.6	tab, 50mg	Clomid	USA	Hoechst Marion Roussel
clomipramine, hydrochloride	24.4	cap, 10mg, 25 mg	Anafranil	Switzerland	Novartis
clonazepam	5	sctab, 500µg	Rivotril	Switzerland	Roche
cloxacillin, sodium	6.2.1	cap, 500mg	Penstaphon	Belgium	Bristol-Myers Squibb
		pwsl, 125mg/5ml	Tegopen	USA	
cyclophosphamide	8.2	tab, 25mg, 50mg	Endoxana	United Kingdom	ASTA Medica
dapsone	6.2.3	tab, 25 mg , 50mg, 100mg	Dapsone	USA	Jacobus
desmopressin, acetate	10.2	nsp, 10µg/metered dose	DDAVP	USA	Ferring
dexamethasone	3	tab, 500µg, 4 mg	Decadron	USA	Merck, Sharp & Dohme
	18.1	tab, 500µg, 4 mg			
diazepam	24.3	sctab, 2mg, 5mg	Valium	USA	Roche
doxazosin mesilate	12.3	tab, 1mg, 2mg, 4mg	Caldura	Germany	Pfizer
doxycycline, hyclate	6.2.2	cap, 100mg	Vibramycin	Germany	Pfizer
		tab, 100mg			
epinephrine, hydrochloride	21.5	eyd, 2%	Suprarenin	Germany	Hoechst Marion Roussel
ergocalciferol	27	cap, 1.25mg (50000IU) osl, 250µg/ml (10000IU/ml)	Drisdol	USA	Sanofi
		tab, 1.25mg (50000IU)			
ethinylestradiol	18.4	tab, 10µg, 20µg, 50µg	Pregnyon C	Germany	Schering
ethinylestradiol + levonorgestrel	18.3.1	tab, 30µg + 150µg, 50µg + 250µg	Nordette-21	USA	Wyeth-Ayerst

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
flucytosine	6.3	cap, 250mg	Ancobon	USA	ICN Pharmaceuticals
fludrocortisone, acetate	18.1	tab, 100µg	Fiorinef	USA	Bristol-Myers Squibb
flourouracil	13.5	oin, 5%	Efudix	USA	Roche
fluphenazine, decanoate	24.1	depot inj, 25mg/ml	Prolixin decanoate	USA	Bristol-Myers Squibb
fluphenazine, enantate	24.1	depot inj, 25mg/ml	Prolixin enantate	USA	Bristol-Myers Squibb
furosemide	16	tab, 40mg	Lasix	Germany	Hoechst Marion Roussel
glyceryl trinitrate	12.1	subtab, 500µg chcap, 800µg	Nitroglycerin Wander	Switzerland	Novartis
griseofulvin	6.3	cap, 125mg, 250mg tab, 125mg, 250mg	Grisactin Fulcin	USA USA	Zeneca
haloperidol	24.1	tab, 2mg, 5mg	Haldol	Belgium	Janssen
hyalazine, hydrochloride	12.3	tab, 25mg, 50mg pwinj, 20mg	Apresoline	Netherlands United Kingdom	Novartis
hydrochlorothiazide	12.3	tab, 25mg, 50mg	Hydrosaluric	United Kingdom	Merck, Sharp & Dohme
ibuprofen	2.1	tab, 200mg	Nurofen	UK	Boots
idoxuridine	21.1	eycd, 0.1%	Herplex	USA	Allergan
imipenem (monohydrate) + cilastin (sodium)	6.2.1	eyo, 0.2% pwinj, 250mg + 250mg, 500mg + 500mg	Tienam	Italy	Merck, Sharp & Dohme
insulin injection (soluble)	18.5	pwinj, 500mg + 500mg inj, 40IU/ml, 80IU/ml; +80IU/ml	Actrapid	Germany	Novo Nordisk
		inj, 40IU/ml, 80IU/ml; 100IU/ml	Actrapid	Zimbabwe	
		inj, 40IU/ml, 80IU/ml; 100IU/ml	Novolin R	Japan, USA	

Table 1 (continued)

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products		
			Trademark	Primary market	Manufacturer
intermediate-acting insulin (as compound insulin zinc suspension)	18.5	inj, 40 IU/ml, 80 IU/ml, 100 IU/ml	Humulin L	USA	Eli Lilly
intermediate-acting insulin (as isophane insulin)	18.5	inj, 40 IU/ml, 80 IU/ml, 100 IU/ml	Humulin N	USA	Eli Lilly
ipratropium bromide	25.1	inh, 20 µg/metered dose	Atrovent	USA	Boehringer Ingelheim
iron dextran	10.1	inj, equiv. to 50 mg iron/ml	Infed	USA	Shein Pharmaceuticals
isosorbide dinitrate	12.1	sbltab, 5 mg	Isordil	USA	Wyeth-Ayerst
ivermectin	6.1.2	sctab, 6 mg	Mectizan/Stromectol	Netherlands	Merck, Sharp & Dohme
ketoconazole	6.3	osp, 100 mg/5 ml tab, 200 mg	Nizoral	Belgium	Janssen
levamisole, hydrochloride	6.1.1	tab, 50 mg, 150 mg	Ergamisol	Belgium	Janssen
levodopa	8.2	tab, 50 mg			
levodopa + carbidopa	9	tab, 100 mg + 10 mg, 250 mg + 50 mg	Sinemet	Italy	Merck, Sharp & Dohme
levonorgestrel	18.3.1	tab, 30 µg	Microval	Germany	Wyeth-Ayerst
lithium carbonate	24.2.2	cap, 300 mg tab, 300 mg	Quilonum	Germany	SmithKline Beecham
mebendazole	6.1.1	chtab, 100 mg, 500 mg	Vermox	Belgium	Janssen
medroxyprogesterone acetate	18.3.1	depot inj, 150 mg/ml	Depo-Provera	USA	Pharmacia-Upjohn
mefloquine, hydrochloride	18.7	tab, 5 mg	Provera		
methylodopa	6.5.3	tab, 250 mg	Lariam	Switzerland	Roche
metoclopramide, hydrochloride	12.3	tab, 250 mg	Aldomet	Spain	Merck, Sharp & Dohme
	17.2	tab, 10 mg	Primperan	France	Synthlabo

miconazole, nitrate	13.1	cre, 2% oin, 2% tab, 500mg	Daktarin	Belgium	Janssen
nalidixic acid	6.2.2	cap, 500 mg	Neggran	USA	Sanofi Winthrop
neostigmine, bromide	20	tab, 15 mg	Prostigmin	Germany	Roche
niclosamide	6.1.1	chtab, 500 mg	Yomesan	Germany	Bayer
nifedipine	12.3	cap, 10 mg (sr) tab, 10 mg (sr)	Adalat 10 Adalat T 10	Germany	Bayer
nifurtimox	6.5.5	tab, 30 mg, 120 mg, 250 mg	Lampit	Argentina	Bayer
nitrofurantoin	6.2.2	tab, 100 mg	Furadantin	Ireland, United Kingdom	Proctor & Gamble
norethisterone enantate	18.3.1	oilsl, 200 mg/ml	Noristerat	Mexico, South Africa	Schering
nystatin	6.3	loz, 100 000 IU pes, 400 000 IU tab, 100 000 IU tab, 500 000 IU vagtab, 100 000 IU	Nystan Mycostatine	United Kingdom France France USA France Brazil	Bristol-Myers Squibb
oxamniquine	6.1.3	cap, 250 mg syr, 250 mg/5 ml	Mansil/Mansil		Pfizer
paracetamol	2.1	sup, 400 mg, 125 mg, 250 mg, 500 mg, 1000 mg	Ben-U-Ron	Germany	Bene
penicillamine	4.2	cap, 250 mg tab, 250 mg	Cuprimine Depen	USA	Merck, Sharp & Dohme Cater-Wallace
phenobarbital	5	tab, 15–100 mg	Luminal (100 mg) Luminaletten (15 mg) V-Cillin K	Germany USA	Desitin Eli Lilly
phenoxymethylpenicillin, potassium	6.2.1	pwosp, 250 mg/5 ml tab, 250 mg	Dilantin Kapseals	USA	Parke-Davis
phenytoin, sodium	5	cap, 25 mg; 30 mg, 50 mg; 100 mg	Dilantin Infatabs Konaktion	Switzerland	Roche
phytomenadione	10.2	tab, 25 mg; 50 mg, 400 mg tab, 10 mg			

Table 1 (continued)

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products		
			Trademark	Primary market	Manufacturer
praziquantel	6.1.1 6.1.3	tab, 150mg, 600 mg tab, 600mg	Biltricide	Germany	Bayer
prednisolone	3 8.3 18.1 21.2 12.2	tab, 5 mg tab, 5 mg tab, 1 mg, 5 mg eycd, 0.5% tab, 250mg, 500 mg	Scherisolon Ultracortenol Pronestyl	Colombia, Uruguay Germany USA	Schering Ciba Vision (Novartis) Bristol-Myers Squibb
procainamide, hydrochloride procarbazine, hydrochloride	8.2	cap, 50 mg	Natlan	Switzerland	Roche
proguanil, hydrochloride	6.5.3	tab, 100 mg	Paludrine	United Kingdom	Zeneca
propranolol, hydrochloride	7.2	tab, 20mg, 40 mg tab, 10mg, 40 mg	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	Zinamide	United Kingdom	Merck, Sharp & Dohme
pyridostigmine, bromide	20	tab, 60mg	Mestinon	Switzerland	Roche
rifampicin	6.2.3	cap, 150mg, 300 mg tab, 150mg, 300 mg	Rifadin	Italy	Gruppo Lepetit
rifampicin + isoniazid	6.2.4	tab, 150mg + 100mg, 300 mg + 150mg	Rifinah	Italy	Gruppo Lepetit
rifampicin + isoniazid + pyrazinamide	6.2.4	tab, 150 mg + 75mg + 400mg, 150 mg + 150mg + 500mg	Rifater	Italy	Hoechst Marion Roussel
silver sulfadiazine	13.2	cre, 1%/500 g	Silvadene	USA	Hoechst Marion Roussel

sulfadoxine + pyrimethamine	6.5.3	tab, 500 mg + 25 mg	Fansidar	Switzerland	Roche
sulfamethoxazole + trimethoprim	6.2.2	osp, 200 mg + 40 mg/5 ml tab, 100 mg + 20 mg, 400 mg + 80 mg	Bactrim	Switzerland	Roche
sulfasalazine	17.4	tab, 500 mg	Azulfidine	USA	Pharmacia-Upjohn
tamoxifen, citrate	8.3	tab, 10 mg, 20 mg	Nolvadex	United Kingdom	Zeneca
testosterone, enantate	18.2	inj, 200 mg/ml, 250 mg/ml	Testorion depot	Argentina, Germany, Mexico	Schering
theophylline	25.1	tab, 400 mg , 125 mg, 200 mg, 250 mg, 375 mg, 500 mg	Euphylong	Germany	BYK-Gulden
timolol, maleate	21.4	sl (eyd), 0.25%, 0.5%	Timoptol ophthalmic solution	France	Merck, Sharp & Dohme
tolbutamide	—	eyd, 0.25%, 0.5% (unit dose)	Timoptol Ocudose		
triclabendazole	6.1.3	gel (eyd), 0.25%, 0.5%	Timoptol LP		
tropicamide	14.1	tab, 500 mg	Rastinon	Germany	Hoechst Marion Roussel
verapamil, hydrochloride	12.1	tab, 40 mg, 80 mg (sr)	Egaten	Egypt	Novartis
	12.2	tab, 40 mg, 80 mg (sr)	Mydracyl	United Kingdom	Alcon
			Isoptin	Germany	Knoll
List B					
acetazolamide	21.4	tab, 250 mg			
acetylsalicylic acid	2.1	sup, 50–150 mg tab, 100–500 mg			
	7.1	tab, 300–500 mg			
	12.5	tab, 100 mg			
aciclovir	6.4.1	tab, 200 mg			
aciclovir (sodium)	6.4.1	pw/inj, 250 mg			
allopurinol	2.3	tab, 100 mg			
aluminium hydroxide	17.1	osp, 320 mg/5 ml tab, 500 mg			

Table 1 (continued)

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products	
			Trademark	Primary market Manufacturer
amoxicillin + clavulanic acid	6.2.1	tab, 500mg + 125mg	*****	
ascorbic acid	27	tab, 50mg	*****	
atropine, sulfate	17.5	tab, 1mg	*****	
azathioprine	8.1	tab, 50mg	*****	
beclometasone, dipropionate	25.1	inh, 50µg/dose	*****	
benzoic acid + salicylic acid	13.1	cre, 6% + 3% oin, 6% + 3%		
benzoyl peroxide	13.5	cre, 5% lot, 5%		
benzoyl benzoate	13.6	lot, 25%		
betamethasone, valerate	13.3	cre, 0.1% oin, 0.1%	***** *****	
calamine lotion	13.3	lot		
chloral hydrate	1.3	sy, 200mg/5ml		
chloramphenicol, palmitate	6.2.2	osp, 150mg/5ml	*****	
chloroquine, phosphate	6.5.3	sy, 50mg/5ml ^{b,c}	*****	
chloroquine, sulfate	6.5.3	sy, 50mg/5ml ^{b,c} tab, 100mg, ^b 150mg ^{b,c}		
chlorpromazine, hydrochloride	24.1	sy, 25mg/5ml tab, 100mg	***** *****	
coal tar	13.5	topsl, 5%		
codeine, phosphate	2.2	tab, 30mg	*****	
	17.7.2	tab, 30mg	*****	
colchicine	2.3	tab, 500µg	*****	

chromoglicic acid, sodium	25.1	inh, 20mg/dose	*****
dextromethorphan	25.2	osl, 3.5mg/5ml	*****
diethylcarbazine, dihydrogen citrate	6.1.2	tab, 50mg	*****
diethyltoluamide	6.6	topsl, 50%, 75%	*****
digitoxin	—	tab, 50µg, 100µg	*****
digoxin	12.4	osl, 50µg/ml	*****
diloxanide, furoate	6.5.1	tab, 62.5µg, 250µg	*****
dimercaprol	4.2	tab, 500mg	*****
dithranol	13.5	oilinj, 50mg/ml	*****
ergometrine, hydrogen maleate	22.1	oin, 0.1–2%	*****
ergotamine, tartrate	7.1	tab, 200µg	*****
erythromycin, ethyl succinate	6.2.2	tab, 1mg	*****
erythromycin, stearate	6.2.2	cap, 250mg	*****
		pwosp, 125mg	*****
		tab, 250mg	*****
		cap, 250mg	*****
		pwosp, 125mg	*****
		tab, 250mg	*****
		tab, 100–400mg	*****
ethambutol, hydrochloride	6.2.4	tab, 35µg + 1.0mg	*****
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	*****
		tab, equiv. to 60mg iron + 250µg folic acid	*****
ferrous salt (sulfate) + folic acid	10.1	tab, 1mg, 5mg	*****
folic acid	10.1	tab, 1mg, 5mg	*****
gentamicin, sulfate	21.1	eyd, 0.3%	*****
glibenclamide	18.5	tab, 2.5mg, 5mg	*****

Table 1 (continued)

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products	
			Trademark	Primary market Manufacturer
hydrocortisone, acetate	13.3	cre, 1% oin, 1% supp, 25mg	***** ***** *****	
hydrogen peroxide	17.4	sl, 3%	*****	
iopanoic acid	—	tab, 500mg	*****	
ipecacuanha	14.2	sy, 0.14%, as emetine		
isoniazid	4.1	tab, 100–300mg	*****	
isoniazid + ethambutol	6.2.4	tab, 150mg + 400mg	*****	
levothyroxine, sodium	6.2.4	tab, 50µg, 100µg	*****	
magnesium hydroxide	18.8	osp, equiv. to 550mg/10ml		
mercaptopurine	17.1	tab, 50mg	*****	
metformin	8.2	tab, 500mg	*****	
DL-methionine	18.5	tab, 250mg	*****	
methotrexate, sodium	4.2	tab, 2.5mg	*****	
metrifonate	8.2	tab, 100mg	*****	
metronidazole	—	sup, 500mg, 1g tab, 200–500mg	***** *****	
metronidazole, benzoate	6.2.2	tab, 200–500mg	*****	
metronidazole, benzoate	6.5.1	osp, 200mg/5ml	*****	
morphine, hydrochloride	6.5.1	osl, 10mg/5ml	*****	
morphine, sulfate	2.2	osl, 10mg/5ml	*****	
neomycin, sulfate + bacitracin zinc	2.2	tab, 10mg		
neomycin, sulfate + bacitracin zinc	13.2	oin, 5mg + 500IU	*****	
nicotinamide	27	tab, 50mg		
norethisterone	18.7	tab, 5mg	*****	
paracetamol	2.1	sy, 125mg/5ml tab, 100–500mg		
	7.1	tab, 300–500mg		

permethrin	13.6	lot, 1%	*****
perthidine, hydrochloride	2.2	tab, 50mg, 100mg	*****
phenobarbital	5	elix, 15mg/5ml	*****
pilocarpine,	21.4	sl (eyd), 2%, 4%	*****
hydrochloride or nitrate			
podophyllum resin	13.5	topsl, 10–25%	
potassium iodide	18.8	tab, 60mg	
primaquine, diphosphate	6.5.3	tab, 7.5mg, 15mg	*****
promethazine,	1.3	elix, 5mg/5ml	*****
hydrochloride		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	
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	tab, 4mg	*****
	25.1	inh, 100µg/dose	*****
		respsl, 5mg/ml	*****
		syr, 2mg/5ml	*****
		tab, 2mg, 4mg	*****
salicylic acid	13.5	topsl, 5%	*****

Table 1 (continued)

Pharmaceutical name	Section no.	Dosage forms and strengths	Comparator pharmaceutical products	
			Trademark	Primary market Manufacturer
senna (sennoside)	17.6	tab, 7.5 mg		
silver nitrate	21.1	sl (eyd), 1%		
sodium fluoride	27	any	*****	
spironolactone	16	tab, 25 mg	*****	
sulfadiazine	6.2.2	tab, 500 mg	*****	
sulfadimidine	—	osp, 500 mg/5 ml	*****	
tetracaine, hydrochloride	21.3	tab, 500 mg	*****	
tetracycline, hydrochloride	21.1	sl (eyd), 0.5% eyo, 1%	*****	
thiamine, hydrochloride	27	tab, 50 mg		
thioacetazone + isoniazid	6.2.4	tab, 50 mg + 100 mg, 150 mg + 300 mg	*****	
trimethoprim	6.2.2	tab, 100 mg, 200 mg	*****	
urea	13.5	cre, 10%		
valproic acid, sodium	5	oin, 10%	*****	
warfarin, sodium	10.2	encotab, 200 mg, 500 mg tab, 1 mg, 2 mg, 5 mg	*****	
zidovudine	6.4.2	cap, 100 mg, 250 mg osl, 50 mg/5 ml	*****	
zinc oxide	—	cre oin	*****	

^a For instructions on the use of the list, see pages 164–167.

^b For curative treatment.

^c For prophylaxis.

Authors

This guidance was discussed during two meetings convened by the Division of Drug Management and Policies and the Department of Essential Drugs and other Medicines, World Health Organization, Geneva, Switzerland, from 12 to 13 February 1996 and from 8 to 9 February 1999. The meetings were attended by the following people:

Mr M.N. Dauramanzi, Drugs Control Council, Harare, Zimbabwe

Professor U. Gundert-Remy, University of Göttingen, Göttingen, Germany

Dr M. Holz-Slomczyk, Federal Institute for Drugs and Medical Devices, Berlin, Germany

Mrs M. Ikeda, Ministry of Health and Welfare, Tokyo, Japan

Dr K. Morimoto, Pharmaceuticals and Medical Devices Evaluation Centre, National Institute of Health Sciences, Tokyo, Japan

Ms A. Poompanich, Division of Drug Analysis, Ministry of Public Health, Nonthaburi, Thailand

Dr R. Williams, Center for Drug Evaluation and Research, Food and Drug Administration, Rockville, MD, USA

Secretariat

Mrs K. Bremer, Quality Assurance and Safety: Medicines, Essential Drugs and other Medicines, WHO, Geneva, Switzerland

Dr M. Demesmaeker, Quality Assurance and Safety: Medicines, Essential Drugs and other Medicines, WHO, Geneva, Switzerland

Dr J. Idänpään-Heikkilä, Special Adviser on Quality Assurance and Safety, Health Technology and Pharmaceuticals, WHO, Geneva, Switzerland

Dr S. Kopp-Kubel, Quality Assurance and Safety: Medicines, Essential Drugs and other Medicines, WHO, Geneva, Switzerland

Mr D. Sato, Drug Management and Policies, WHO, Geneva, Switzerland

Miss M. Schmid, Quality Assurance and Safety: Medicines, Essential Drugs and other Medicines, WHO, Geneva, Switzerland

Miss A. Wehrli, Regulatory Support, Drug Management and Policies, WHO, Geneva, Switzerland

Mr Y. Yoshida, Quality Assurance and Safety: Medicines, Essential Drugs and other Medicines, WHO, Geneva, Switzerland

Acknowledgements

Acknowledgement was made by the WHO Secretariat to the following people, for their valuable contributions to the discussions: Miss M. Cone, International Federation of Pharmaceutical Manufacturers Associations (IFPMA), Geneva, Switzerland; Dr I. Kanfer, International Generic Pharmaceutical Alliances, Genpharm Inc., Etobicoke, Ontario, Canada; and Dr R. Patnaik, Deputy Director, Division of Bioequivalence, Center for Drugs Evaluation and Research, Food and Drug Administration, Rockville, MD, USA.

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 (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.