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COMMISSION OF THE EUROPEAN COMMUNITIES

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**Annual Report (2008)**

**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**

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This is the fifth annual report foreseen under Article 11 of Regulation (EC) No 953/2003<sup>1</sup>, 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 2008.

## 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 framework<sup>2</sup> to accelerate action targeted at the three major diseases – HIV/AIDS, malaria and tuberculosis (TB). A Programme for Action (PfA)<sup>3</sup> was developed outlining specific measures to be taken. The state of play with this programme was described in the Second Progress Report<sup>4</sup> 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 medicines<sup>5</sup> ("the Regulation").

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<sup>1</sup> 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.*"

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

<sup>3</sup> 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.

<sup>4</sup> 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.

<sup>5</sup> 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): <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2005:267:0019:0021:EN:PDF>

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

This report covers the period from 1 January to 31 December 2008. 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>
<b>EPIVIR 150 mg x 60</b>	US\$ 121.81 – US\$ 395.78	US\$ 5.70
<b>COMBIVIR 300/150 mg x 60</b>	US\$ 177.49 – US\$ 767.59	US\$ 19.50
<b>EPIVIR Oral Solution 10mg/ml - 240 ml</b>	US\$ 33.32– US\$ 71.73	US\$ 6.73
<b>RETROVIR 100 mg x 100</b>	US\$ 104.07 – US\$ 219.42	US\$ 15.77
<b>RETROVIR 300 mg x 60</b>	US\$ 125.15 – 295.42	US\$ 17.40
<b>RETROVIR 250 mg x 40</b>	US\$ 83.84 – US\$ 205.16	US\$ 13.27
<b>TRIZIVIR 750 mg x 60</b>	US\$ 539.09 – 887.97	US\$ 102.00
<b>ZIAGEN 300 mg x 60</b>	US\$ 152.64 – US\$ 411.42	US\$ 72.90
<b>RETROVIR Oral Solution 10 mg/ml – 200 ml</b>	US\$ 17.85 – US\$ 73.83	US\$ 7.10

It should be noted that both the prices offered ("tiered" prices) and 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 and the prices offered can be found in Annex I, together with the volumes sold in 2008 for each product registered under 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, negotiated<sup>6</sup>.

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 **20** of the countries listed in Annex II of the Regulation. These were: Armenia, Botswana, Burkina Faso, Cambodia, Democratic Republic of Congo, Ghana, Guinea, Haiti, Ivory Coast, Kenya, Madagascar, Malawi, Mauritania, Namibia, Nicaragua, Nigeria, South Africa, Uganda, Zambia, and Zimbabwe.

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.

Detailed information on the volumes of exports to each of the 7 sub-regions (Europe and Central Asia, East Asia and Pacific, Latin America and the Caribbean, West Africa, Central Africa, East Africa and Southern Africa) 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 2008, the diseases covered in this report remain identical, i.e. exclusively treatment of HIV/AIDS.

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<sup>6</sup> 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/fr/procurement/pqr/?lang=fr>

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	2006	2007	2008	% difference (2007/2008)
Retrovir 250 mg x 40	585	643	2.700	<b>320%</b>
Retrovir 100 mg x 100	132.176	92.467	136.571	<b>48%</b>
Combivir 300/150 mg x 60	397.450	153.793	178.216	<b>16%</b>
Epivir 150 mg x 60	975.250	1.125.986	971.689	<b>-14%</b>
Ziagen 300 mg x 60	40.208	35.884	26.872	<b>-25%</b>
Trizivir 750 mg x 60	4.903	17.102	7.475	<b>-56%</b>
Retrovir 300 mg x 60	48.410	118.725	47.682	<b>-60%</b>
Epivir Oral Solution 10mg/ml 240 ml	406.287	155.523	33.311	<b>-79%</b>
Retrovir Oral Solution 10 mg	119.807	272.063	13.502	<b>-95%</b>
<b>Total</b>	<b>2.125.076</b>	<b>1.972.186</b>	<b>1.418.018</b>	<b>-28%</b>

Of all the products registered, only *Retrovir 250 mg x 40*, *Retrovir 100 mg x 100* and *Combivir 300/150 mg x 60* showed an increase in volumes sold at tiered prices, with increases of 320%, 48% and 16% respectively. Sales volumes for the other 6 products decreased with a drop between 14 and 95%. Overall sales decreased by 28 %.

This further decrease in 2008 is again primarily due to more customers *purchasing* ARVs from other producers and in particular from generic manufacturers, including those licensed by GSK. As stated in last year's report, GSK has granted voluntary licences to eight generic companies for the manufacture and supply of ARVs (Retrovir, Epivir 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 2008 GSK licencees supplied 279 million tablets of their versions of Epivir and Combivir and GSK supplied 70 million tablets making a total of 349 million tablets in 2008 compared with a total of 268 million in 2007. It should, therefore once again be underlined that, overall, access to preferentially priced medicines has increased significantly.

## ANNEX 1: DETAILS OF VOLUMES OF MEDICINES SOLD IN 2008

<b>EPIVIR Oral Solution 10mg/ml – 240 ml</b>	<b>Sub-region</b>	<b>Volumes sold (units)<sup>7</sup></b>
<b>Date of Approval: 19 April 2004</b>		<b>- 1 January 2008 to 31 December 2008</b>
Disease targeted: HIV infection	Latin America and the Caribbean	2,844
Active ingredient: lamivudine	East Africa	7,457
	Southern Africa	23,010
<b>Price offered (per unit): US\$ 5.42</b>	<b>Total no. of packs sold</b>	<b>33,311</b>
	<i>per month</i>	<i>2,776</i>
Lowest OECD list price: US\$ 39.58		
Preferential/lowest OECD list price: 13.69%		

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<sup>7</sup> 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**

**Date of Approval: 19 April 2004**

**Sub-region**

**Volumes sold (units) -  
1 January 2008 to 31  
December 2008-**

Disease targeted: HIV infection

Latin America and the  
Caribbean

6,000

Active ingredient: lamivudine

East Africa

8,233

Southern Africa

957,456

**Price offered (per unit): US\$ 5.23**

**Total no. of packs sold**

**971,689**

*Per month*

80,974

Lowest OECD list price: US\$ 147.49

Preferential/lowest OECD list price: 3.55%

**COMBIVIR 300/150 mg x 60**

**Sub-region**

**Volumes sold (units)  
- 1 January 2008 to 31  
December 2008-**

**Date of Approval: 19 April 2004**

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Disease targeted: HIV infection

Latin America and the  
Caribbean

3,912

Active ingredient: lamivudine + zidovudine

West Africa

31

Central Africa

120

East Africa

41,000

Southern Africa

133,153

**Price offered (per unit): US\$ 16.19**

**Total no. of packs sold**

**178,216**

*Per month*

14,851

Lowest OECD list price: US\$ 302.85

Preferential/lowest OECD list price: 5.35%

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

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**Sub-region**

**Volumes sold (units) -  
1 January 2008 to 31  
December 2008-**

Disease targeted: HIV infection

West Africa

2,104

Active ingredient: zidovudine

East Africa

7,242

Southern Africa

127,225

**Price offered (per unit): US\$ 12.17**

**Total no. of packs sold**

**136,571**

*Per month*

11,381

Lowest OECD list price: US\$ 101.69

Preferential/lowest OECD list price: 11.97 %

**RETROVIR 300 mg x 60**

**Sub-region**

**Volumes sold (units) -  
1 January 2008 to 31  
December 2008-**

**Date of Approval: 19 April 2004**

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Disease targeted: HIV infection

East Africa

1,166

Active ingredient: zidovudine

Southern Africa

46,516

**Price offered (per unit): US\$ 13.24**

**Total no. of packs sold**

**47,682**

*Per month*

3,974

Lowest OECD list price: US\$ 211.09

Preferential/lowest OECD list price: 6.27%

**RETROVIR 250 mg x 40**

**Sub-region**

**Volumes sold (units) -  
1 January 2008 to 31  
December 2008-**

**Date of Approval: 19 April 2004**

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Disease targeted: HIV infection

East Asia and Pacific

2,400

Active ingredient: zidovudine

West Africa

250

Southern Africa

50

**Price offered (per unit): US\$ 11.03**

**Total no. of packs sold**

**2,700**

*per month*

225

Lowest OECD list price: US\$ 109.16

Preferential/lowest OECD list price: 10.10%

**TRIZIVIR 750 mg x 60**

**Sub-region**

**Volumes sold (units) -  
1 January 2008 to 31  
December 2008-**

**Date of Approval: 19 April 2004**

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Disease targeted: HIV infection

West Africa

5,884

Active ingredient: abacavir sulphate (300 mg) + lamivudine  
(150 mg) + zidovudine (300 mg)

East Africa

130

Southern Africa

1,461

**Price offered (per unit): US\$ 53.71**

**Total no. of packs sold**

**7,475**

*Per month*

623

Lowest OECD list price: US\$ 545.81

Preferential/lowest OECD list price: 9.84 %



**ZIAGEN 300 mg x 60**

**Sub-region**

**Volumes sold (units) -  
1 January 2008 to 31  
December 2008-**

**Date of Approval: 20 September 2004**

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Disease targeted: HIV infection

Active ingredient: abacavir sulphate

Latin America and the  
Caribbean

533

West Africa

4,168

East Africa

3,865

Southern Africa

18,306

**Price offered (per unit): US\$ 35.91**

**Total no. of packs sold**

**26,872**

*per month*

2,239

Lowest OECD list price: US\$ 255.92

Preferential/lowest OECD list price: 14.03%

**RETROVIR Oral Solution 10 mg/ml – 200 ml****Sub-region****Volumes sold (units) –  
1 January 2008 to 31  
December 2008-****Date of Approval : 20 September 2004**

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Disease targeted: HIV infection

Europe and Central Asia

24

Active ingredient: zidovudine

West Africa

516

East Africa

5,919

Southern Africa

7,043

**Price offered (per unit): US\$ 6.35****Total no. of packs sold****13,502**

Lowest OECD list price: US\$ 25.72

*Per month*

1,125

Preferential/lowest OECD list price: 24.69%

**ANNEX 2: VOLUMES OF TIERED PRICED PRODUCTS SOLD BY SUB-REGION BETWEEN  
1 JANUARY 2008 AND 31 DECEMBER 2008**

<b>Sub-regions</b>	<b>Products</b>	<b>Units</b>
Europe and Central Asia	RETROVIR Oral Solution	24
East Asia and Pacific	RETROVIR 250 mg x40	2,400
Latin America and the Caribbean	EPIVIR Oral Solution	2,844
	EPIVIR 150 mg x 60	6,000
	COMBIVIR 300/150 mg x 60	3,912
	ZIAGEN 300 mg x 60	533
West Africa	COMBIVIR 300/150 mg x 60	31
	RETROVIR 100mgx100	2,104
	RETROVIR 250mgx40	250
	RETROVIR Oral Solution	516
	TRIZIVIR 750 mg x 60	5,884
	ZIAGEN 300 mg x 60	4,168
Central Africa	COMBIVIR 300/150 mg x 60	120
East Africa	EPIVIR Oral Solution	7,457
	EPIVIR 150 mg x 60	8,233
	COMBIVIR 300/150 mg x 60	41,000
	RETROVIR 100mgx100	7,242
	RETROVIR 300 mg x 60	1,166
	RETROVIR Oral Solution	5,919
	TRIZIVIR 750 mg x 60	130
Southern Africa	ZIAGEN 300 mg x 60	3,865
	EPIVIR Oral Solution	23,010
	EPIVIR 150 mg x 60	957,456
	COMBIVIR 300/150 mg x 60	133,153
	RETROVIR 100 mg x 100	127,225
	RETROVIR 250mgx40	50

RETROVIR 300 mg x 60	46,516
RETROVIR Oral Solution	7,043
TRIZIVIR 750 mg x 60	1,461
ZIAGEN 300 mg x 60	18,306