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Unit B.3 Intellectual Property & Public Procurement

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Evaluation of council regulation (EC) 953/2003 to avoid trade diversion into the European Union of certain key medicines

Executive Summary - Draft report for discussion at 15th of July workshop

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Executive Summary

Charles River Associates (CRA) has been commissioned by DG Trade of the European Commission to evaluate the council regulation (EC) 953/2003 to avoid trade diversion into the European Union of certain key medicines as part of the Commission's regulatory fitness and performance programme (REFIT). In line with the Commission's evaluation standards there are four points to be considered:

1. Effectiveness: To what extent did the Regulation achieve its goals?
2. Efficiency: Were the costs involved justified, given the achievements? This includes in particular an assessment of administrative burden for businesses, especially SMEs.
3. Coherence: To what extent is the Regulation coherent internally, with other EU policies, with Treaty objectives, and with the activities of other actors?
4. Relevance: To what extent do the (original) objectives (still) correspond to the EU needs? What is the role of a Regulation?

Based on these findings, CRA was also asked to provide recommendations on the continuing need for EU-level policy intervention in support of tiered pricing schemes; and on the most appropriate form that any such intervention should take and a clear conclusion on whether the existing regulatory framework should be maintained and if so, to outline how the functioning of the Regulation could be improved.

The report also seeks to identify some of the factors which must be taken into account in order to build a successful scheme; and seeks to identify examples of best practices in the design and implementation of existing tiered pricing schemes from either the public or private sector.

To undertake the assessment, CRA has undertaken an extensive literature review, assessed the impact of the Regulation on prices and volumes, and undertaken 34 interviews with companies with products eligible for registration under the Regulation, European Commission staff, national customs authorities, Non-Governmental Organisations (NGOs), international bodies and academics.

This draft report has been prepared for discussion at a public workshop on the 15th of July 2015. It will be revised following discussion at the workshop and any additional comments received.

Context of the Regulation's adoption

In the early 2000s, HIV/AIDS, tuberculosis and malaria together were responsible for approximately 6 million deaths a year.[1] There was an international consensus that something

[1] The Global Fund website - Fighting AIDS, Tuberculosis and Malaria, retrieved at http://www.theglobalfund.org/en/about/diseases/

had to be done about access to health care and more specifically access to medicines in developing countries.

In response to these challenges, a number of international initiatives were initiated. New international organisations were set up to improve access to HIV/AIDS, malaria, and tuberculosis medicines in developing countries, such as the Global Fund in 2002 (of which, the European Union is a significant financial contributor) and United States President's Emergency Plan for AIDS Relief (PEPFAR), in 2003, which set aside US$15 billion for HIV/AIDS prevention, care, and treatment programmes.

Given the international focus on improving access to medicines for HIV/AIDS, malaria and TB in the early 2000s by improving affordability in lower income countries, it was predicted that the volumes of products in these markets would increase significantly. For HIV/AIDS, in particular, there were many new innovative medicines that had been developed to address the disease, offering significant benefits to patients and healthcare systems.

As HIV/AIDS was (and remains) a disease affecting a significant patient population in high income countries, the same products were being marketed in high income markets at a much higher prices (reflecting both the value these delivered to patients and the need to reward progress and incentivise further R&D). There was therefore a tangible risk that trade diversion would increase and this could discourage the flow of medicines reaching the poorest developing countries at affordable prices. Indeed, there is evidence of a number of cases of trade diversion into the EU for HIV/AIDS medicines occurring prior to the introduction of the Regulation.

In the European Union, in February 2001, the Council adopted a Communication on "Accelerated Action targeted at major communicable diseases within the context of poverty reduction", creating a policy framework on the way the EC could play its part in the efforts to tackle the three major communicable diseases, which were severely restricting social and economic development in many Lower Middle Income (LMICs) and Low income Countries (LICs), namely: HIV/AIDS, malaria and TB.[2] One element of this communication was to find ways to make medicines more affordable through a comprehensive global approach. This provided the impetus for the introduction of regulation EC 953/200, which came into force on the 26th May 2003.

The Regulation's mechanism and application

Under the Regulation, companies can register pharmaceutical products which they are supplying at a 'heavily' discounted price[3] in beneficiary countries (defined in Annex II of the Regulation). Imports of these products into the EU are then prohibited.

The Regulation created a procedure designed to ensure that medicines for the treatment of HIV/AIDS, tuberculosis and malaria sold to the poorest developing countries at discounted

2 COMMUNICATION OF THE COMMISSION TO THE COUNCIL AND THE EUROPEAN PARLIAMENT - Accelerated action targeted at major communicable diseases within the context of poverty reduction, COM (2000) 585

3 Defined in Article 3 of the Regulation as a maximum 75% of the average ex-factory price in OECD countries, or the direct production cost plus 15%.

prices would be blocked from re-importation into the EU. It provided the customs authorities the legal title to suspend the release of, or detain, products if they are registered under the Regulation.

Manufacturers of tiered priced products must differentiate the appearance of tiered priced products to facilitate the task of customs authorities by affixing a permanent logo on any packaging of tiered priced products.

There are 76 potential beneficiary countries when the Regulation was adopted. These included 48 Least Developed Countries and 24 low-income countries with a GNP per capita of less than USD 765 and those countries where HIV/AIDS is particularly prevalent. This includes a small number of Lower middle income countries such as China and South Africa.

Effectiveness of the Regulation

To assess whether the Regulation met it objectives, we need to go back to the original goals as set out in the Regulation and by those involved in its creation. As stated in Regulation 953/2003, the objective was "*to encourage the pharmaceutical producers to make pharmaceutical products available at heavily reduced prices in significantly increased volumes by ensuring through this Regulation that these products remain on those markets*".[4] It was recognised this was adding an additional regulation to existing safeguards preventing trade diversion. Whilst legislative and regulatory instruments have been in place in the EU to prevent importation of pharmaceutical products in certain circumstances, it was also recognised that "*these instruments risk becoming insufficient where substantial volumes of heavily discounted pharmaceuticals are sold to the poorest developing country markets and the economic interest in trade diversion into high priced markets therefore may increase significantly*," [5] and that it was necessary to "*reinforce safeguards against diversion of low priced pharmaceuticals destined for poor markets and prevent price erosion in developed countries markets*".[6] The Regulation 953/2003 therefore served the purpose of preventing tiered priced[7] products from being imported into the Community".

One company (GSK) registered products under the Regulation. In terms of the volumes of products sold in Annex II countries, the volumes were initially high, reflecting the importance of GSK's HIV/AIDS medicines at the time. However, these volumes fell dramatically, as GSK adopted a strategy of voluntary licensing for the products registered under the Regulation (and

4 Council Regulation (EC) No 953/2003 of 26 May 2003 to avoid trade diversion into the European Union of certain key medicines - Official Journal of the European Union 3.6.2003, recital 7

5 Ibid, recital 6

6 Ibid recital 2

7 According to Regulation 953/2003, 'tiered priced product' means any pharmaceutical product used in the prevention, diagnosis and treatment of a disease referred to in Annex IV which is priced in accordance with one of the optional price calculations set out in Article 3, verified by the Commission or an independent auditor as provided for in Article 4 and entered in the list of tiered priced products set out in Annex I;

ultimately GSK's products lost patent protection). At the same time, other ARV treatments from other companies, which were not registered under the Regulation grew in importance.

Using international databases on HIV/AIDS medicine prices, we have compared the distribution of prices of products registered under the Regulation to those outside of the Regulation. We find no evidence that the Regulation resulted in lower prices, or improved affordability. The price in Annex II countries generally declined after 2004, but there were many factors changing in the environment and we conclude that there is no statistical significant difference between the tiered-price of products using the Regulation and those that do not use the Regulation.

However, we do find a significant positive impact on volumes where on average, the Regulation increased the volumes purchased of registered molecules by Annex II countries by 79% during this period. We therefore conclude that for the period 2004-2008, products registered under the Regulation had higher volume in Annex II countries.

It appears the risk of product diversion, anticipated in the Regulation, was mitigated in other ways:

- Companies used other approaches to mitigate the risk of product diversion such as different packaging and product reformulation, second brands and programmes to allow product traceability. The growing use of modern IT/Communication data bases made it increasingly possible for companies to trace relatively quickly cases of diversion and take appropriate action to avoid repetition. Indeed some companies had already developed these approaches prior to the Regulation.
- The development of international organisations such as the Global Fund, PEPFAR, UNAIDS have significantly increased the security of the supply chain thereby reducing the risk of diversion.

We find no evidence of products registered under the Regulation being seized by customs and other companies were able to mitigate the risk in other ways and preferred to follow this approach rather than use the Regulation.

In terms of direct impact on reducing the risk of product diversion, or the ultimate objective of lowering prices and raising access in the poorest developing countries, we find little impact of the Regulation. However, in terms of the wider benefits, many interviewees highlighted that the Regulation did provide less tangible but wider benefits 'signalling' the Commission's commitment to tiered pricing and in broad terms its opposition to exploiting the price differences through international arbitrage. The signal was described in a number of different ways:

- It was a signal that companies should be adopting tiered pricing
- It was a signal that lower prices in low income countries should not be used as a reference for the price to be paid for the same products in developed country markets as noted in Recital 5 of the Regulation
- The need for a wider discussion on the factors affecting access to medicines in developing markets

To test this, we have compared what happened before and after the introduction of the Regulation. Although clearly there have been other factors in play, there is no question that the affordability of HIV medicines and access to them improved significantly during this period.

In terms of differential or tiered pricing, many companies had developed programmes for their HIV/AIDS medicine by 2001/2, so it seems unlikely that the Regulation had a significant impact on the choice of companies to develop tiered pricing regime. Apart from GSK's registration of its HIV/AIDS medicines, all other companies chose not to register their products under the Regulation. Even so, many companies adopted a tiered pricing approach.

Other factors have also played a very significant role in improving access, including global programmes such as the Global Fund, PEPFAR, UNAIDS. These have dramatically enhanced the funding of HIV/AIDS and driven forward successful PPP initiatives in many countries. Additionally, HIV/AIDS was recognised as a public health issue by many governments and programs were implemented to control the epidemic. Some products have also lost patent protection meaning that generic companies, notably from India and China, have entered the world market, increasing competition and lowering prices even further.

In conclusion, although none of the products registered under the Regulation were imported into the Community it is difficult to attribute this solely to the Regulation. The Regulation did not succeed directly in encouraging producers to make pharmaceutical products available at heavily reduced prices in significantly increased volumes. However, based on the interviews, it appears that the Regulation may have contributed to an improvement in the dialogue between the diverse categories of stakeholders with an interest in how to improve access and led to a more cooperative approach. In reality, there has been a significant increase in access, which in association with improvement in diagnosis and care has reduced mortality significantly. Although it is very difficult to associate any of this directly to the Regulation, it likely made a small positive contribution to this agenda.

Efficiency of the Regulation

There were modest costs incurred in terms of the creating, administering and complying with the Regulation. The cost incurred by the European Commission in introducing and managing the operation of the scheme are small. They largely consisted of the sunk costs of introducing the Regulation. There were costs for an expert committee assessing GSK's application for registering products. There are costs associated with drawing up annual reports but these are not substantial.

Turning to the administrative costs on businesses in meeting the legal obligations of the regulation, Regulation 953/2003 is a voluntary scheme and as such, there is no obligation on pharmaceutical companies to implement these measures. We find that companies who decided not to use the Regulation did not face any administrative burden.

For companies who registered some of its products, our estimates suggest that the cost of complying with the Regulation are relatively small and are not prohibitive. The administrative costs consist of two different cost components: the administrative burden defined as the costs incurred in meeting the administrative measures introduced by the Regulation and the compliance costs which are changes in the business operations to take part in the scheme.

The administrative burden involves a staffing cost associated with the administration of the scheme when new products are registered and data is submitted regarding the volume and price of the products.

In terms of the compliance cost, the incremental cost of adding a logo on the pack and registering new package designs is small in contrast with the costs of other anti-diversion strategies.

According to GSK, the Regulation did serve to reduce the need to use other anti-diversion processes for some products in some areas (but it is not possible to estimate this cost offset) but many other tools are being used by GSK alongside the Regulation. Given that GSK continues to register its products under the Regulation and intends to register additional products, the administrative costs appear to be offset by the benefits.

Customs authorities have not incurred significant costs as no additional actions were required on top of their routine control activities.

Although the achievements were limited, the costs involved were also limited. Therefore one can conclude that the costs involved were justified.

Coherence of the Regulation

To test the coherence of the Regulation with other initiatives, we examined policies and initiatives of the Commission which may have some links to key aspects of the Regulation 953/2003. The goal of the Regulation to encourage tiered pricing by reducing the risk of product diversion appears entirely consistent with the European Commission's trade policy. In terms of EU legislation, the trade mark legislation and legislation on medicinal products for human use appears to have the largest implications for Regulation 953/2003.

The enforcement of trade marks provides tools to address potential infringement associated with parallel trade from outside of the EU. This reinforces the objectives of and is entirely coherent with the Regulation 953/2003.

The legislation on medicinal products for human use ensures control is exercised over the entire chain of distribution of medicinal products, from their manufacture or import into the Community through to supply to the public. These requirements also facilitate the withdrawal of defective products from the market and allow more effective efforts against counterfeit products. Given the objectives on strengthening the detection of counterfeited products, these will eventually serve to reinforce the vigilance mechanism at customs which is entirely coherent with the Regulation 953/2003.

Turning to development policies, the EU has played a leading role in helping developing countries access medicines particularly through the support of international organisations such as Global Fund. We find these are entirely coherent with the objectives of Regulation 953/2003 and are in fact highly complementary.

In conclusion, we find that the Regulation is coherent with other EU policies.

Relevance of the Regulation

The Regulation aimed to encourage greater access to medicines in the 'poorest developing countries' by encouraging companies to lower the price of their medicines to Annex II countries and increase volume, by reducing the risk of trade diversion. To test the relevance of the Regulation, we need to look at the extent to which access to medicines remains a significant challenge, what contribution tiered pricing can make, if there a is role for policy intervention at EU level in support of tiered pricing and if so, if a Regulation is the most appropriate instrument for intervention and if there is a role for a Regulation to prevent the import of tiered priced products into the EU. We find that:

- Access to medicines in HIV/AIDS has increased rapidly in low- and middle-income countries since the introduction of the Regulation, from just 400,000 in 2003 to 11.7 million by the end of 2013.[8] There has been an improvement in access for malaria and TB but this relates primarily to off-patent medicines (as there has not been the same success in developing new innovative medicines). There has been a major improvement in access for TB as the MDG goal to halt and reverse TB has been achieved by all WHO regions and most of the high burden countries. However, innovation has resulted in new TB products introducing new access challenges. For all three diseases, access has improved but there continues to be patients without access to medicines.
- Most companies with HIV/AIDS medicines are using tiered pricing to address affordability of their medicines without registering their product under the Regulation. Some HIV/AIDS products are losing patent protection reducing the value of tiered pricing. Companies are using tiered pricing for TB and for malaria medicines without registering products under the Regulation.
- In terms of product diversion, the risk varies considerably depending on the medicines. For HIV/AIDS medicines the risk in 2003 was clear. The risk of product diversion for malaria and TB products was smaller from the outset because malaria is largely a disease affecting low income countries and middle income countries and there is therefore not a substantial market in high income countries (indeed, some products do not have a European marketing authorisation) and therefore the risk of product diversion was small. For TB most products were already off-patent and trade diversion was not a particular concern for the few innovative products as the market for TB in developed countries is not sufficient large to encourage diversion. Given changes in the market environment, the risk of product diversion is smaller today. International agencies or national programmes are actively involved in the purchase of medicines in all of the diseases covered by the Regulation, significantly limiting the risk of product diversion. Companies have other mechanisms to mitigate the risk of product diversion that they have used effectively over the last ten years. The Community code on

8 World Health Organisation (2013) Global Health Observatory (GHO) data, accessible at: http://www.who.int/gho/hiv/epidemic_response/ART_text/en/

medicinal products introduced measures to protect the supply chain against falsified medicines, notably measures introduced to uniquely identify products in the supply chain, which will reduce the risk of product diversion even more. It is also notable that although the one company that uses the Regulation intends to register future products under the Regulation, the potential for other companies to register products under the Regulation appears small. No other companies expressed an intention to register products under the Regulation.

- At the same time, companies have adopted other types of access programmes that have reduced prices and improved access to the poorest developing countries including voluntary licensing and non-assertion of intellectual property rights. And other factors have also played a very significant role in improving access, including global programmes such as the Global Fund, PEPFAR, and UNAIDS. These have fundamentally changed the funding of HIV/AIDS and improved access. Additionally, HIV/AIDS was recognised as a public health issue by many governments and programs were implemented to control the epidemic. Some products have also lost patent protection meaning that generic providers have entered the market, increasing competition and lowering prices even further. Other approaches to improve access to innovative medicines, including the development of the Medicines Patent Pool have contributed to the improved access to medicines. However, it is important to note that each of these has its limitations and hence, we conclude these are complements to the use of tiered pricing. These alternative mechanisms reduce the relevance of the Regulation (but do not suggest tiered pricing is not an important tool for improving affordability and access).

In conclusion, the objective to encourage greater access to medicines in the poorest developing countries remains relevant. There clearly remains the need to improve access to medicines in HIV/AIDS, TB and malaria. However, we do not find that the Regulation's role in reducing the risk of trade diversion is relevant today.

Recommendations on the future of the Regulation

Using the Commission's evaluation structure, we have examined the Regulation under four different dimensions (i.e. Effectiveness, Efficiency, Coherence, Relevance), we do not find a continuing need for the Regulation as it currently is stands (focusing on product diversion for HIV, malaria and TB). However, there are a number of considerations that need to be taken into account to determine the merits of maintaining the Regulation versus removing the Regulation.

- Given the Regulation does not impose any unjustified costs, it is possible that removing the regulation would be more burdensome then maintaining the current scheme in place.
- The Regulation was seen as a signal that companies should be adopting tiered pricing and the role of tiered pricing. Removing the Regulation could be seen as the Commission retracting its support for the concept of tiered pricing.

- It could provide a safety net or backstop, improving confidence of manufacturers. There is some evidence that this was a valid argument in 2003 but we find little evidence to support this today.

We also explore the case for modifying the regulation. We conclude that given the nature of Regulation 953/2003 as a trade mechanism and the restriction outlined in the recitals which limits the instruments to preventing trade diversion as well as the scope to communicable diseases, there is little scope in the current context for improving the effectiveness of the regulation by simply modifying it.

Stakeholders raised several points in the interviews regarding the need for EU-level policy intervention in support of tiered pricing schemes which extend beyond the current Regulation, as well as the need to overcome barriers to tiered pricing and the different forms this could take. These are beyond the scope of the assessment and these suggestions have therefore been included in Annex to inform future discussions.