

EN

EN

EN



COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 20.11.2008
COM(2008) 764 final

Annual Report (2007)

**on the application of Council Regulation (EC) No 953/2003 of 26 May 2003 to avoid
trade diversion into the European Union of certain key medicines**

TABLE OF CONTENTS

1.	Background	3
2.	Commission Reporting under Regulation (EC) No 953/2003	4
3.	Products registered	4
4.	Countries of destination	5
5.	Diseases covered	6
6.	Application of Price Formulae	6
7.	Evaluating the impact of the Regulation over time.....	7
	ANNEX 1: Details of volumes of medicines sold in 2007	8
	ANNEX 2: Volumes of tiered priced products sold by sub-region between 1 January 2007 and 31 December 2007	17

This is the fourth annual report foreseen under Article 11 of Regulation (EC) No 953/2003¹, which is designed to prevent parallel trade in discounted medicines intended for the least developed countries. This report covers the period from 1 January to 31 December 2007.

1. BACKGROUND

In 2000 the UN Millennium Summit set the Millennium Development Goals (MDGs), one of which is to fight HIV/AIDS, malaria and other diseases. In response to this commitment, on 20 September 2000 the European Commission adopted a comprehensive framework² to accelerate action targeted at the three major diseases – HIV/AIDS, malaria and tuberculosis (TB). A Programme for Action (PfA)³ was developed outlining specific measures to be taken. The state of play with this programme was described in the Second Progress Report⁴ released on 26 October 2004. Subsequently, on 27 April 2005 the Commission adopted a European Programme for Action to confront HIV/AIDS, Malaria and TB through External Action (COM(2005)179) covering the period 2007-2011.

Supplying poor and developing countries with medicines at sustainable low prices is one of the key objectives in the fight against these major diseases. In order to achieve this, the European Commission has consistently advocated a policy of "tiered pricing" for medicines, combined with market segmentation between rich and poor countries. The advantage of such a policy is that it encourages manufacturers to distribute the drugs in question in the target countries at the lowest possible ("tiered") price, while at the same time recouping their research and development expenditure with the higher prices charged in developed (OECD) countries. This approach is designed to promote sustainable supplies and continuous distribution of life-saving medicines. It is also less prone to the constraints often encountered in "partnership schemes".

To support tiered pricing, specific safeguards were devised to prevent diversion of medicines. In May 2003 the EU adopted Council Regulation (EC) No 953/2003 to avoid trade diversion into the European Union of certain key medicines⁵ ("the Regulation").

¹ Article 11 of Regulation (EC) No 953/2003 foresees: "(1) The Commission shall monitor on an annual basis the volumes of exports of tiered priced products listed in Annex I and exported to the countries defined in Article 1 on the basis of information provided to it by pharmaceutical manufacturers and exporters. For this purpose a standard form will be issued by the Commission. Manufacturers and exporters must submit such sales reports annually for each tiered priced product to the Commission on a confidential basis.

(2) The Commission shall periodically report to the Council on the volumes exported under tiered prices, including on the volumes exported within the framework of a partnership agreement agreed between the manufacturer and the government of a country of destination. The report shall examine the scope of countries and diseases and general criteria for the implementation of Article 3."

² Accelerated action targeted at major communicable diseases within the context of poverty reduction, COM(2000)585.

³ Programme for Action: Accelerated action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction COM(2001)96. Update on the EC Programme for Action: Accelerated action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction. Outstanding policy issues and future challenges COM(2003)93.

⁴ Second Progress report on the EC Programme for Action: Accelerated action on HIV/AIDS, malaria and tuberculosis in the context of poverty reduction SEC(2004)1326.

⁵ OJ L 135, 3.6.2003, pages 5 – 11. The Regulation has last been updated by Commission Regulation 1662/2005 of 11 October 2005 (OJ L 267, 12.10.2005, pages 19 – 21).

2. COMMISSION REPORTING UNDER REGULATION (EC) NO 953/2003

This report covers the period from 1 January to 31 December 2007. During the reporting period, no new products were registered.

The report contains the following information:

- The volumes exported under tiered prices for each product registered in annex I of the Regulation;
- The sub-regions benefiting from these exports at tiered prices;
- The diseases treated with the products at question;
- An assessment of the application of the price formulae in Article 3 of the Regulation in relation to each of the products concerned.

This report is mainly based on the information received from the applicant under Article 11(1) of the Regulation. The Commission respects the confidentiality of the data provided by applicants and neither guarantees nor questions their accuracy.

In order to keep the public informed of all products registered under the Regulation, their producers, distinctive features, countries of destination, and other relevant details, the Commission has established a website where this information is continuously updated:

- <http://trade-info.cec.eu.int/cgi-bin/antitradediversion/index.pl>

The same website also provides assistance to manufacturers who wish to register a new product.

3. PRODUCTS REGISTERED

The products listed below were registered in 2004 by GlaxoSmithKline (GSK), Brentford (UK).

<i>PRODUCT NAME</i>	<i>OECD PRICE RANGE</i>	<i>PRICE OFFERED</i>
EPIVIR 150 mg x 60	US\$ 121.81 – US\$ 395.78	US\$ 5.70
COMBIVIR 300/150 mg x 60	US\$ 177.49 – US\$ 767.59	US\$ 19.50
EPIVIR Oral Solution 10mg/ml - 240 ml	US\$ 33.32– US\$ 71.73	US\$ 6.73
RETROVIR 100 mg x 100	US\$ 104.07 – US\$ 219.42	US\$ 15.77
RETROVIR 300 mg x 60	US\$ 125.15 – 295.42	US\$ 17.40
RETROVIR 250 mg x 40	US\$ 83.84 – US\$ 205.16	US\$ 13.27

TRIZIVIR 750 mg x 60	US\$ 539.09 – 887.97	US\$ 102.00 ⁶
ZIAGEN 300 mg x 60	US\$ 152.64 – 411.42	US\$ 72.90 ⁷
RETROVIR Oral Solution 10 mg/ml – 200 ml	US\$ 17.85 – 73.83	US\$ 7.10

The “tiered” prices in the right hand column are those quoted in the application. Medicines can be bought from the applicant at these prices in any volume desired, provided that they are intended for one of the target countries listed in Annex II to the Regulation. Under the Regulation, no distinction can be made between purchasers – public or private - for products at these prices in the countries listed. However, it must be noted that these prices are indicative. The actual sales prices have not been reported, as Article 11(1) of the Regulation places no obligation on applicants to do so. It therefore cannot be excluded that in some instances lower prices for the products can be and, indeed have been, negotiated⁸.

It should also be noted that the OECD price ranges shown in the table above are those reported by the producer at the time when the applications were submitted. An update of these price ranges can be found in Annex I, together with the volumes sold for each product registered under the Regulation.

Over the reporting period, no attempts illegally to re-import tiered-priced products registered under the Regulation back into the EU were reported to the Commission.

As HIV/AIDS, Malaria and TB are chronic diseases, purchases of medication have to be sustainable. The Commission has been informed that most sales are part of long- standing agreements with purchasers. No exports under specific “partnership agreements” have been notified to the Commission.

4. COUNTRIES OF DESTINATION

In the reporting period, tiered priced products have been supplied to **18** of the countries listed in Annex II of the Regulation. These were: Armenia, Botswana, Burkina Faso, Cambodia, Democratic Republic of Congo, Ghana, Guinea, Haiti, Kenya, Malawi, Nicaragua, Nigeria, Rwanda, South Africa, Sudan, Uganda, Zambia, and Zimbabwe. The reduction in the countries of destination (34 in 2006) can be explained by the fact that the producer is now increasingly signing voluntary licences with generic companies in Africa. These licences are now supplying almost twice the number of their versions of ARVs than is the original producer. This has led to a reduction in the number of countries supplied originally, since they are now sourcing from the generic companies in Africa.

⁶ In a press release issued on 30 May 2006, GlaxoSmithKline announced a reduction of its not-for-profit price of Trizivir 750 mg x 60 by 31% (from US\$ 102.00 to US\$ 70.00) The price indicated in the table corresponds to the price submitted by the applicant at the time of submission of the application.

⁷ In a press release issued on 30 May 2006, GlaxoSmithKline announced a reduction of its not-for-profit price of Ziagen 300 mg x 60 by 28% (from US\$ 72.90 to US\$ 52.29). The price indicated in the table corresponds to the price submitted by the applicant at the time of submission of the application.

⁸ Readers interested in obtaining information on actual sales prices may find it on the website of the Global Fund to Fight AIDS, TB and Malaria.
http://www.theglobalfund.org/en/funds_raised/price_reporting/default.asp

With the exceptions of Armenia, Cambodia, Haiti and Nicaragua, all the countries concerned are in Sub-Saharan Africa, the region where the prevalence of HIV/AIDS is highest.

As it was indicated in the 2006 report, sales volumes are reported for 8 sub-regions, as follows: Europe and Central Asia, East Asia and Pacific, South Asia, Latin America and the Caribbean, West Africa, Central Africa, East Africa and Southern Africa.

Detailed information on the volumes of exports to each sub-region can be found in Annex 2 to this report.

5. DISEASES COVERED

HIV/AIDS, malaria and tuberculosis are generally considered the gravest public health concerns for developing countries and a major obstacle to development. This is why EC development policy, including the Regulation, is specifically focusing on these three diseases. Considering that the list of registered products remained unchanged in 2007, the diseases covered in this report remain identical, i.e. exclusively treatment of HIV/AIDS.

However, there are certainly some pharmaceuticals for treating malaria and tuberculosis that would benefit from registration under the Regulation. Medicines to treat opportunistic infections associated with HIV/AIDS are also eligible and suitable for coverage under the Regulation, but there have been no applications so far.

6. APPLICATION OF PRICE FORMULAE

To date the application of the price formulae provided for in Article 3 of the Regulation has caused no practical problem. The applicant has not found it necessary to avail itself of the services of an independent auditor in order to protect sensitive business data (a possibility allowed by Article 4(2)(ii) of the Regulation). For all nine products, it proved sufficient to show that the price offered (i.e. the “tiered” price) was less than 25% of the lowest OECD list price. Both the tiered price and the OECD list prices are available to the public.

7. EVALUATING THE IMPACT OF THE REGULATION OVER TIME

The table below gives some indication of the sales trends per product registered under the Regulation over the last three years:

Product/unit	2005	2006	2007	% difference (2006/2007)
Trizivir 750 mg x 60	3.119	4.903	17.102	249%
Retrovir 300 mg x 60	102.236	48.410	118.725	145%
Retrovir Oral Solution 10 mg	365.938	119.807	272.063	127%
Eпивir 150 mg x 60	1.274.711	975.250	1.125.986	15%
Retrovir 250 mg x 40	905	585	643	10%
Eпивir Oral Solution 10mg/ml 240 ml	173.673	406.287	155.523	-62%
Combivir 300/150 mg x 60	691.466	397.450	153.793	-61%
Retrovir 100 mg x 100	95.109	132.176	92.467	-30%
Ziagen 300 mg x 60	33.924	40.208	35.884	-11%
Total	2.741.081	2.125.076	1.972.186	-7%

Of all the products registered, *Trizivir 750 mg x 60*, *Retrovir 300 mg x 60* and *Retrovir Oral Solution 10 mg* showed the biggest increases in volumes sold at tiered prices, with 249%, 145% and 127% respectively. Two products, *Eпивir 150 mg x 60* and *Retrovir 250 mg x 40* showed a marginal increase; whereas the other four in the table *Eпивir Oral Solution 10mg/ml 240 ml*, *Combivir 300/150 mg x 60*, *Retrovir 100 mg x 100* and *Ziagen 300 mg x 60* displayed relatively large decreases in sales volumes. Overall sales decreased by 7 %.

This further decrease in 2007⁹ was expected and is again primarily due to more customers *purchasing* ARVs from other producers and in particular from generic manufacturers. As stated in last year's report, GSK has granted voluntary licences to eight generic companies for the manufacture and supply of ARVs (Retrovir, Eпивir and Combivir, all used mainly as first line treatment) to both the public and private sectors in sub-Saharan Africa. This trend is welcome as it improves the availability of affordable ARVs for customers in developing countries and helps to maintain a sustainable supply. In 2007 licencees supplied 183 million tablets of their versions of Eпивir and Combivir and GSK supplied 85 million tablets making a total of 268 million tablets in 2007 compared with a total of 206 million in 2006. It should, therefore once again be underlined that, overall, access to preferentially priced medicines has increased significantly.

⁹ In February 2008, GSK announced significant new price reductions for its ARVs offered on a not for profit basis; sales volumes can thus be expected to increase for 2008.

ANNEX 1: DETAILS OF VOLUMES OF MEDICINES SOLD IN 2007

EPIVIR Oral Solution 10mg/ml – 240 ml	Sub-region	Volumes sold (units) ¹⁰ - 1 January 2007 to 31 December 2007
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Europe and Central Asia	72
Active ingredient: lamivudine	Latin America and the Caribbean	2,016
	East Africa	137,968
	Southern Africa	15,467
	Total no. of packs sold	155,523
	<i>per month</i>	12,960
Highest OECD list price: US\$ 86.11		
Lowest OECD list price: US\$ 41.16		
Preferential/highest OECD list price: 7.82%		
Preferential/lowest OECD list price: 16.35%		

¹⁰ In this and the following tables, “units” are the packages in which the products concerned are packed. For example, one “unit” of EPIVIR Oral Solution 10mg/ml – 240 ml is one bottle of 240 ml. One unit of EPIVIR 150 mg x 60 (see following table) is one package containing 60 tablets.

EPIVIR 150 mg x 60	Sub-region	Volumes sold (units) - 1 January 2007 to 31 December 2007-
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Europe and Central Asia	23
Active ingredient: lamivudine	Latin America and the Caribbean	180
	East Africa	93,649
	Southern Africa	1,032,134
Price offered (per unit): US\$ 5.70	Total no. of packs sold	1,125,986
	<i>Per month</i>	93,832
Highest OECD list price: US\$ 427.09		
Lowest OECD list price: US\$ 153.38		
Preferential/highest OECD list price: 1.33%		
Preferential/lowest OECD list price: 3.72%		

COMBIVIR 300/150 mg x 60

Sub-region

**Volumes sold (units)
- 1 January 2007 to 31
December 2007-**

Date of Approval: 19 April 2004

Disease targeted: HIV infection

Europe and Central Asia

519

Active ingredient: lamivudine + zidovudine

Latin America and the
Caribbean

7,100

West Africa

11,516

Central Africa

850

East Africa

16,370

Southern Africa

117,438

Price offered (per unit): US\$ 19.50

Total no. of packs sold

153,793

Per month

12,816

Highest OECD list price: US\$ 834.82

Lowest OECD list price: US\$ 315.73

Preferential/highest OECD list price: 2.34%

Preferential/lowest OECD list price: 6.18%

RETROVIR 100 mg x 100
Date of Approval: 19 April 2004

Sub-region

**Volumes sold (units) -
1 January 2007 to 31
December 2007-**

Disease targeted: HIV infection

East Africa

11,354

Active ingredient: zidovudine

Southern Africa

81,113

Price offered (per unit): US\$ 15.77

Total no. of packs sold

92,467

Per month

7,706

Highest OECD list price: US\$ 257.15

Lowest OECD list price: US\$ 106.01

Preferential/highest OECD list price: 6.13 %

Preferential/lowest OECD list price: 14.88 %

RETROVIR 300 mg x 60**Sub-region****Volumes sold (units) -
1 January 2007 to 31
December 2007-****Date of Approval: 19 April 2004**

Disease targeted: HIV infection

Europe and Central Asia

7

Active ingredient: zidovudine

Latin America and the
Caribbean

50

East Africa

8,548

Southern Africa

110,120

Price offered (per unit): US\$ 17.40**Total no. of packs sold****118,725***Per month*

9,894

Highest OECD list price: US\$ 395.54

Lowest OECD list price: US\$ 221.56

Preferential/highest OECD list price: 4.40%

Preferential/lowest OECD list price: 7.85%

RETROVIR 250 mg x 40

Sub-region

**Volumes sold (units) -
1 January 2007 to 31
December 2007-**

Date of Approval: 19 April 2004

Disease targeted: HIV infection

East Asia and Pacific

450

Active ingredient: zidovudine

Southern Africa

193

Price offered (per unit): US\$ 13.27

Total no. of packs sold
per month

643

54

Highest OECD list price: US\$ 305.78

Lowest OECD list price: US\$ 113.80

Preferential/highest OECD list price: 4.34%

Preferential/lowest OECD list price: 11.66%

TRIZIVIR 750 mg x 60	Sub-region	Volumes sold (units) - 1 January 2007 to 31 December 2007-
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	West Africa	7,337
Active ingredient: abacavir sulphate (300 mg) + lamivudine (150 mg) + zidovudine (300 mg)	East Africa	5,211
	Southern Africa	4,554
Price offered (per unit): US\$ 70.00	Total no. of packs sold	17,102
	<i>Per month</i>	1,425
Highest OECD list price: US\$ 1,274.89		
Lowest OECD list price: US\$ 569.03		
Preferential/highest OECD list price: 5.49%		
Preferential/lowest OECD list price: 12.30 %		

ZIAGEN 300 mg x 60

Sub-region

**Volumes sold (units) -
1 January 2007 to 31
December 2007-**

Date of Approval: 20 September 2004

Disease targeted: HIV infection	Europe and Central Asia	8
Active ingredient: abacavir sulphate	East Asia and Pacific	651
	Latin America and the Caribbean	1,200
	West Africa	1,223
	Central Africa	33
	East Africa	25,792
	Southern Africa	6,977
Price offered (per unit): US\$ 52.29	Total no. of packs sold	35,884
	<i>per month</i>	2,990
Highest OECD list price: US\$ 499.3		
Lowest OECD list price: US\$ 266.8		
Preferential/highest OECD list price: 10.47%		
Preferential/lowest OECD list price: 19.60%		

RETROVIR Oral Solution 10 mg/ml – 200 ml**Sub-region****Volumes sold (units) –
1 January 2007 to 31
December 2007-****Date of Approval : 20 September 2004**

Disease targeted: HIV infection

Europe and Central Asia

108

Active ingredient: zidovudine

East Africa

202,873

Southern Africa

69,082

Price offered (per unit): US\$ 7.10**Total no. of packs sold****272,063***Per month*

22,672

Highest OECD list price: US\$ 88.39

OECD weighted average price: US\$ 41.76

Preferential/highest OECD list price: 8.03%

Preferential/OECD weighted average price: 17%

**ANNEX 2: VOLUMES OF TIERED PRICED PRODUCTS SOLD BY SUB-REGION BETWEEN 1
JANUARY 2007 AND 31 DECEMBER 2007**

Sub-regions	Products	Units
Europe and Central Asia	EPIVIR Oral Solution	72
	EPIVIR 150 mg x 60	23
	COMBIVIR 300/150 mg x 60	519
	RETROVIR 300 mg x 60	7
	RETROVIR Oral Solution	108
	ZIAGEN 300 mg x 60	8
East Asia and Pacific	RETROVIR 250 mg x40	450
	ZIAGEN 300 mg x 60	651
Latin America and the Caribbean	EPIVIR Oral Solution	2,016
	EPIVIR 150 mg x 60	180
	COMBIVIR 300/150 mg x 60	7,100
	RETROVIR 300 mg x 60	50
	ZIAGEN 300 mg x 60	1,200
West Africa	COMBIVIR 300/150 mg x 60	11,516
	TRIZIVIR 750 mg x 60	7,337
	ZIAGEN 300 mg x 60	1,223
Central Africa	COMBIVIR 300/150 mg x 60	850
	ZIAGEN 300 mg x 60	33
East Africa	EPIVIR Oral Solution	137,968
	EPIVIR 150 mg x 60	93,649
	COMBIVIR 300/150 mg x 60	16,370
	RETROVIR 100mgx100	11,354
	RETROVIR 300 mg x 60	8,548
	RETROVIR Oral Solution	202,873
	TRIZIVIR 750 mg x 60	5,211
	ZIAGEN 300 mg x 60	25,792
Southern Africa	EPIVIR Oral Solution	15,467

EPIVIR 150 mg x 60	1,032,134
COMBIVIR 300/150 mg x 60	117,438
RETROVIR 100 mg x 100	81,113
RETROVIR 250mgx40	193
RETROVIR 300 mg x 60	110,120
RETROVIR Oral Solution	69,082
TRIZIVIR 750 mg x 60	4,554
ZIAGEN 300 mg x 60	6,977