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COMMISSION STAFF WORKING DOCUMENT

Annual report (2006) on 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 third annual report under Article 11 of Regulation 953/2003,[1] 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 2006.

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[2] 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 Report[4] 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. The first progress report under this programme will be prepared in 2008.

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 medicines in question in the target countries at the lowest possible ("tiered") price, while at the same time recouping their research and development

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1 Article 11 of Regulation 953/2003: *"(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.

expenditure by charging higher prices 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".[5]

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**[6] **("the Regulation").**

2. COMMISSION REPORTING UNDER REGULATION 953/2003

This report covers the period from 1 January to 31 December 2006. 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 and listed in Annex I to the Regulation;

– the countries of destination benefiting from these exports at tiered prices;

– the diseases treated with the products in question;

– an assessment of application of the price formulae in Article 3 of the Regulation to each of the products concerned.

This report is mainly 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 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).

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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, 3.6.2003, pp 5–11. The Regulation was last updated by Commission Regulation 1662/2005 of 11 October 2005: OJ L 267, 12.10.2005, pp 19–21.

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
EPIVIR Oral solution 10 mg/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 – US$ 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 – US$ 887.97	US$ 102.00[7]
ZIAGEN 300 mg x 60	US$ 152.64 – US$ 411.42	US$ 72.90[8]
RETROVIR Oral solution 10 mg/ml – 200 ml	US$ 17.85 – US$ 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[9] in any volume desired, provided 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, negotiated.[10]

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.

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

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

9 These are the prices 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", 9th ed., July 2006: (http://www.accessmed-msf.org/prod/publications.asp?scntid=12120071627123&contenttype=PARA&). The MSF document provides information on pricing and suppliers to help purchasers make informed decisions when buying ARVs.

10 Information on actual sales prices can be found on the website of the Global Fund to Fight AIDS, TB and Malaria: http://www.theglobalfund.org/en/funds_raised/price_reporting/default.asp.

Based on the usual daily dose prescribed for each product, the reported sales volumes could have been used to treat an estimated 140 000 persons infected with HIV during the period covered by this report. However, it must be added that all the products registered so far are used as part of a combination therapy together with other medicines which have not yet been registered.

To put this estimate into perspective in terms of the overall supply of ARV therapies to poor and developing countries, it must be remembered that in December 2006 approximately 2 million people were on ARV therapy in low- and middle-income countries,[11] including some not listed as "countries of destination" in Annex II to the Regulation and, therefore, not covered by this report. Some 1.3 million people were receiving ARV treatment in Sub-Saharan Africa, 355 000 in Latin America and the Caribbean, 280 000 in East, South and South-East Asia, 35 000 in Eastern Europe and Central Asia and 5 000 in North Africa and the Middle East.

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 were supplied to 34 of the countries listed in Annex II to the Regulation. These were: Armenia, Benin, Botswana, Burkina Faso, Burundi, Cambodia, Cameroon, the Central African Republic, the Democratic Republic of Congo, Côte d'Ivoire, Ethiopia, Gambia, Ghana, Guinea-Bissau, Haiti, Honduras, Kenya, Madagascar, Malawi, Mauritania, Moldova, Mozambique, Nepal, Nigeria, Rwanda, Senegal, South Africa, Sudan, Tanzania, Togo, Uganda, Vietnam, Zambia and Zimbabwe. With the exceptions of Armenia, Cambodia, Haiti, Honduras, Moldova, Nepal and Vietnam, all the countries concerned are in Sub-Saharan Africa, the region where the prevalence of HIV/AIDS is highest.

In the two previous reports, sales volumes were reported country by country. Since producers report the sales volumes in each country to the Commission on a confidential basis and in order to protect the data of the countries themselves, from now on the volumes will be reported for eight 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.

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[11] cf. Towards Universal Access. Scaling up priority HIV/AIDS interventions in the health sector. Progress report, April 2007. Available at: http://www.who.int/hiv/mediacentre/univeral_access_progress_report_en.pdf.

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 2006, 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 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

7.1. The 2005 report and this report both cover a calendar year (from January to December). The table below gives some indication of the sales trends per product registered under the Regulation and provides a year-on-year comparison with the 2005 figures.

Product/unit	2005	2006	% difference
Epivir Oral solution 10 mg/ml 240 ml	173 673	406 287	133.94%
Trizivir 750 mg x 60	3 119	4 903	57.20%
Retrovir 100 mg x 100	95 109	132 176	38.97%
Ziagen 300 mg x 60	33 924	40 208	18.52%
Retrovir Oral solution 10 mg/ml 200 ml	365 938	119 807	-67.26%
Retrovir 300 mg x 60	102 236	48 410	-52.65%
Combivir 300/150 mg x 60	691 466	397 450	-42.52%
Retrovir 250 mg x 40	905	585	-35.36%
Epivir 150 mg x 60	1 274 711	975 250	-23.49%
Total	2 741 081	2 125 076	***-22%***

Of all the products registered, *Epivir Oral solution 10 mg/ml – 240 ml, Trizivir 750 mg x 60* and *Retrovir 100 mg x 100* showed the biggest increases in volumes sold at tiered prices, with 133.94%, 57.20% and 38.97% respectively. Another product, *Ziagen 300 mg x 60,* showed a marginal increase, whereas the other five in the table – *Retrovir Oral solution 10 mg/ml – 200 ml*, *Retrovir 300 mg x 60, Combivir 300/150 mg x 60, Retrovir 250 mg x 40* and *Epivir 150 mg x 60* displayed relatively large decreases in sales volumes. Overall sales decreased by 22%. This

was expected and is primarily due to more customers purchasing ARVs from other producers and in particular from generic manufacturers. It is part of the producer's policy to grant voluntary licences to generic manufacturers in order to increase access. Over the last year GSK has granted voluntary licences to eight generic manufacturers and suppliers 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 2006 licensees supplied over 120 million tablets (2 million units) of their versions of Epivir and Combivir and GSK supplied 86 million tablets making a total of over 206 million tablets in 2006 compared with a total of 126 million in 2005. It should, therefore, be underlined that, overall, access to preferentially priced medicines has increased substantially.

The variations in volumes between individual products can also be attributed to fluctuation of stocks. Supply chain management is one of the main challenges facing developing countries trying to scale up their HIV programmes. Purchase of medicines is not the biggest issue, but it is widely recognised that the other two aspects of supply chain management – planning and delivery – are almost non-existent in some countries. Planning includes commodity selection, quality control, forecasting and financing. Delivery includes storage, decentralisation of distribution, effective use of the medicines and monitoring. Lack of proper forecasting at country level in particular can lead either to overstocking (some countries tend to order large quantities of products when they receive payments from donors) or to a shortage.

7.2 Overall trend since 2004

The 2004 report covered a maximum of 8.5 months (registration of products started in April 2004). The 2005 report and this report each cover a calendar year (from January to December). The table set out below therefore compares volumes on a monthly basis to give some indication of the volume trends per product registered under the Regulation since 2004.

	Year (monthly figures)				
Product	**2004 (8.5 months)**	**2005 (12 months)**	**2006 (12 months)**	**Diff. 2004/2006**	**Overall trend**
Trizivir 750 mg x 60	135	260	409	274	202.96%
Retrovir 100 mg x 100	6 734	7 926	11 015	4 281	63.57%
Epivir Oral solution 10 mg/ml 240 ml	22 129	14 473	33 857	11 728	53.00%
Retrovir Oral solution 10 mg/200 ml	62 689	30 495	9 984	-52 705	-84.07%
Retrovir 250 mg x 40	146	75	49	-97	-66.44%
Ziagen 300 mg x 60	3 522	2 827	3 350	-172	-4.88%
Retrovir 300 mg x 60	3 059	8 520	4 034	975	31.87%
Epivir 150 mg x 60	51 099	106 226	81 271	30 172	59.05%
Combivir 300/150 mg x 60	44 498	57 622	33 121	-11 377	-25.57%
Total	194 011	228 424	177 090	-16 921	-8.72%

Between 2004 and 2005 the volumes increased overall. However, in 2006 overall volumes decreased substantially and were even lower than in 2004. This change of trend is explained by the scheme for granting licences to producers of generic versions of the medicines, as explained in Section 7.1. Sales of products currently registered under the Regulation are therefore expected to continue to decrease and, considering that some of the licences granted have not yet been activated, producers of generic versions will continue to gain market share, essentially for the triple-dose combination (Retrovir, Epivir and Combivir) which will remain a leading option for first-line treatment. The producer expects volumes of Ziagen to hold steady or rise, as Ziagen is currently used in second-line treatment and demand for second-line products should increase. However, generic versions of Ziagen already exist. Trizivir should remain stable. The trend for the oral solutions of Epivir and Retrovir is more difficult to predict, as more and more children should be treated. However, oral solutions are not always easy to use and doctors and nurses sometimes prefer to administer crushed tablets instead.

8. CONCLUSIONS

8.1 Tiered pricing makes supply of discounted medicines sustainable. While the Commission regrets that no additional products were registered in 2006, it is very satisfactory 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 is aware that other producers are also selling 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 tiered-pricing schemes for developing countries,[12] and in

[12] See the 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);

some cases these prices are comparable with those of generics. While the Regulation covers both tiered-priced and donated products, the European Commission believes that tiered pricing is a useful way forward, for the following reasons:

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

- 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.

- By contrast, donations are not a sustainable solution. They are sometimes considered to be working well in disease eradication programmes and emergencies. But it cannot be sustainable for companies to give away products for free indefinitely 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 unsuitable products are supplied, even lead to damage to health.

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

8.2. Responsible prices for medicines

Council Regulation 953/2003 is part of a package of political measures adopted to secure affordable access to medicine in poor countries, in particular for HIV/AIDS, malaria and tuberculosis. These measures include the Decision[13] of the WTO General Council to allow compulsory licences on patented drugs for export purposes, the EU Regulation[14] to implement this WTO Decision at Community level, greater funding for research and development and various other initiatives.[15]

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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).

13 Amendment of the TRIPS Agreement, Decision of 6 December 2005 (WT/L/641 – 8 December 2005), currently under ratification by the European Parliament.

14 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 L 157, 9.6.2006.

15 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.

However, lower prices for medicines will not suffice to secure access. It is of the utmost importance that sufficient and continuous funding be made available for purchasing these drugs, that efforts be stepped up to strengthen local health systems and that further incentives be provided to ensure research and development of new medicines. Specific proposals for action by national and international stakeholders in this connection were highlighted in a report[16] released in April 2006 by an independent body – the Commission on Intellectual Property Rights, Innovation and Public Health (CIPIH) – at the request of the WHO. These and other proposals are being discussed currently at the WHO Inter Governmental Working Group on public health, innovation and intellectual property[17]. Working closely with EU Member States, the Commission is playing a constructive role in this Inter Governmental Working Group, in order to promote medicine availability, affordability and access[18].

16 http://www.who.int/intellectualproperty/en/.

17 http://www.who.int/phi/en/; http://www.who.int/gb/phi-igwg/index-phi-igwg-E.html

18 In April 2007, the Commission hosted a stakeholder workshop on this issue, co-chaired by the EU Presidency: http://ec.europa.eu/health/ph_international/documents/summary_report.pdf

ANNEX 1: VOLUMES OF MEDICINES SOLD IN 2006

EPIVIR Oral solution 10 mg/ml – 240 ml

Date of approval: 19 April 2004

Disease targeted: HIV infection

Active ingredient: lamivudine

Price offered (per unit): US$ 6.73

Highest OECD list price: US$ 85.09

Lowest OECD list price: US$ 34.53

Preferential/highest OECD list price: 7.91%

Preferential/lowest OECD list price: 19.49%

The oral solution is for paediatric use; the dose depends on the weight of the child. According to WHO treatment guidelines,[20] the recommended dose for a child weighing less than 60 kg is 4 mg/kg/dose twice daily. The 406 287 units reported therefore would equal the amount needed to treat 33 857 children weighing 10 kg for 12 months if used in a combination recommended by the WHO (see Annex 3).

According to information published by the WHO on the source and prices of active pharmaceutical ingredients (API) for ARVs available on the world market in 2006,[21] the selling price for lamivudine on the international market is between US$ 250 and US$ 480 per kg.

Sub-region	**Volume sold (units)[19] – 1 January 2006 to 31 December 2006**
Europe and Central Asia	36
East Asia and Pacific	3 408
West Africa	5 049
East Africa	127 531
Southern Africa	270 263
Total	406 287
per month	33 857

[19] In this and the subsequent tables "units" means the packages in which the products concerned are packed. For example, one "unit" of EPIVIR Oral solution 10 mg/ml – 240 ml is one bottle of 240 ml. One unit of EPIVIR 150 mg x 60 (see next table) is one package containing 60 tablets.

[20] http://www.who.int/hiv/pub/prev_care/en/arvrevision2003en.pdf.

[21] http://www.who.int/hiv/amds/sourcespricesAPI.pdf.

EPIVIR 150 mg x 60

Date of approval: 19 April 2004

Disease targeted: HIV infection

Active ingredient: lamivudine

Price offered (per unit): US$ 5.70

Highest OECD list price: US$ 476.45

Lowest OECD list price: US$ 128.66

Preferential/highest OECD list price: 1.20%

Preferential/lowest OECD list price: 4.43%

According to WHO treatment guidelines, the recommended dose of lamivudine is 150 mg twice daily or 300 mg once daily, which means that one "unit" would suffice for one patient for one month. On this basis the 975 250 units of Epivir 150 mg x 60 reported would equal the amount needed to treat an estimated 81 271 persons for 12 months if used in a combination recommended by the WHO (see Annex 3).

According to information published by the 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$ 250 and US$ 480 per kg.

Sub-region	**Volume sold (units) – 1 January 2006 to 31 December 2006**
Europe and Central Asia	13
East Asia and Pacific	5 400
West Africa	17 014
East Africa	308 763
Southern Africa	644 060
Total	975 250
Per month	81 271

COMBIVIR 300/150 mg x 60

Date of approval: 19 April 2004

Disease targeted: HIV infection

Active ingredient: lamivudine + zidovudine

Price offered (per unit): US$ 19.50

Highest OECD list price: US$ 931.31

Lowest OECD list price: US$ 264.54

Preferential/highest OECD list price: 2.09%

Preferential/lowest OECD list price: 7.37%

According to WHO treatment guidelines, the recommended dose of lamivudine is 150 mg twice daily or 300 mg once daily and the recommended dose of zidovudine is 300 mg twice daily. One "unit" of COMBIVIR, containing 60 tablets, would therefore suffice to treat one person for one month. On this basis, the 397 450 units reported would equal the amount needed to treat an estimated 33 121 infected persons for 12 months if used in a combination recommended by the WHO (see Annex 3).

According to the WHO, the selling prices on the international market are between US$ 250 and US$ 480 per kg for lamivudine and between US$ 360 and US$ 550 per kg for zidovudine.

Sub-region	**Volume sold (units) – 1 January 2006 to 31 December 2006**
Europe and Central Asia	211
East Asia and Pacific	1 300
Latin America and the Caribbean	186
West Africa	56 137
Central Africa	1 220
East Africa	155 234
Southern Africa	183 162
Total	397 450
Per month	33 121

RETROVIR 100 mg x 100

Date of approval: 19 April 2004

Disease targeted: HIV infection

Active ingredient: zidovudine

Price offered (per unit): US$ 15.77

Highest OECD list price: US$ 261.33

Lowest OECD list price: US$ 105.09

Preferential/highest OECD list price: 7.19%

Preferential/lowest OECD list price: 15%

According to WHO treatment guidelines, the recommended dose of zidovudine is 300 mg twice daily. The 100 mg capsules are available for dose variations and should not therefore be included in the calculation.

Sub-region	**Volume sold (units) – 1 January 2006 to 31 December 2006**
Latin America and the Caribbean	12
West Africa	7 584
East Africa	29 842
Southern Africa	94 738
Total	132 176
Per month	11 015

RETROVIR 300 mg x 60

Date of approval: 19 April 2004

Disease targeted: HIV infection

Active ingredient: zidovudine

Price offered (per unit): US$ 17.40

Highest OECD list price: US$ 342.12

Lowest OECD list price: US$ 184.16

Preferential/highest OECD list price: 5.08%

Preferential/lowest OECD list price: 9.45%

According to WHO treatment guidelines, the recommended dose of zidovudine is 300 mg (one tablet) twice daily. On this basis, the 48 410 units reported would equal the amount needed to treat an estimated 4 034 infected persons for 12 months if used in a combination recommended by the WHO (see Annex 3).

Sub-region	**Volume sold (units) – 1 January 2006 to 31 December 2006**
Europe and Central Asia	13
Latin America and the Caribbean	16
West Africa	3 560
East Africa	20 917
Southern Africa	23 904
Total	48 410
Per month	4 034

RETROVIR 250 mg x 40

Date of approval: 19 April 2004

Disease targeted: HIV infection

Active ingredient: zidovudine

Price offered (per unit): US$ 13.27

Highest OECD list price: US$ 263.17

Lowest OECD list price: US$ 101.27

Preferential/highest OECD list price: 5.047%

Preferential/lowest OECD list price: 13.10%

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

Sub-region	**Volume sold (units) – 1 January 2006 to 31 December 2006**
East Asia and Pacific	141
Southern Africa	444
Total	**585**
per month	**49**

TRIZIVIR 750 mg x 60

Date of approval: 19 April 2004

Disease targeted: HIV infection

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

Price offered (per unit): US$ 70.00

Highest OECD list price: US$ 1 141.68

Lowest OECD list price: US$ 499.05

Preferential/highest OECD list price: 6.13%

Preferential/lowest OECD list price: 14.03%

According to WHO treatment guidelines, the recommended doses are 300 mg twice daily for abacavir, 150 mg twice daily or 300 mg once daily for lamivudine and 300 mg twice daily for zidovudine. The normal prescription would therefore be two capsules of TRIZIVIR 750 mg per day. On this basis, the 4 903 units reported would equal the amount needed to treat an estimated 409 infected persons for 12 months. According to the WHO, the selling prices on the international market are between US$ 250 and US$ 480 per kg for lamivudine and between US$ 360 and US$ 550 per kg for zidovudine. For abacavir, the price range is between US$ 1 500 and US$ 2 900.

Sub-region	**Volumes sold (units) – 1 January 2006 to 31 December 2006**
Europe and Central Asia	300
West Africa	2 581
Central Africa	690
East Africa	307
Southern Africa	1 025
Total	**4 903**
Per month	**409**

ZIAGEN 300 mg x 60

Date of approval: 20 September 2004

Disease targeted: HIV infection

Active ingredient: abacavir sulphate

Price offered (per unit): US$ 52.29

Highest OECD list price: US$ 504.32

Lowest OECD list price: US$ 244.79

Preferential/highest OECD list price: 10.36%

Preferential/lowest OECD list price: 21.36%

According to WHO treatment guidelines, the recommended dose of abacavir is 300 mg (i.e. one capsule) twice daily. On this basis, the 40 208 units reported would therefore equal the amount needed to treat an estimated 3 351 persons for 12 months if used in accordance with WHO recommendations (see Annex 3).

According to the WHO, the selling price for abacavir on the international market is between US$ 1 500 and US$ 2 900.

Sub-region	**Volumes sold (units) – 1 January 2006 to 31 December 2006**
Europe and Central Asia	12
East Asia and Pacific	2 053
South Asia	518
Latin America and the Caribbean	1 521
West Africa	6 904
Central Africa	3 187
East Africa	10 026
Southern Africa	15 987
Total	40 208
per month	3 351

RETROVIR Oral solution 10 mg/ml – 200 ml

Date of approval: 20 September 2004

Disease targeted: HIV infection

Active ingredient: zidovudine

Price offered (per unit): US$ 7.10

Highest OECD list price: US$ 87.63

Lowest OECD list price: US$ 20.25

Preferential/highest OECD list price: 8.10%

Preferential/lowest OECD list price: 35.06%

The oral solution is for paediatric use; the quantity to be administered depends on the age of the child. According to WHO treatment guidelines, the recommended dose for a child of less than 4 weeks is 4 mg/kg/dose twice daily. The 119 807 units reported would therefore equal the amount needed to treat 9 .984 children weighing approximately 10 kg for 12 months if used in a combination recommended by the WHO (see Annex 3).

Sub-region	**Volume sold (units) – 1 January 2006 to 31 December 2006**
Europe and Central Asia	36
East Asia and Pacific	1 692
West Africa	9 198
East Africa	103 615
Southern Africa	5 266
Total	119 807
Per month	9 984

ANNEX 2: VOLUMES OF TIERED-PRICED PRODUCTS SOLD BY SUB-REGION BETWEEN 1 JANUARY 2006 AND 31 DECEMBER 2006

Sub-region	Product	Units
Europe and Central Asia	EPIVIR Oral solution	36
	EPIVIR 150 mg x 60	13
	COMBIVIR 300/150 mg x 60	211
	RETROVIR 300 mg x 60	13
	RETROVIR Oral solution	36
	TRIZIVIR 750 mg x 60	300
	ZIAGEN 300 mg x 60	12
East Asia and Pacific	EPIVIR Oral solution	3 408
	EPIVIR 150 mg x 60	5 400
	COMBIVIR 300/150 mg x 60	1 300
	RETROVIR 250 mg x40	141
	RETROVIR Oral solution	1 692
	ZIAGEN 300 mg x 60	2 053
South Asia	ZIAGEN 300 mg x 60	518
Latin America and the Caribbean	COMBIVIR 300/150 mg x 60	186
	RETROVIR 100 mg x 100	12
	RETROVIR 300 mg x 60	16
	ZIAGEN 300 mg x 60	1 521
West Africa	EPIVIR Oral solution	5 049
	EPIVIR 150 mg x 60	17 014
	COMBIVIR 300/150 mg x 60	56 137
	RETROVIR 100 mg x 100	7 584
	RETROVIR 300 mg x 60	3 560
	RETROVIR Oral solution	9 198
	TRIZIVIR 750 mg x 60	2 581
	ZIAGEN 300 mg x 60	6 904
Central Africa	COMBIVIR 300/150 mg x 60	1 220

	TRIZIVIR 750 mg x 60	690
	ZIAGEN 300 mg x 60	3 187
East Africa	EPIVIR Oral solution	127 531
	EPIVIR 150 mg x 60	308 763
	COMBIVIR 300/150 mg x 60	155 234
	RETROVIR 100 mg x 100	29 842
	RETROVIR 300 mg x 60	20 917
	RETROVIR Oral solution	92 683
	TRIZIVIR 750 mg x 60	307
	ZIAGEN 300 mg x 60	10 026
Southern Africa	EPIVIR Oral solution	270 263
	EPIVIR 150 mg x 60	644 060
	COMBIVIR 300/150 mg x 60	183 162
	RETROVIR 100 mg x 100	94 738
	RETROVIR 250 mg x 40	444
	RETROVIR 300 mg x 60	23 904
	RETROVIR Oral solution	16 198
	TRIZIVIR 750 mg x 60	1 025
	ZIAGEN 300 mg x 60	15 987

ANNEX 3: FIXED-DOSE ARV COMBINATIONS

The WHO encourages use of the following fixed-dose combinations:

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)