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**Annual Report (2004/2005)
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 second annual report foreseen under Article 11 of Regulation 953/2003¹, covering the period of 1 January to 31 December 2005. A first report was published on 23 June 2005, covering the period 2003-2004.

1. BACKGROUND

In 2000, the UN Millennium Summit defined the Millennium Development Goals (MDGs), one of which is the fight against HIV/AIDS, malaria and other diseases. In view of this commitment the European Commission adopted on 20 September 2000 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 as a framework for implementation, outlining specific measures to be taken. The latest state of play of this programme is described in a Second Progress Report⁴ released on 26 October 2004. Furthermore, 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).

In the fight against the major diseases, the supply of poor and developing countries with medicines at sustainable low prices is a key objective. In order to achieve this objective, the European Commission has consistently advocated a policy of tiered pricing for medicines and 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 expenditures with the higher prices charged in developed (OECD) countries. This approach is likely to promote the sustainability of supplies and the continuous distribution of life-saving medicines.

¹ Article 11 of Regulation 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

It is also less subject to the constraints often encountered in so called partnership schemes.⁵

For tiered pricing to be effective, however, specific safeguards are needed in order to prevent trade diversion of medicines sold at tiered prices into high price markets such as the EU. Therefore, the EU has adopted **Council Regulation (EC) No 953/2003 of 26 May 2003 to avoid trade diversion into the European Union of certain key medicines**⁶ (hereafter ‘the Regulation’).

2. COMMISSION REPORTING UNDER REGULATION 953/2003

The reporting period covered by this report is from 1 January to 31 December 2005. During the reporting period, no new products were registered; however Annex I of the Regulation was updated on 11 October 2005 in order to modify the distinctive features of two products registered in 2004.

The following information is presented in this report:

- the volumes exported under tiered prices for each product registered in annex I of the Regulation, and the countries of destination of such exports
- (where appropriate) the volumes of tiered priced products exported “within the framework of a partnership agreement”⁷
- The countries of destination 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 solely based on the information received from applicants under Article 11 (1) of the Regulation. The Commission respects the confidentiality of the data provided by applicants. It does neither guarantee nor question the exactitude of these data.

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 an internet website where this information is continuously updated:

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

This website also provides assistance to manufacturers wishing to register a new product.

⁵ For a comprehensive assessment of partnership and donation programmes in selected low and middle income countries see:

<http://www.ippph.org/index.cfm?page=/ippph/newsmedia/news&thechoice=show&id=594>

⁶ Official Journal L 135, 3 June 2003, pages 5 – 11. The Regulation has last been updated by Commission Regulation 1662/2005 of 11 October 2005, OJ L 267, 12 October 2005, pages 19 - 21

⁷ For more information, see Annual Report (2003/2004), footnote 8 – SEC (2005) 896

3. PRODUCTS REGISTERED

In the reporting period, 2 applications, both filed by GlaxoSmithKline, Brentford (UK), were received and processed. These two applications were not for the registration of new products. The applicant requested a change of distinctive features for two products, which had been previously registered under this Regulation. The two products below, when sold at tiered prices, are differentiated with red tablets as opposed to white tablets when they are sold in the OECD markets:

Product name	OECD price range	Price offered
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

The other 7 products registered in the course of 2004 have remained unchanged:

Product name	OECD price range	Price offered
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 ⁸
ZIAGEN 300 mg x 60	US\$ 152.64 – 411.42	US\$ 72.90 ⁹
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 that have been quoted in the application. Medicines can be bought at these prices from the applicant¹⁰ in any volume desired, provided that they are intended for one of the target countries identified in Annex II of the Regulation. Under the provisions of the Regulation, there can be no distinction made between purchasers – public or private - for products at these prices in the countries identified. 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 does not oblige applicants to do so. It is therefore not

⁸ 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.

⁹ 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.

¹⁰ These prices correspond to those reported by Médecins sans frontières in its brochure “Untangling the web of price reductions: a pricing guide for the purchase of ARVs for developing countries”, 8th ed., June 2005 (<http://www.accessmedmsf.org/prod/publications.asp?scentid=28620051846504&contenttype=PARA&>). The MSF document is intended to provide information on pricing and suppliers that will help purchasers make informed decisions when buying ARVs.

excluded that in some instances lower prices for the products can be and, indeed, have been negotiated.¹¹

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

Based on the usual daily prescription for each product, it can be estimated that the reported volumes of sale could be used to treat roughly 175.000 persons during the period concerned by this report. However, it must be noted that all of the products registered so far are used as part of a combination therapy together with other drugs which so far have not been registered.

To put this estimate into a relation with the overall supply of ARV therapies to poor and developing countries it must be noted that currently 1.3 million people are on ARV therapy in low and middle-income countries¹² - including such countries that are not defined as “countries of destination” in Annex II of the Regulation and, therefore, not covered by this report. 810.000 patients receive ARV treatment in Sub-Saharan Africa, 315.000 in Latin America and the Caribbean, 180.000 in East, South and South-East Asia, 21.000 in Eastern Europe and Central Asia and 4.000 in North Africa and the Middle East.

In the reporting periods, no attempts to illegally re-import tiered-priced products registered under the Regulation back into the EU have been reported to the Commission.

4. COUNTRIES OF DESTINATION

In the reporting period, tiered priced products have been supplied to 36 of the countries listed in Annex II of the Regulation. These countries were: Botswana, Burkina Faso, Burundi, Cambodia, Cameroon, Central African Republic, Democratic Republic of Congo, Republic of Congo, Djibouti, East Timor, Eritrea, Ethiopia, Gambia, Ghana, Guinea, Haiti, India, Kenya, Madagascar, Malawi, Mali, Mauritania, Moldova, Mozambique, Nicaragua, Nigeria, Rwanda, Senegal, South Africa, Sudan, Tanzania, Togo, Uganda, Vietnam, Zambia, and Zimbabwe. With the exceptions of East Timor, Haiti, India, Moldova, Nicaragua and Vietnam all countries concerned are situated in Sub-Saharan Africa. This corresponds to the fact that the prevalence of HIV/AIDS is strongest in this region.

Detailed information on the volumes of exports to each country of destination is found in Annex II of this report.

¹¹ 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.

¹² http://www.theglobalfund.org/en/funds_raised/price_reporting/default.asp
cf. WHO and UNAIDS “3 by 5” Progress on Global Access to HIV Antiretroviral Therapy. A Report on “3 by 5” and Beyond”, March 2006, published on the internet at http://www.who.int/hiv/fullreport_en_highres.pdf

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

5. DISEASES COVERED

HIV/AIDS, malaria and tuberculosis are generally considered the gravest public health concerns for developing countries and an important obstacle for development. This is why EC Development policy, including the Regulation, specifically focuses on these three diseases. Considering that the list of registered products did not change in 2005, the diseases covered in this report remain identical, i.e. exclusively the treatment of HIV/AIDS.

However, there are certainly some pharmaceuticals for the treatment of malaria and tuberculosis that would benefit from registration under the Regulation. Medicines for opportunistic infections associations with HIV/AIDS are also eligible and suitable for coverage under the Regulation.

While not directly targeted by the Regulation, it is important to note that of new medicines developed over the last 25 years, only 1% were for the treatment of tuberculosis and tropical diseases, which account for 11 % of the global disease burden. These “neglected” diseases¹³ continue being an area where, due to the absence of solvable market demand, incentives are generally insufficient to stimulate the research and development of new treatments.

6. APPLICATION OF PRICE FORMULAE

To date the application of the price formulae (as foreseen in Article 3 of the Regulation) has not caused any practical problem. Indeed, the applicant did not find it necessary to avail himself of the services of an independent auditor in order to protect sensitive business data (possibility foreseen in Article 4(2)(ii) of the Regulation). For 7 out of 9 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. In the two other cases (Ziagen 300 mg x 60 and Retrovir Oral Solution), the producer submitted calculations detailing weighted averages of OECD prices. Both the tiered price and all OECD list prices are information available to the public.

¹³ “Neglected diseases” are generally understood to be diseases that are not targeted by private research and development efforts. However, some differentiate further between “neglected diseases” (which affect many persons in poor countries, and which, due to the poverty of these patients, fail to attract research and development efforts), and “orphan diseases” (which affect people in developed countries, but are very rare, so that it is their rarity which makes research and development economically unviable).

7. CONCLUSIONS

7.1. Evaluating the impact of the Regulation over time

Last year's report covered the period from the adoption of the Regulation (26 May 2003) until the end of 2004, i.e. 19 months. However, the first set of products was only registered on 19 April 2004 and the second set of products on 20 September 2004. Consequently the reporting on volumes actually covered a period of maximum 8.5 months. This year's report, on the other hand, covers a period of 12 months (Jan.-Dec. 2005). The comparison of volumes was therefore done on a monthly basis. The table below provides some indication of the volume trends per product registered under the Regulation:

Product	2004 (monthly average)	2005 (monthly average)	% difference
Retrovir 300 mg x 60	3.059	8.520	+179%
Epivir 150 mg x 60	51.099	106.226	+108%
Trizivir 750 mg x 60	135	260	+93%
Combivir 300/150 mg x 60	44.498	57.622	+29%
Retrovir 100 mg x 100	6.734	7.926	+18%
Ziagen 300 mg x 60	3.522	2.827	-20%
Epivir Oral solution 10mg/ml - 240 ml	22.129	14.473	-35%
Retrovir 250 mg x 40	146	75	-48%
Retrovir Oral solution 10 mg/ml - 200 ml	62.689	30.495	-51%
<i>Average</i>			+30%

Of all products registered, *Retrovir 300 mg x 60*, *Epivir 150 mg x 60* and *Trizivir 750 mg x 60* experienced the biggest increase in monthly volumes sold at tiered prices, with increases of respectively 178.5%, 107.88% and 92.53%. Two products, *Combivir 300/150 mg x 60* and *Retrovir 100 mg x 100* have only marginally increased in terms of monthly sales volumes; while the last 4 products in the table – *Ziagen 300 mg x 60*, *Epivir Oral Solution 10 mg/ml – 240 ml*, *Retrovir 250 mg x 40* and *Retrovir Oral Solution 10 mg/ml – 200 ml*- experienced relatively high decreases in monthly sales volumes. Overall, monthly volume trends have increased on average by approximately 30%.

The producer considers that the variations of volumes can be attributed to the fluctuation of stocks. Supply Chain Management is one of the main challenges facing developing countries trying to scale up their HIV programmes. If the purchase of medicines is not the biggest issue, it is widely recognised that the two other aspects of the Supply Chain Management: planning and delivery are almost inexistent in certain countries. Planning includes commodities selection, quality control, forecasting and financing; delivery includes storage and decentralisation of the distribution, effective use of the medicines and monitoring. The lack of proper forecasting at a country level in particular can lead to either over stock (some countries tend to order large quantity of products when they receive disbursements from donors) or problems of shortage.

Disappointingly, no new products were registered over the reporting period; however, the Commission continues to believe that the Regulation is a forward-looking measure, addressing situations that will arise in the future as volume sales of

ARVs and other medicines increase. Sales volumes of the products currently registered under the Regulation (and hence the importance of a measure addressing the problem of trade diversion) are likely to increase when and if demand for them increases. Presently, the situation is that the prices for these drugs have been strongly reduced – yet there is still a need for public funding, because the vast majority of people in need of these drugs are not able to afford them. Once more funding and better distribution under strengthened health systems are in place, sales volumes will increase.

The Regulation is also relevant in encouraging access to newer second-line AIDS treatments and to make these available in poor countries in future. Likewise (and even more importantly), the Regulation should help ensuring access to an effective HIV/AIDS vaccine, if and when such a vaccine becomes available. Equally relevant for protection under this Regulation are medicines and/or vaccines for the other two targeted diseases under the Regulation, i.e. malaria and tuberculosis.

It can also be expected that the scope of countries supplied with tiered priced medicines will broaden, when more funding and more efficient distribution channels become available. Since last year, the number of countries supplied with the registered products has already increased from 26 to 36.

7.2. Tiered pricing makes supply of discounted medicines sustainable

While the Commission regrets the fact that no additional products were registered in 2005, it can still be considered an achievement that GlaxoSmithKline is prepared to supply poor and developing countries with the nine products listed above at the prices indicated above on a sustainable basis. The Commission remains aware that other producers also sell key medicines at reduced prices or make donations. Most companies producing anti-retrovirals, including Abbot, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, Merck and Roche, have reduced pricing schemes for developing countries¹⁴, and in some cases these prices are comparable to those of generics. The Commission has actively encouraged these pharmaceutical companies to register their products under the Regulation.

While the Regulation covers both tiered priced and donated products, the European Commission has never concealed its view that it sees tiered pricing as the best way forward:

- Tiered pricing is a sustainable solution. In the best of cases, tiered prices are prices that would be reached in a competitive market, and allow the sale of medicines to be profitable. Indeed, the concept is founded on the principle that profits gained in developed countries support lower priced sales in poor countries.

¹⁴

Cf. following websites:

http://www.abbott.com/global/url/content/en_US/40.20:20/general_content/General_Content_00050.htm (Abbot); http://www.boehringer-ingelheim.fr/html/presse/presse_detail2.asp (Boehringer Ingelheim); <http://www.bms.com/landing/data/index.html> (Bristol Myers Squibb); http://www.gilead.com/wt/sec/patient_assist (Gilead); http://www.merck.com/cr/enabling_access/developing_world/hiv/ (Merck); http://www.roche.com/sus_eth_pat (Roche)

- Therefore, this approach leads to the development of viable, competitive markets for pharmaceutical products in developing countries. It makes it possible for pharmaceutical companies to include developing countries in their business development strategies.
- Contrary to this, donations are not a sustainable solution. They are sometimes considered as working well in disease eradication programmes and in emergencies. But it cannot be sustainable for companies to give away products for free indefinitely and in significant quantities.
- In the worst case, donations can even have hidden costs. They can distort national healthcare priorities, undermine the development of competitive local markets and, if they involve unsuitable products, lead to health damages.

7.3. Responsible drug prices

Council Regulation 953/2003 is part of a package of political measures adopted by the EC in order to facilitate affordable access to medicine in poor countries, in particular with regard to HIV/AIDS, malaria and tuberculosis. These measures include the Decision¹⁵ of the WTO General Council to allow compulsory licenses on patented drugs for export purposes, the EU Regulation¹⁶ to provide implementation of this Decision at Community level, enhanced funding for Research and Development and various other initiatives.¹⁷

Last year's report highlighted the historic decline in prices of anti-retrovirals (ARVs), from over US\$ 10,000 in 2000 to as little as US\$200 per patient/year more recently. However, these prices refer to first-line ARVs, used by most of the estimated 1.3 million currently receiving treatment. Once resistance to first-line ARVs develops, patients will increasingly need to switch to second-line ARVs, which remain priced out of reach or are not available at all. As awareness about the issue is growing, one could expect that a similar combination of public advocacy, market transparency and competition will again lead to the availability and affordability of these second-line medicines.

Lower prices for drugs, do not, however, suffice to ensure access. It is of the utmost importance that sufficient and continuous funding be made available for the purchase of these drugs that efforts are reinforced to strengthen local health systems and that further incentives are provided to ensure the research and development of new medicines. In this respect, some concrete proposals for action by national and international stakeholders were highlighted in a report¹⁸ released last April by an independent body, the Commission on Intellectual Property Rights, Innovation and Public Health (CIPRH) at the request of WHO.

¹⁵ Amendment of the TRIPS Agreement, Decision of 6 December 2005 (WT/L/641 – 8 December 2005)

¹⁶ Regulation (EC) No 816/2006 of the European Parliament and of the Council of 17 May 2006 on compulsory licensing of patents relating to the manufacture of pharmaceutical products for export countries with public health problems. Official Journal, L157, 9.6.2006

¹⁷ cf. Communication from the Commission to the Council and the European Parliament - A Coherent European Policy Framework for External Action to Confront HIV/AIDS, Malaria and Tuberculosis; COM(2004) 726 final, 26 October 2004

¹⁸ <http://www.who.int/intellectualproperty/en/>

ANNEX 1: DETAILS OF VOLUMES OF MEDICINES SOLD IN 2005

EPIVIR Oral Solution 10mg/ml – 240 ml	Country of Destination	Volumes sold (units)¹⁹ – 01/01/05 to 31/12/05
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Central African Republic	216
Active ingredient: lamivudine	Congo, Republic of	255
	Eritrea	108
Price offered (per unit): US\$ 6,73	Ethiopia	26,604
	Haiti	9,192
Highest OECD list price: US\$ 71.73 ²⁰	Kenya	34,797
Lowest OECD list price: US\$ 33.32 ²¹	Mozambique	2,500
Preferential/highest OECD list price: 9.38% ²²	Nigeria	28,759
Preferential/lowest OECD list price: 20.20% ²³	Senegal	750
	South Africa	14,425
	Sudan	1,176
The oral solution is for paediatric use; the dosage depends on the weight of the child. According to WHO treatment guidelines ²⁴ the recommended dosage for a child weighing less than 60 kg is 4 mg/kg/dose twice daily. The 173,673 units reported below would thus correspond to the amount of drugs needed for the treatment of 14,473 children of 10 kg during 12 months if used in a combination recommended by WHO (See Annex III below).	Togo	315
	Uganda	19,848
	Vietnam	2,208
	Zambia	32,520
	Total	173,673
According to information published by WHO on the source and prices of active pharmaceutical ingredients (API) for ARVs available on the world market ²⁵ , the selling price for lamivudine on the international market is between US\$ 295,- and US\$ 480,- per kg.	<i>per month</i>	14,473

¹⁹ 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.

²⁰ The highest OECD list price for Epivir Oral Solution, as reported in June 2006, is now US\$ 85.09

²¹ The lowest OECD list price for Epivir Oral Solution, as reported in June 2006, is now US\$ 34.53

²² Revised preferential/highest OECD list price: 7.91%

²³ Revised preferential/lowest OECD list price: 19.49%

²⁴ http://www.who.int/hiv/pub/prev_care/en/arvrevision2003en.pdf

²⁵ http://www.who.int/3by5/amds/API_0905.pdf

EPIVIR 150 mg x 60	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Botswana	99,271
Active ingredient: lamivudine	Burkina Faso	3,000
	Cambodia	508
Price offered (per unit): US\$ 5,70	Congo, Republic of	900
	Djibouti	217
Highest OECD list price: US\$ 395.78 ²⁶	East Timor	120
Lowest OECD list price: US\$ 121.81 ²⁷	Ethiopia	90,589
Preferential/highest OECD list price: 1.44% ²⁸	Haiti	6,136
Preferential/lowest OECD list price: 4.68% ²⁹	Kenya	313,594
	Mali	1,967
	Mauritania	212
According to WHO treatment guidelines, the recommended dosage of lamivudine is 150 mg twice daily or 300 mg once daily, which means that one “unit” would suffice for one patient during one month. On this basis it can be estimated that the 1,274,711 units of Eпивir 150 mg x 60 reported correspond to the amount needed to treat 106,226 persons during 12 months if used in combination recommended by WHO (See Annex III below).	Nigeria	164,109
	Senegal	2,920
	South Africa	354,597
	Sudan	54
	Tanzania	27,600
According to information published by WHO on the source and prices of active pharmaceutical ingredients (API) for ARVs available on the world market, the selling price for lamivudine on the international market is between US\$ 295,- and US\$ 480,- per kg.	Togo	1,975
	Uganda	113,419
	Vietnam	11,100
	Zambia	73,961
	Zimbabwe	8,462
	Total	1,274,711
	<i>Per month</i>	106,226

²⁶ The highest OECD list price for Eпивir 150 mg x 60, as reported in June 2006, is now US\$ 231.49

²⁷ The lowest OECD list price for Eпивir 150 mg x 60, as reported in June 2006, is now US\$ 128.66

²⁸ Revised preferential/highest OECD list price: 2.46%

²⁹ Revised preferential/lowest OECD list price: 5.23%

COMBIVIR 300/150 mg x 60**Country of Destination** **Volumes sold (units) –
– 01/01/05 to 31/12/05****Date of Approval: 19 April 2004**

Disease targeted: HIV infection	Botswana	150,650
Active ingredient: lamivudine + zidovudine	Burkina Faso	7,500
	Burundi	2,500
	Cambodia	900
Price offered (per unit): US\$ 19.50	Congo, Democratic Republic of	170
	Djibouti	1,947
Highest OECD list price: US\$ 767.59 ³⁰	Ethiopia	87,250
Lowest OECD list price: US\$ 177.49 ³¹	Gambia	438
Preferential/highest OECD list price: 2.54% ³²	Ghana	5,050
Preferential/lowest OECD list price: 10.99% ³³	Haiti	30,705
	India	80
According to WHO treatment guidelines, the recommended dosage of lamivudine is 150 mg twice daily or 300 mg once daily and the recommended dosage of zidovudine is 300 mg twice daily. One “unit” of COMBIVIR, containing 60 tablets, would thus suffice for the treatment of one person during one month. On this basis, it can be estimated that the 691,466 units reported below would correspond to the amount of drugs needed for the treatment of 57,622 infected persons during 12 months if used in combination recommended by WHO (See Annex III below).	Kenya	115,349
	Madagascar	210
	Malawi	80
	Mali	1,966
	Mauritania	25
	Nigeria	65,364
	Rwanda	601
According to WHO, the selling prices on the international market are for lamivudine between US\$ 295,- and US\$ 480,- per kg and for zidovudine between US\$ 360,- and US\$ 510,- per kg.	Senegal	5,760
	South Africa	46,153
	Sudan	134
	Togo	600
	Uganda	72,583
	Vietnam	6,801
	Zambia	83,372
	Zimbabwe	40
	Total	691,466
	<i>Per month</i>	57,622

³⁰ The highest OECD list price for Combivir, as reported in June 2006, is now US\$ 931.308

³¹ The lowest OECD list price for Combivir, as reported in June 2006, is now US\$ 264.54

³² Revised preferential/highest OECD list price: 2.09%

³³ Revised preferential/lowest OECD list price: 7.37%

RETROVIR 100 mg x 100	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval: 19 April 2004	Botswana	35,478
Disease targeted: HIV infection	Cambodia	39
Active ingredient: zidovudine	Ethiopia	2,897
	Gambia	100
Price offered (per unit): US\$ 15.77	Haiti	940
	India	20
Highest OECD list price: US\$ 219.42 ³⁴	Kenya	12,957
Lowest OECD list price: US\$ 104.07 ³⁵	Nigeria	11,814
Preferential/highest OECD list price: 7.19% ³⁶	Senegal	616
Preferential/lowest OECD list price: 15.15% ³⁷	South Africa	16,465
According to WHO treatment guidelines, the recommended dosage of zidovudine is 300 mg twice daily. The 100 mg capsules are available for dose variations; thus they should not enter the calculation.	Sudan	77
	Uganda	4,836
	Zambia	8,870
	Total	95,109
	<i>Per month</i>	7,926

³⁴ The highest OECD list price for Retrovir 100 mg x 60, as reported in June 2006, is now US\$ 261.33

³⁵ The lowest OECD list price for Retrovir 100 mg x 60, as reported in June 2006, is now US\$ 105.09

³⁶ Revised preferential/highest OECD list price: 6.03%

³⁷ Revised preferential/lowest OECD list price: 15.00%

RETROVIR 300 mg x 60	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Bostwana	4,450
Active ingredient: zidovudine	Congo, Republic of	100
	Djibouti	183
Price offered (per unit): US\$ 17.40	East Timor	120
	Ethiopia	2,360
Highest OECD list price: US\$ 295.42 ³⁸	Haiti	1,008
Lowest OECD list price: US\$ 125.15 ³⁹	Kenya	25,090
Preferential/highest OECD list price: 5.89% ⁴⁰	Madagascar	70
Preferential/lowest OECD list price: 13.90% ⁴¹	Mali	987
	Nigeria	36,827
According to WHO treatment guidelines, the recommended dosage of zidovudine is 300 mg (one tablet) twice daily. On this basis, it can be estimated that the 102,236 units reported would correspond to the amount of drugs needed for the treatment of 8,520 infected persons during 12 months if used in combination recommended by WHO (see Annex III below).	Senegal	525
	South Africa	14,774
	Togo	30
	Uganda	14,685
	Zambia	840
	Zimbabwe	187
	Total	102,236
	<i>Per month</i>	8,520

RETROVIR 250 mg x 40	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Cambodia	39
Active ingredient: zidovudine	Guinea	750

³⁸ The highest OECD list price for Retrovir 300 mg x 60, as reported in June 2006, is now US\$ 342.12

³⁹ The lowest OECD list price for Retrovir 300 mg x 60, as reported in June 2006, is now US\$ 184.16

⁴⁰ Revised preferential/highest OECD list price: 5.09%

⁴¹ Revised preferential/lowest OECD list price: 9.45%

⁴² The highest OECD list price for Retrovir 250 mg x 40, as reported in June 2006, is now US\$ 263.17

⁴³ The lowest OECD list price for Retrovir 250 mg x 40, as reported in June 2006, is now US\$ 101.27

⁴⁴ Revised preferential/highest OECD list price: 5.04%

⁴⁵ Revised preferential/lowest OECD list price: 13.10%

	South Africa	116
Price offered (per unit): US\$ 13.27	Total	905
	<i>per month</i>	75
Highest OECD list price: US\$ 205.16 ⁴²		
Lowest OECD list price: US\$ 83.84 ⁴³		
Preferential/highest OECD list price: 6.47% ⁴⁴		
Preferential/lowest OECD list price: 15.83% ⁴⁵		

According to WHO treatment guidelines, the recommended dosage of zidovudine is 300 mg twice daily. The 250 mg capsules are used for smaller dosage

TRIZIVIR 750 mg x 60	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval: 19 April 2004		
Disease targeted: HIV infection	Central African Republic	505
Active ingredient: abacavir sulphate (300 mg) + lamivudine (150 mg) + zidovudine (300 mg)	Gambia	25
	Kenya	237
Price offered (per unit): US\$ 102.00 ⁴⁶	Moldova	360
	Mozambique	689
Highest OECD list price: US\$ 887.97 ⁴⁷	Nigeria	822
	South Africa	31
Lowest OECD list price: US\$ 539.09 ⁴⁸	Uganda	50
	Zambia	400
Preferential/highest OECD list price: 11.49% ⁴⁹		
Preferential/lowest OECD list price: 18.92% ⁵⁰		
	Total	3,119
	<i>Per month</i>	260

According to WHO treatment guidelines, the recommended dosage of abacavir is 300 mg twice daily, the recommended dosage of lamivudine is 150 mg twice daily or 300 mg once daily, the recommended dosage of zidovudine is 300 mg twice daily. The normal prescription would therefore be two capsules of TRIZIVIR 750 mg per day. On this basis, it can be estimated that the 3,119 units reported above would correspond to the treatment of 260 infected persons during 12 months. According to WHO, the selling prices on the international market are for lamivudine between US\$ 295,- and US\$ 480,- per kg and for zidovudine between US\$ 360,- and US\$ 510,- per kg. For abacavir, the price range is between US\$ 1.500,- and US\$ 3.500,-.

⁴⁶ 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.

⁴⁷ The highest OECD list price for Trizivir 750 mg x 60, as reported in June 2006, is now US\$ 1,141.68

⁴⁸ The lowest OECD list price for Trizivir 750 mg x 60, as reported in June 2006, is now US\$ 499.05

⁴⁹ Revised preferential/highest OECD list price: 6.13%

⁵⁰ Revised preferential/lowest OECD list price: 14.03%

ZIAGEN 300 mg x 60	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval: 20 September 2004		
Disease targeted: HIV infection	Botswana	2,500
Active ingredient: abacavir sulphate	Burkina Faso	590
	Cambodia	762
Price offered (per unit): US\$ 72.90 ⁵¹	Cameroon	26
	Central African Republic	722
Highest OECD list price: US\$ 411.42 ⁵²	Congo, Republic of	300
Lowest OECD list price: US\$ 152.64 ⁵³	Congo, Democratic Republic of	84
Preferential/highest OECD list price: 17.72% ⁵⁴	Djibouti	300
Preferential/lowest OECD list price: 47.76% ⁵⁵	Eritrea	305
According to WHO treatment guidelines, the recommended dosage of abacavir is 300 mg (i.e. one capsule) twice daily. On this basis, it can be estimated that the 33,924 units reported above would thus correspond to the amount of drugs needed for the treatment of 2,827 persons during 12 months if used in accordance with WHO recommendations (see Annex III below).	Guinea	410
	Haiti	1,161
	Kenya	2,129
According to WHO, the selling prices on the international market for abacavir are between US\$ 1.500,- and US\$ 3.500,-.	Madagascar	70
	Malawi	40
	Mauritania	30
	Mozambique	1,559
	Nicaragua	85
	Nigeria	7,890
	Rwanda	4,300
	South Africa	2,179
	Tanzania	4,480
	Uganda	1,966

⁵¹ 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.

⁵² The highest OECD list price for Ziagen 300 mg x 60, as reported in June 2006, is now US\$ 504.324

⁵³ The lowest OECD list price for Ziagen 300 mg x 60, as reported in June 2006, is now US\$ 244.79

⁵⁴ Revised preferential/highest OECD list price: 10.37%

⁵⁵ Revised preferential/lowest OECD list price: 21.36%

Vietnam	2,000
Zambia	36
Total	33,924
<i>per month</i>	2,827

RETROVIR Oral Solution 10 mg/ml – 200 ml	Country of Destination	Volumes sold (units) – – 01/01/05 to 31/12/05
Date of Approval : 20 September 2004		
Disease targeted: HIV infection	Botswana	174,215
Active ingredient: zidovudine	Ethiopia	37,656
	Haiti	11,810
Price offered (per unit): US\$ 7.10	Kenya	69,582
	Mozambique	2,500
Highest OECD list price: US\$ 73.83 ⁵⁶	Nigeria	31,265
Lowest OECD list price: US\$ 17.85 ⁵⁷	South Africa	8,050
Preferential/highest OECD list price: 9.62% ⁵⁸	Sudan	108
Preferential/lowest OECD list price: 39.77% ⁵⁹	Togo	20
The oral solution is paediatric; the quantity to administer depends on the age of the child. According to WHO treatment guidelines, the recommended dosage for a child of less than 4 weeks is 4 mg/kg/dose twice daily. The 365,938 units reported would thus correspond to the amount of drugs needed for the treatment of 30.495 children of approximately 10 kg during 12 months if used in combination recommended by WHO (see Annex III below).	Uganda	19,380
	Vietnam	1,704
	Zambia	9,648
	Total	365,938
	<i>Per month</i>	30,495

⁵⁶ The highest OECD list price for Retrovir Oral Solution, as reported in June 2006, is now US\$ 87.63

⁵⁷ The lowest OECD list price for Retrovir Oral Solution, as reported in June 2006, is now US\$ 20.25

⁵⁸ Revised preferential/highest OECD list price: 8.10%

⁵⁹ Revised preferential/lowest OECD list price: 35.06%

**ANNEX 2: VOLUMES OF TIERED PRICED PRODUCTS SOLD BY COUNTRY BETWEEN 1
JANUARY 2005 AND 31 DECEMBER 2005**

Country	Products	Units
Botswana	EPIVIR 150 mg x 60	99,271
	COMBIVIR 300/150 mg x 60	150,650
	RETROVIR 100 mg x 100	35,478
	RETROVIR 300 mg x 60	4,450
	ZIAGEN 300 mg x 60	2,500
	RETROVIR Oral Solution	174,215
Burkina Faso	EPIVIR 150 mg x 60	3,000
	COMBIVIR 300/150 mg x 60	7,500
	ZIAGEN 300 mg x 60	590
Burundi	COMBIVIR 300/150 mg x 60	2,500
Cambodia	EPIVIR 150 mg x 60	508
	COMBIVIR 300/150 mg x 60	900
	RETROVIR 100 mg x 100	39
	RETROVIR 250 mg x 40	39
	ZIAGEN 300 mg x 60	762
Cameroon	ZIAGEN 300 mg x 60	26
Central African Republic	EPIVIR Oral Solution	216
	TRIZIVIR 750 mg x 60	505
	ZIAGEN 300 mg x 60	722
Congo, Democratic Republic of	COMBIVIR 300/150 mg x 60	170
	ZIAGEN 300 mg x 60	84
Congo, Republic of	EPIVIR Oral Solution	255
	EPIVIR 150 mg x 60	900
	RETROVIR 300 mg x 60	100
	ZIAGEN 300 mg x 60	300
Djibouti	EPIVIR 150 mg x 60	217
	COMBIVIR 300/150 mg x 60	1,947

	RETROVIR 300 mg x 60	183
	ZIAGEN 300 mg x 60	300
East Timor	EPIVIR 150 mg x 60	120
	RETROVIR 300 mg x 60	120
Eritrea	EPIVIR Oral Solution	108
	EPIVIR 150 mg x 60	90,589
	ZIAGEN 300 mg x 60	305
Ethiopia	EPIVIR Oral Solution	26,604
	COMBIVIR 300/150 mg x 60	87,250
	RETROVIR 100 mg x 100	2,897
	RETROVIR 300 mg x 60	2,360
	RETROVIR Oral Solution	37,656
Gambia	COMBIVIR 300/150 mg x 60	438
	RETROVIR 100 mg x 100	100
	TRIZIVIR 750 mg x 60	25
Ghana	COMBIVIR 300/150 mg x 60	5,050
Guinea	RETROVIR 250 mg x 40	750
	ZIAGEN 300 mg x 60	410
Haiti	EPIVIR Oral Solution	9,192
	EPIVIR 150 mg x 60	6,136
	COMBIVIR 300/150 mg x 60	30,705
	RETROVIR 100 mg x 100	940
	RETROVIR 300 mg x 60	1,008
	ZIAGEN 300 mg x 60	1,161
	RETROVIR Oral Solution	11,810
India	COMBIVIR 300/150 mg x 60	80
	RETROVIR 100 mg x 100	20
Kenya	EPIVIR Oral Solution	34,797
	EPIVIR 150 mg x 60	313,594
	COMBIVIR 300/150 mg x 60	115,349
	RETROVIR 100 mg x 100	12,957

	RETROVIR 300 mg x 60	25,090
	TRIZIVIR 750 mg x 60	237
	ZIAGEN 300 mg x 60	2,129
	RETROVIR Oral Solution	69,582
Madagascar	COMBIVIR 300/150 mg x 60	210
	RETROVIR 300 mg x 60	70
	ZIAGEN 300 mg x 60	70
Malawi	COMBIVIR 300/150 mg x 60	80
	ZIAGEN 300 mg x 60	40
Mali	EPIVIR 150 mg x 60	1,967
	COMBIVIR 300/150 mg x 60	1,966
	RETROVIR 300 mg x 60	987
Mauritania	EPIVIR 150 mg x 60	212
	COMBIVIR 300/150 mg x 60	25
	ZIAGEN 300 mg x 60	30
Moldova	TRIZIVIR 750 mg x 60	360
Mozambique	EPIVIR Oral Solution	2,500
	TRIZIVIR 750 mg x 60	689
	ZIAGEN 300 mg x 60	1,559
	RETROVIR Oral Solution	2,500
Nicaragua	ZIAGEN 300 mg x 60	85
Nigeria	EPIVIR Oral Solution	28,759
	EPIVIR 150 mg x 60	164,109
	COMBIVIR 300/150 mg x 60	65,364
	RETROVIR 100 mg x 100	11,814
	RETROVIR 300 mg x 60	36,827
	TRIZIVIR 750 mg x 60	822
	ZIAGEN 300 mg x 60	7,890
	RETROVIR Oral Solution	31,265
Rwanda	COMBIVIR 300/150 mg x 60	601
	ZIAGEN 300 mg x 60	4,300

Senegal	EPIVIR Oral Solution	750
	EPIVIR 150 mg x 60	2,920
	COMBIVIR 300/150 mg x 60	5,760
	RETROVIR 100 mg x 100	616
	RETROVIR 300 mg x 60	525
South Africa	EPIVIR Oral Solution	14,425
	EPIVIR 150 mg x 60	354,597
	COMBIVIR 300/150 mg x 60	46,153
	RETROVIR 100 mg x 100	16,465
	RETROVIR 300 mg x 60	14,774
	RETROVIR 250 mg x 40	116
	TRIZIVIR 750 mg x 60	31
	ZIAGEN 300 mg x 60	2,179
	RETROVIR Oral Solution	8,050
	Sudan	EPIVIR Oral Solution
EPIVIR 150 mg x 60		54
COMBIVIR 300/150 mg x 60		134
RETROVIR 100 mg x 100		77
RETROVIR Oral Solution		108
Tanzania	EPIVIR 150 mg x 60	27,600
	ZIAGEN 300 mg x 60	4,480
Togo	EPIVIR Oral Solution	315
	EPIVIR 150 mg x 60	1,975
	COMBIVIR 300/150 mg x 60	600
	RETROVIR 300 mg x 60	30
	RETROVIR Oral Solution	20
Uganda	EPIVIR Oral Solution	19,848
	EPIVIR 150 mg x 60	113,419
	COMBIVIR 300/150 mg x 60	72,583
	RETROVIR 100 mg x 100	4,836
	RETROVIR 300 mg x 60	14,685

	TRIZIVIR 750 mg x 60	50
	ZIAGEN 300 mg x 60	1,966
	RETROVIR Oral Solution	19,380
Vietnam	EPIVIR Oral Solution	2,208
	EPIVIR 150 mg x 60	11,100
	COMBIVIR 300/150 mg x 60	6,801
	ZIAGEN 300 mg x 60	2,000
	RETROVIR Oral Solution	1,704
Zambia	EPIVIR Oral Solution	32,520
	EPIVIR 150 mg x 60	73,961
	COMBIVIR 300/150 mg x 60	83,372
	RETROVIR 100 mg x 100	8,870
	RETROVIR 300 mg x 60	840
	TRIZIVIR 750 mg x 60	400
	ZIAGEN 300 mg x 60	36
	RETROVIR Oral Solution	9,648
Zimbabwe	EPIVIR 150 mg x 60	8,462
	COMBIVIR 300/150 mg x 60	40
	RETROVIR 300 mg x 60	187

ANNEX 3: FIXED-DOSE ARV COMBINATIONS

WHO encourages the use of fixed-dose combinations as follows:

- Three drug fixed-dose combinations:
- Stavudine (40 mg) + Lamivudine (150 mg) + Nevirapine (200 mg)
 - Stavudine (30 mg) + Lamivudine (150 mg) + Nevirapine (200 mg)
 - Zidovudine (300 mg) + Lamivudine (150 mg) + Abacavir (300 mg)
 - Zidovudine (300 mg) + Lamivudine (150 mg) + Nevirapine (200 mg)
- Two drug fixed-dose combinations:
- Stavudine (30 mg) + Lamivudine (150 mg)
 - Stavudine (40 mg) + Lamivudine (150 mg)
 - Zidovudine (300 mg) + Lamivudine (150 mg)