Policies to Combat Counterfeit Medicines

Contribution to Impact Assessment

Europe Economics
Chancery House
53-64 Chancery Lane
London WC2A 1QU
Tel: (+44) (0) 20 7831 4717
Fax: (+44) (0) 20 7831 4515
www.europe-economics.com

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1 INTRODUCTION

1.1 Scope of the report

1.1.1 This report is a contribution by Europe Economics to an Impact Assessment by DG Enterprise and Industry of policy options to combat the risk of counterfeit medicines. These options were set out by the European Commission in its consultation paper of 11 March 2008. Europe Economics' research for the impact assessment was substantially completed in May, with subsequent 'stock taking' of some related issues in June.

1.1.2 As instructed by DG Enterprise, the policy proposals were considered mainly as a package rather than as alternatives between which choices would have to be made. Consideration was given to the possible initial impact cost of the proposed package to possible benefits, and to the overall impacts.

1.1.3 Some comments are made on ways in which the package might be made most cost-effective. However the work reported here did not extend to the refinement of the package of possible policies or to the assessment of a modified package such as was subsequently proposed by DG Enterprise.

1.1.4 The main estimates are presented in this report, with more detailed explanations of sources and estimation methods and four 'stock-taking' briefs in Annexes.

1.2 Disclaimer

1.2.1 Every effort has been made to provide the best estimates possible of the likely effects of the policies under consideration. However, this is a difficult area to research and all estimates are subject to considerable uncertainties. Estimates of the benefits and of downstream impacts are by their nature subject to more uncertainty than costings.

2 PROBLEM DEFINITION

2.1 The problem

2.1.1 A consultation paper published by the European Commission on 11 March 2008 stated that in the last few years counterfeit medicines have become an increasing threat to public health.[1] Greatly increased numbers of counterfeits have been intercepted by Customs and Excise authorities, and there are reports from some medicines regulatory authorities that counterfeit medicines are being found among products used to treat life-threatening conditions. International organisations are giving increased priority to the problem.

2.1.2 The World Health Organization (WHO) estimates that less than one per cent of the drugs on the market in the developed world are counterfeit. But the scale of the problem is hard to estimate for several clear reasons: it would be understandable if pharmaceutical companies were reluctant to make public their findings, for fear of damaging the reputation of their products; it is difficult for the consumer to detect a counterfeit product; when medicines fail to work as hoped it may be hard for doctors to discover why; and the problem has not had a high police priority.

2.1.3 Counterfeit medicines came to Europe's attention as a significant issue in 1998. Since then the number of cases reported each year has risen substantially.[2] As of 11 March 2008, the UK MHRA (Medicines and Health products Regulatory Authority) has reported 14 incidents of counterfeit medicines entering the supply chain. In nine of these, counterfeit medicines reached the patient and needed to be recalled, while in the other five, the counterfeit medicines were intercepted at the wholesaler.

2.1.4 In 2007, the EU reported that 4,081,056 medical products were confiscated by customs officials at borders. This is a 56 per cent increase from the 2006 border seizures, which totaled 2,711,410 medical items. A majority of these products were in transit through EU ports and airports to developing country markets.

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1 "Public consultation in preparation of a legal proposal to combat counterfeit medicines for human use." 11 Mar. 2008. EUROPEAN COMMISSION. 27 Mar. 2008 <http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_03/consult_counterfeit_20080307.pdf>.

2 Harper, Jonathan, Julian Morris, Graham Satchwell, Philip Stevens, David Taylor, and Michael Tremblay. "Coincidence or Crisis? Prescription Medicine Counterfeiting." Ed. Peter J. Pitts. 19 June 2006. The Stockholm Network. 27 Mar. 2008 <http://www.stockholm-network.org/downloads/publications/d41d8cd9-Coincidence%20or%20Crisis.pdf>.

2.1.5 Counterfeiting is not only growing in volume, it is also targeting more important medicines. Until recently the most common targets in the developed countries were those that treat erectile dysfunction, facilitate weight loss, lower cholesterol, and fight aging.[3] Some antibiotics and antivirals were also discovered to be counterfeits. But as the scale of counterfeiting grows, so does the fear that counterfeit drugs are being substituted for those which are prescribed to treat serious ailments such as cancer, heart disease, and psychiatric illnesses. In 2007 there were indications that counterfeit psychiatric and heart disease drugs did reach the supply chains in Europe.[4] This new trend of counterfeiting life-saving drugs increases the potential human loss caused by this problem. In the UK in 2005, an anti-psychotic medication for the treatment of schizophrenia and acute bipolar mania, Zyprexa, had to be withdrawn; the bogus tablets contained only 60 per cent active ingredient. There were two alerts concerning 75 mg tablets of Plavix, an anti-platelet drug that is administered after heart attacks or stroke.

2.2 The underlying causes

2.2.1 It is believed by some experts in this field that the risk-reward ratio for supplying counterfeit medicines has become extremely attractive, perhaps offering criminals even higher potential rewards than supply of other illegal substances. The profit margins could indeed be huge; for illustration, a legitimate manufacturer of a successful patented medicine might incur production costs of about five per cent of its selling price; the counterfeiter would not spend nearly so much in producing the imitation (which might contain no, or only trace amounts of, active ingredient). The supply chain is often complex and obscure. Moreover the chances of detection and conviction are thought to be less in counterfeit medicines than in other illegal substances, and so are the penalties.

2.2.2 The increasing use of the internet has made it easier for criminals to act on a large scale with small risks of detection. Those purchasing medicines over the internet include pharmacists, hospitals and wholesalers, individuals seeking legitimate supplies without the trouble of obtaining repeat prescriptions, and even more reckless people seeking a bargain price for non-prescription (and other) drugs. Many of those trading in medicines over the internet are behaving legally, while others may have criminal intent.

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[3] Harper, Jonathan, Julian Morris, Graham Satchwell, Philip Stevens, David Taylor, and Michael Tremblay. "Coincidence or Crisis? Prescription Medicine Counterfeiting." Ed. Peter J. Pitts. 19 June 2006. The Stockholm Network. 27 Mar. 2008 <http://www.stockholm-network.org/downloads/publications/d41d8cd9-Coincidence%20or%20Crisis.pdf>.

[4] "Public consultation in preparation of a legal proposal to combat counterfeit medicines for human use." 11 Mar. 2008. EUROPEAN COMMISSION. 27 Mar. 2008 <http://ec.europa.eu/enterprise/pharmaceuticals/pharmacos/docs/doc2008/2008_03/consult_counterfeit_20080307.pdf>.

2.2.3 A third factor is the increasing globalisation of production of medicines (as of many other products). Manufacturers based in the industrialised countries have increasingly established manufacturing plants in parts of the world where production costs are much lower; and as a consequence technical manufacturing and other skills have been transferred. This is in general an excellent development for the world economy, but it has had the side effect of increasing the number of people able to produce counterfeit versions of legitimate products; sometimes (it is said) using the same facilities as have been established and are in use for legitimate production. It is thought that much of the production of counterfeits may be in China, India and other parts of Asia, rather than in the EU or other developed economies (although of course this is not known for sure).

2.2.4 In this context, the European Commission's March 2008 consultation paper identifies potential weaknesses in present EU legislation and its enforcement. These include whether brokers and business-to-business platforms dealing in pharmaceuticals are covered by the legislation, general lack of transparency in the supply chain and possible poor standards, packs being opened for repackaging and changed for re-labelling purposes, difficulties in targeted recalls, legal uncertainty and differing practices between Member States regarding imports for the purpose of export, and active substances that may be manufactured in unknown locations and to low standards.

2.3 Those affected

2.3.1 Those primarily affected are patients and healthcare service providers.

2.3.2 For the purpose of the policy options considered in this Impact Assessment, individuals purchasing over the internet for their own use are not taken into account.

2.4 Prospects on unchanged policies

2.4.1 It is impossible to be certain how the problem would evolve under a continuation of present policies, but there is a consensus among those who have been studying the issues in many countries that the risk of a serious escalation cannot be ignored. For the purpose of this report, three possible scenarios have been assumed on how the incidence of counterfeit medicines within the EU might evolve over the next 10 years.

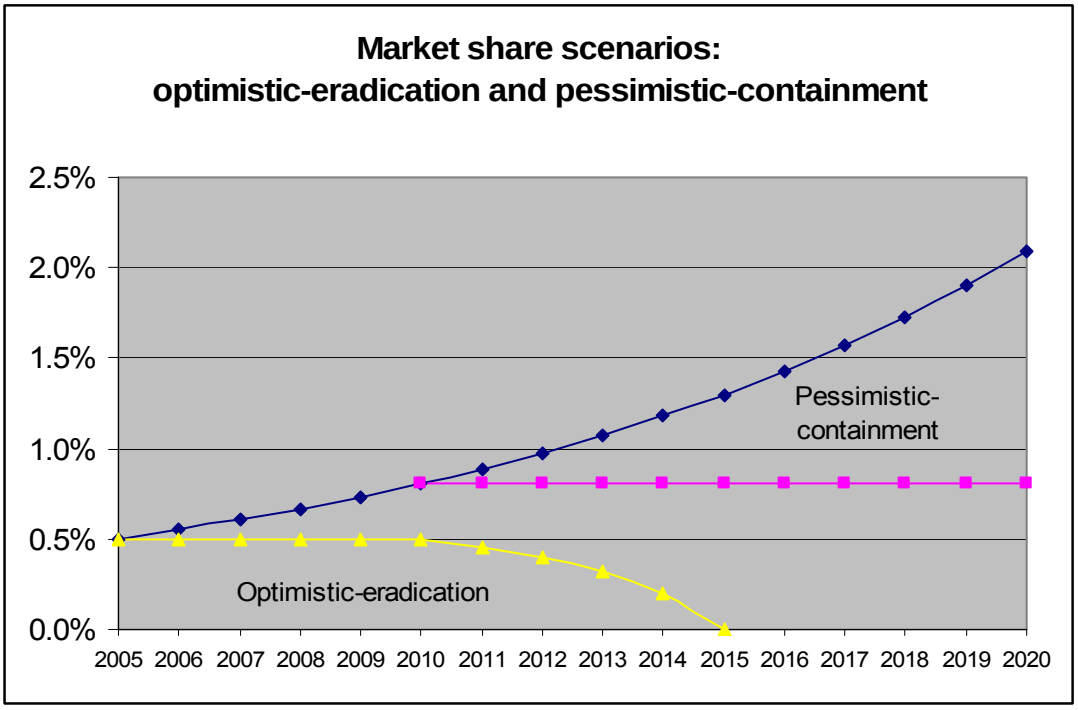
2.4.2 The magnitude of the benefits that could be credibly attributed to the proposed counter-measures depend on the assumed counterfactual – the extent to which counterfeit medicines are *already* penetrating the EU market, and the rate at which this would grow, in a business-as-usual scenario. Two such cases are illustrated, assuming that the policies come into force in 2011:

(a) An "optimistic" base case: the EU market share of counterfeit medicines was *one-half per cent* in 2005 (consistent with the WHO estimate of "less than one per cent for developed countries), and would remain at that level;

(b) A "pessimistic" base case: the EU market share of counterfeit medicines was one-half per cent in 2005, and is growing by 10 per cent a year.[5]

2.4.3 In the "optimistic" case, which implies that there are many more counterfeits in the EU legitimate supply chain than have been identified as such, it would be a realistic target to eradicate counterfeit medicines from the legitimate supply chain by 2015. In the "pessimistic" base case, it would be more realistic to consider containment at 2011 levels. These two cases are illustrated below, as the "optimistic-eradication" and "pessimistic-containment" scenarios respectively.

Chart 2.1: Market Share Scenarios



2.4.4 The cumulative policy impact in the two scenarios over the ten-year period 2011-2020 would be equivalent to respectively 5.3 per cent and 3.1 per cent of the 2011 EU market for medicines.

2.5 Does the EU have the right to act?

2.5.1 There is in general no question about this; some at least of the measures needed to limit the risks of receiving counterfeit medicines would require action in EU legislation; others will involve international co-operation to which the EU would be able to contribute, and

[5] Far more optimistic or pessimistic scenarios are easily imagined.

others will involve action by the EU Member States, in which the Commission would be able to assist.

2.5.2 Analysis of the legal basis and of the issue of subsidiarity was made by the Commission services and not considered here.

3 OBJECTIVES

3.1 The general policy objective

3.1.1 The 11 March consultation paper stated that the general objective of the European Commission is to assess various policy options to prevent the counterfeiting of medicinal products in the EU. As part of this, it is considering key ideas for amending the regulatory framework for medicinal products.[6]

3.2 The specific policy objectives

3.2.1 The specific policy objectives set out for the EU by DG Enterprise and Industry are to:

(a) prevent manufacturing and distribution of counterfeit active substances;

(b) prevent manufacturing of counterfeit medicines;

(c) prevent importation of counterfeit medicines;

(d) protect the legal distribution chain against counterfeit medicines;

(e) prevent the establishment of illegal distribution chains;

(f) contribute to the international fight against counterfeit medicines.

3.2.2 The policies being proposed to achieve these objectives are put forward as a coherent whole rather than as alternatives, although it is understood that some significant fine-tuning of the individual policies may be made.

[6] 11 March consultation paper from DG Enterprise and Industry, paragraph 1. The terms 'medicines' and 'medicinal products' are used to mean the same.

4 POLICY OPTIONS

4.1.1 DG Enterprise and Industry has identified three broad areas (or 'pillars') in which it believes that improvements to the regulatory framework could make a significant contribution to protecting against counterfeit medicinal products being supplied through the legal supply chain:

(a) More effective regulatory requirements for manufacture, placing on the market of medicinal products, and inspections.

(b) Tighter regulation of the import/export/transit (transhipment) of medicinal products.

(c) Tighter requirements for manufacture, placing on the market of active substances and inspections.

4.2 More effective regulatory requirements for manufacture, placing on the market of medicinal products, and inspections

4.2.1 The March consultation paper proposed six policies for this purpose:

(a) Subject all actors in the distribution chain to pharmaceutical legislation (Reference 4.1.1 in the consultation paper).

(b) Tighten rules on inspections (Reference 4.1.2).

(c) Improve product integrity through a unique seal from the manufacturer to the retailer or wholesaler, using a risk-based approach, supported by a ban on repackaging (Reference 4.1.3).

(d) Centrally accessible record to facilitate traceability of batches throughout the distribution chain (Reference 4.1.4).

(e) Mass serialisation for pack-tracing and authenticity checks on a case - by - case basis (Reference 4.1.5).

(f) Increasing transparency concerning authorised wholesalers through a Community database (Reference 4.1.6).

4.3 Tighter regulation of the import/export/transit (transhipment) of medicinal products

4.3.1 Two policies are to be assessed in this category:

(a) Prohibit the import of medicinal products in the EU territory not fulfilling EU requirements (Reference 4.2.1). This option is not discussed in the Consultation paper but it was included in the brief for the Impact Assessment.

(b) Ensure that imported medicinal products intended for export are subject to the rules for other imports of medicinal products (Reference 4.2.2).

4.4 Tighter requirements for manufacture, placing on the market of active substances and requirements for inspections

4.4.1 Three policies are proposed by DG Enterprise for this purpose:

(a) Requirement of a mandatory notification procedure for manufacturers/ importers of active substances (Reference 4.3.1).

(b) Enhancing audit and enforceability of GMP (Reference 4.3.2).

(c) Enhancing GMP inspections (Reference 4.3.3).

4.4.2 Several of these policies have sub-options. There are thus a large number of proposed policies whose combined likely costs and benefits are to be assessed.

5 ANALYSIS OF IMPACTS

5.1 The counterfactual

5.1.1 In assessing the impacts of proposed policies comparison is made with the situation to be expected under a continuation of present policies, so that the estimated effects are those that would result from the proposed new EU policies; comparison is with this counterfactual and not with the present situation. Under present policies national Customs and Excise authorities, the police, national medicines regulatory authorities and international agencies will continue to develop their own strategies to address the problem, as presumably will leading pharmaceutical companies. The effects of such activities are treated as part of a continuation of present policies, which is defined as Option 1 for the purposes of the Impact Assessment.

5.1.2 The extent of the threat from counterfeit medicines under a continuation of present policies is of course uncertain, as explained earlier (in Section 2, e.g. Chart 2.1).

5.2 More effective regulatory requirements for manufacture, placing on the market of medicinal products and inspections[7]

Subject all actors in the distribution chain to pharmaceutical legislation (Reference 4.1.1 in the Consultation paper)[8]

Policy 4.1.1 (a), Good Distribution Practice (GDP) licensing and inspection of brokers and traders including business to business platforms

5.2.1 This policy has been proposed due to the great uncertainty regarding parties in the wholesale distribution chain that do not necessarily handle products. This very uncertainty means that the effects of this policy option are difficult to determine, both in terms of the number of firms that will be affected and whether any businesses would be discouraged from their activities - whether legitimate or illegitimate - as a result of the (relatively small) cost impact.

5.2.2 The cost estimates presented here are based on the fees for regulators and industry opinion on the internal costs associated with inspections. One-off and annual costs are

[7] Consultation paper section 4.1.

[8] In this section, there are frequently several sources for a single cost category. Annex 1 describes in detail the procedure by which final estimates for each cost category are derived and provides greater information on the sources of the information used to formulate these estimates.
Further, the calculations of many one-off and annual costs are quite involved. The equations used for these calculations are provided in Annex 1.

calculated as well as the net present value (NPV) of the policy option over a time horizon of ten years.[9]

5.2.3 Before receiving authorisation, firms would need to be inspected. The one-off costs of this policy option therefore include the initial cost of all brokers, traders and business-to-business platform providers being inspected, including the administrative costs for business associated both with the application and inspection. Administrative costs are calculated as per the standard administrative cost model (SACM) specified in the EC Impact Assessment Guidelines. It is assumed that the individual undertaking administrative duties earns the average EU wage in industry for the EU 27. This is the appropriate basis for this approximation, since although wages in the pharmaceutical industry are higher for those with special skills, most of the additional work of form-filling scanning batches etc is likely to be carried out by workers able to command only the average industry and services wage..

5.2.4 The ongoing annual cost of this proposed policy is calculated by multiplying inspection costs (fees plus administration costs) by the population of firms and dividing this by the frequency of inspection before adding the on-going cost of registration of new firms to account for entry and exit. The estimates assume that once registered, a broker is not inspected during the first year of his registration and thereafter one-third of brokers are inspected each year. Fuller details are given in the Annex.

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[9] The net present value of a stream of expenditure accounts for the fact that, in an investment decision, expenditure that occurs several years into the future should be considered less important than an equivalent volume of expenditure that occurs today. In general, the expression for calculating NPV is:

$$NPV=C_1+ \sum^{T}_{(t=2)} (C_t /(1+r)^t)$$

where C_1 is the sum of the one-off cost and annual running cost for year 1 of the policy, T is the time horizon, C_t is the cost in year t and r is the discount rate.

In this case, net present values for a ten year horizon are calculated. It is assumed that one-off costs are incurred upon implementation and that annual costs are incurred both in the year of implementation and in each future year during the ten-year horizon. In common with the European Commission Impact Assessment Guidelines, Annex 12, a discount rate of 4 per cent is used.

Therefore, the expression used in our NPV calculations is:

$$NPV=C_1+ \sum^{10}_{(t=2)} (C_t /(1+0.04)^t)$$

Table 5.1: Estimated cost of policy 4.1.1(a) (€, 2007 prices)

COST CATEGORY	Value	Source(s)
Number of currently unlicensed finished products brokers/traders etc. in EU	1,000	EC, MHRA[10]
Proportion of new entrants per year	20%	Industry source
Administration hours for firm submitting wholesaler application (one-off cost)	4.00	Europe Economics estimate
GDP inspection fees for these (non-complex) firms (3/4 of day)	€ 1,976	MHRA
Frequency of GDP inspection (current) (years between)	-	Regulators
Frequency of GDP inspection (required) (years between)	3	Europe Economics assumption
Administration hours for firm per inspection (2 people, 3/4 day)	11.25	GIRP, EMEA, Europe Economics estimate
Hourly wage including overheads	€ 23.45	Eurostat
POLICY COST ESTIMATES		
Administrative cost (one-off)	€ 357,600	
Administrative cost (annual)	€ 159,500	
One- off cost total	**€ 2,333,000**	
Annual cost total	**€ 1,213,000**	
Net present value	**€ 12,566,000**	

For detail of sources and calculations please refer to Annex.

5.2.5 If a firm supplies counterfeits, it should not be too difficult for them to apply for a wholesale authorisation and to be inspected and authorised. Most EU counterfeit suppliers that have been caught in the past possessed GDP licenses. In order to make a contribution to policies to combat counterfeits any future authorisation/inspection scheme would need specifically to address the risk of counterfeit medicines and possible company strategies to avoid detection. Greater transparency concerning legitimate suppliers might also assist the police in investigations into dubious transactions.

5.2.6 The costs of this policy proposal would, however, fall largely on legitimate businesses.

[10] The UK Medicines and Healthcare Regulatory Authority

Policy 4.1.1(b), Mandatory Good Manufacturing Practice (GMP) audit of contract manufacturers and mandatory (when suspicion of non-compliance) GDP audit of suppliers

5.2.7 The cost of this policy would depend significantly on the type of implementation, and in particular on whether each purchaser had to carry out its own audit or was allowed to rely on an audit performed by an independent third party the cost of which could be shared with other purchasers.

5.2.8 A single contract manufacturer could have contracts with (be hired by) 100 other different firms so that third party recognition of GMP audits would imply costs substantially below those if third party audits were not accepted. However, broad third party acceptance of audits would approximately equate to the current inspection regime. It was established that some industry groups are planning co-ordination that would reduce the costs of auditing all suppliers by 75 per cent.

5.2.9 The sources for the estimates of GMP audit cost are mainly manufacturer organisations including European Self-Medication Industry (AESGP) and European Generic Medicines Association (EGA), whilst for GDP audit cost sources are wholesaler organisations such as the European Association of Euro-Pharmaceutical Companies (EAEPC) and the European Association of Pharmaceutical Wholesalers (GIRP), as well as regulators.

5.2.10 This policy imposes additional costs only on those firms that are not currently audited to the required standard of at least once in every three years. Annual GMP audit costs were calculated for a scenario in which firms are audited at least once every three years and for a second scenario in which the firms are audited at least once every five years (the assumed current frequency of audits for those not audited at least every three years). Subtracting the latter from the former gives the annual incremental cost of this policy.

5.2.11 A similar methodology is used for the calculation of GDP audit costs, but a different rate of inspection is assumed to be current practice.

Table 5.2: Estimated cost of 4.1.1(b)

Mandatory GMP audit of contract manufacturers		
Cost category	**Value**	**Source(s)**
Total number of audits of contract manufacturers supplying the EU if third-party audits are not accepted	500,000	AESGP, EAEPC, EGA, EMEA
Number of sites of contract manufacturers supplying to the EU (including non-EU sites)	10,000	EAEPC, EFPIA, EGA, EMEA
Total third-country (i.e. non-EU) audits of contract manufacturers if third-party audits are not accepted	300,000	AESGP, EGA
Number of sites of contract manufacturers supplying to the EU based outside EU	6,000	EAEPC, EFPIA firm, EGA
Cost of travel to these non-EU sites, expenses etc.	€ 30,000	EGA, EMEA, German inspector for Nordrhein-Westfalen
Proportion not being adequately audited (every 3 years)	20%	AESGP, Audit firm EAEPC, EGA, EMEA
Target frequency of audit (years between audit)	3	Europe Economics assumption
Current frequency of audit of those below target (years between audit)	5	EMEA
Cost of audit firm carrying out audit	€ 8,500	Audit firms, AESGP, EAEPC, EGA
Cost of manufacturer carrying out the audit themselves	€ 12,500	AESGP, EFPIA, EGA
Administration hours (2 people, 2 days)	30.00	Europe Economics assumption
Wage	€ 23.45	Eurostat
POLICY COST ESTIMATES		
Annual administrative cost (assumes policy would accept third-party audits)	€ 0.19m	
Annual administrative cost (do not accept third-party audits)	€ 9.38m	
Annual cost (accept third-party audits, conducted by audit firm)	**€ 26.45m**	
Annual cost (accept third-party audits, conducted by manufacturer)	**€ 27.52m**	
Annual cost (do not accept third-party audits)	**€ 1,376.05m**	
Net present value (accept third-party audits, conducted by audit firm)	**€ 223.15m**	
Net present value (accept third-party audits, conducted by manufacturer)	**€ 232.15m**	
Net present value (do not accept third-party audits)	**€ 11,607.41m**	

Table 5.2 Estimated cost of 4.1.1(b) (cont'd)

Mandatory GDP finished product supplier audit (in case of suspicion)		
Cost category	**Value**	**Source(s)**
Total number of supplier audits (independent audits)	700,000	EAEPC, EMEA,
Total number of supplier audits (if third party audits are accepted)	7,000	EAEPC, EMEA
Target frequency of audit (years between audit)	3	EE assumption
Proportion not being adequately audited (independent)	95%	Industry groups
Proportion not being adequately audited (joint)	90%	Industry groups
Current frequency of audit of these firms	-	EE assumption
Cost of audit firm conducting audit	€ 4,000	AESGP, Audit firms, EAEPC, EGA
Costs of carrying out the audit themselves	€ 6,000	AESGP, EFPIA, EGA
Hours required for administration (2 people, 1 day)	15.00	EE estimate
Wage	€ 23.45	Eurostat
POLICY COST ESTIMATES		
Annual administrative cost (accept third-party audits)	€ 0.74m	
Annual administrative cost (do not accept third-party audits)	€ 77.97m	
Annual costs total (accept third-party audits, conducted by audit firm)	**€ 9.14m**	
Annual costs total (accept third-party audits, conducted by manufacturer)	**€ 13.34m**	
Annual costs total (do not accept third-party audits)	**€ 1,407.97m**	
Net present value (accept third-party audits, conducted by audit firm)	**€ 77.09m**	
Net present value (accept third-party audits, conducted by manufacturer)	**€ 112.52m**	
Net present value (do not accept third-party audits)	**€ 11,876.70m**	

5.2.12 Firms consulted in the course of the Impact Assessment reported that they had not found counterfeits on any audits of their contract manufacturers or suppliers. Firms will normally inform their contract manufacturers and suppliers of their intention to conduct an audit and thus the contract manufacturer would have time to prepare and remove any evidence of

trade in counterfeits. No firm has mentioned auditing at night (when sites can start producing counterfeits after the end of the normal shift). Firms could also choose to make surprise visits and if they were not given adequate access they might interpret this as a reason for concern.

5.2.13 The main benefit of this policy would probably be to contribute to improved transparency and knowledge about the quality of the contract manufacturer in general, and to help legitimate firms raise standards through more thorough assessment.

Tighten rules on inspections (Reference 4.1.2)

Policy 4.1.2 (a) Strengthen provisions on inspections and supervisions, in particular regarding inspections in countries outside the EU. For example, make it compulsory to follow the Compilation of Community Procedures on Inspections and Exchange of Information (CoCP).

5.2.14 The sources for the cost estimates of this policy option are largely the trade associations AESGP and EGA for GMP inspections and GIRP and EAEPC for GDP inspections (as well as information on fees obtained from regulators).

5.2.15 DG Enterprise suggested that all GMP inspections within the EU currently apply Compilation of Community Procedures (CoCP). On this basis, the introduction of this policy has no impact on such inspections and no costs or benefits are associated with it.

5.2.16 At present there are few procedures laid down for GDP inspections and so these would need to be further developed prior to the introduction of a policy mandating application of CoCP to GDP inspections. It is assumed that the procedures that would be put in place would not exceed the standards of the most rigorous current inspections so that some GDP inspections already 'apply' these procedures. The incremental cost of this policy option applies only for those GDP inspections whose practices must change so as to apply CoCP (number of annual GDP inspections multiplied by the extra fee and administration costs of applying CoCP multiplied by proportion not following CoCP currently).

5.2.17 Regulators believe that CoCP demands a more rigorous and time-consuming inspection than is generally the case today and would mean that all GDP inspections would be required to happen at least every three years. This would increase the number of GDP inspections (full cost of GDP inspection following CoCP including administration costs multiplied by number of extra inspections). Further, the new GDP inspections for brokers, traders and business to business platforms would need to follow CoCP. The full cost of the inspections is calculated and so this policy slightly duplicates policy 4.1.1(a) in which these inspections happen without CoCP (fee and administration costs of CoCP basic GDP inspection multiplied by number of inspections per year).

5.2.18 For the cost of GMP inspections in countries outside the EU, the calculation is the cost of the inspection (including fees, travel and other expenses for inspectors and administration costs) multiplied by the number of firms that would be inspected (adjusting for the proportion being adequately inspected at present) divided by the frequency of inspection.

All the costs in this section are annual (with no set-up costs) and so NPV calculations are simple.

5.2.19 One important reason — but by no means the only reason — that the costs of GMP inspections in third countries exceed those within the EU is substantially increased travel costs. The costs estimated for this policy may only fall indirectly on EU purchasers through the higher prices paid for using these suppliers. This may have a marginal impact in encouraging firms to use more local suppliers (that may be easier to inspect or audit).

5.2.20 Both EMEA and an inspector for the German region Nordrhein-Westfalen said that they were not aware of counterfeit medicines being found during an inspection. Inspections (at least the regular ones for GDP and GMP) are usually announced and aim to check that equipment and procedures are working properly. These inspections may improve the compliance of bona fide firms, but have little impact on the business of counterfeiters.

Table 5.3: Estimated cost of 4.1.2(a)

Apply Compilation of Community Procedures to all GMP and GDP inspections in EU		
Cost category	**Value**	**Source(s)**
Proportion of non-CoCP GMP inspections	0%	Assumption proposed by EC
Extra cost for GMP inspections to apply CoCP (fee)	€ 0	Follows from assumption above
Extra administration hours for CoCP GMP inspections	0.00	Follows from assumption above
Number of GMP inspections by EU authorities (annual)	3,500	EMEA, EudraGMP
Extra number of GMP inspections required	0	Industry sources
Proportion of GDP inspections following simplified standards in the absence of harmonised CoCP	80%	EE assumption
Total cost of CoCP GDP inspection (fee for 1 day)	€ 3,951	MHRA and EE estimate
Total administration hours for CoCP GDP inspections	22.50	EE estimate
Extra cost for current GDP inspections to apply CoCP (fee)	€ 1,317	AESGP, EMEA, German inspector for Nordrhein-Westfalen, MHRA and EE estimate
Extra administration hours for current GDP inspections	7.50	EE estimate
Number of GDP inspections by EU authorities at present (annual)	4,000	EMEA
Extra number of GDP inspections by EU authorities if follow CoCP in the future	3,000	EE estimate
Proportion of GDP inspections following simplified standards in the absence of harmonised CoCP for unlicensed brokers/traders	100%	EE assumption
Total cost of CoCP GDP broker/trader inspection (fee- ¾ of a day)	€ 2,964	MHRA and EE estimate
Total administration hours for CoCP GDP broker/trader inspections	16.875	EE estimate
Number of unlicensed broker/trader inspections required (annual)	333	EE calculation
Wage	€ 23.45	Eurostat
POLICY COST ESTIMATES		
Annual administrative cost	€ 2,278,000	
Annual cost	**€ 19,333,000**	
Net present value	**€ 163,080,000**	

Table 5.4: Estimated cost of 4.1.2(b)

GMP finished product inspections in third countries		
Cost category	**Value**	**Source(s)**
Number of sites of pharmaceutical manufacturers supplying EU based outside EU	8,000	AESGP, EGA, EMEA
Proportion of firms being inspected	80%	AESGP, EMEA
Target inspection frequency (years between inspection)	3	EE assumption
Cost (fees + expenses) of GMP inspection in third countries	€ 35,000	EGA, EMEA, German inspector for Nordrhein- Westfalen
Administration hours of audited firm (2 people, 3 days due to language, unfamiliarity etc.)	45	EE estimate
Administrative wage in non-EU countries not currently inspected	€ 1.25	YDL Management Consultants
POLICY COST ESTIMATES		
Annual administrative cost	€ 30,000	
Annual cost total	**€ 18.7m**	
Net present value	**€ 157.71m**	

Improve product integrity through a unique seal from the manufacturer to the retailer or wholesaler, using a risk-based approach, supported by a ban on repackaging (Reference 4.1.3).

5.2.21 EFPIA regards the banning of repackaging as a pre-requisite for pack serialisation, but pack serialisation could help to protect the supply chain without banning repackaging. Any dishonest re-packagers would be able to replace the genuine product with a counterfeit but if they could not create their own serialisation codes (and were required to keep the codes on the incoming packs) then they could only supply one packet for every genuine pack purchased. If serialisation and authentication were linked to national reimbursement schemes then it would not be possible for re-packagers to sell the genuine product obtained from this substitution in the legitimate supply chain and they may have to resort to supplying the genuine product via illegitimate (non-reimbursed) routes. The re-packager would have bought one genuine (serialised) pack and one counterfeit and sold one counterfeit serialised pack and one genuine medicine through illegitimate routes. It is unlikely this would be very profitable given the costs of the repackaging process and may not be worthwhile for firms that could get detected or prosecuted.

5.2.22 EFPIA and manufacturers have provided us with information used to formulate our estimate of the costs associated with this policy option. In general, the upper-limit of EFPIA's estimates was accepted by manufacturers (some of whom thought it should be higher or that some costs had been missed). EFPIA said that many firms had stopped sealing packs because it is not worthwhile whist repackaging remains legal, but that

sealing is still happening on a risk-based approach. The annual cost is calculated as the number of packs multiplied by the cost per pack multiplied by the reduction for existing sealing of packs. These annual cost estimates do not include any forward-looking reduction in the cost of sealing as processes improve.

5.2.23 One of the advantages of this option is that supply chains are shortened.

5.2.24 The effects of this policy include the dramatic reduction (of maybe 80 per cent or more) in the parallel trade industry and an equivalent reduction in the number of firms and employment (currently about 100 firms and 12,000 employees).

Downstream impacts

5.2.25 The environmental effects of a major reduction in parallel trade would include reduced waste from re-boxing 50 million packs a year, and reduced transport-related costs from additional movement of products from lower income Member States to higher income Member States.

5.2.26 As explained in detail in Europe Economics' contribution to an impact assessment of the effects of policies to ensure safe medicines through parallel trade, the effects of a ban on repackaging and re-labelling of patented medicines that are to be reimbursed through healthcare services would be beneficial to patients and to the EU economy, for two essential reasons. By removing almost all parallel trade in these products, this policy would both:

(a) Allow market forces to lead to prices for essential medicines that are more closely in line with the ability of healthcare services to pay for them, thus improving the working of the EU internal market.

(b) Remove the inherent systemic risk to patients resulting from original packages of medicine being re-opened and relabelled, in an unnecessarily complicated and non-transparent supply chain.

5.2.27 Ensuring greater transparency in the supply chain would be directly relevant to the major policy objective of making it more difficult for counterfeiters to sell their fake medicines.

5.2.28 The right to open the outer packaging would be strictly limited to the market authorisation holder (e.g. in case of need for a recall) and of the patient and his or her health care professional.

Table 5.5: Estimated cost of 4.1.3

Unique seal and ban repackaging		
Cost category	**Value**	**Source(s)**
Number of packs in EU (all prescriptions)	29bn	AESGP
Number of packs in EU (non-generic)	14.5bn	AESGP, EGA
Cost of a seal or hologram	€ 0.02[11]	AESGP, EFPIA, EGA
Proportion of non-generic packs already being sealed	20%	EFPIA
POLICY COST ESTIMATES		
Total annual cost (all prescriptions)	**€ 522.00m**	
Total annual cost (risk-based/non-generic)	**€ 232.00m**	
Net present value (all prescriptions)	**€ 4,403.24m**	
Net present value (risk-based/non-generic)	**€ 1,957.00m**	

Centrally accessible record to facilitate traceability of batches throughout the distribution chain (Reference 4.1.4).

5.2.29 At present, pharmaceutical packaging must display the batch number and manufacturers and wholesalers are required to keep records of their transactions relating to batches. Therefore, this policy would not require any additional printing and should not be associated with additional data-entry costs – rather than entering the information onto their own database, manufacturers and wholesalers would instead enter the information onto the central database.

5.2.30 The incremental costs of the policy are calculated for two scenarios – one in which authentication at retail level is not required and an alternative in which it is. Incremental costs of the policy arise from the creation of the new database and, if required, from additional verification at pharmacy level. The only one-off cost is the development cost of the database whilst annual costs are the multiple of the total number of pharmacies in the EU, the average number of batches per pharmacy, the time per entry onto the database and the average wage in the EU. Such costs arise with retail-level authentication because pharmacists are not currently required to keep records of these transactions.

[11] Higher estimates are also made.

5.2.31 Batch traceability may not help early detection of counterfeits since it could be possible to by-pass the system by, for example, claiming that the products were bought from pharmacists after observing a pharmacist with that batch number. A counterfeiter could sell individual packs of counterfeits to which a false batch number had been attached, referencing a pharmacist that had received a genuine batch with that number. The counterfeiter need not be in cahoots with the pharmacist, merely able to find out some batch numbers. There would be no way of knowing that the individual packs were counterfeit, and the false batch number could even lend a spurious impression of reliability. The policy of batch traceability may be advantageous in terms of increasing the speed that the source of counterfeits is tracked down after an incident has been discovered, but it appears that there is often no significant delay to detecting the source firm of counterfeits at the moment. In order for firms to thoroughly check that all the packs received are from the stated batch it may be necessary to check them all individually.

Table 5.6: Estimated cost of 4.1.4

Batch-traceability		
Cost category	**Value**	**Source(s)**
Database costs (exclusive of the cost of option 4.1.6)	€ 20m	EFPIA, EGA, Technology firm
Number of batches per pharmacy (annual)	125	EAEPC, EFPIA, Manufacturer
Time per entry (hours)	0.01	EE assumption
Wage	€ 23.45	Eurostat
Number of pharmacies in EU	160,000	EFPIA, EGA, GIRP, PGEU[12]
POLICY COST ESTIMATES		
Total cost (one off)	**€ 20m**	
Total cost (annual, if retail authentication is required)	**€ 4.69m**	
Net present value (no retail authentication)	**€ 20m**	
Net present value (with retail authentication)	**€ 59.56m**	

Mass serialisation for pack-tracing and authenticity checks on a case-by-case basis (Reference 4.1.5).

5.2.32 This policy would require the possibility to trace each pack and perform authenticity checks. This could be achieved through a mass serialisation feature on the individual

[12] PGEU - Pharmaceutical Group of the European Union

packaging. Technical details would be further defined in implementing legislation and/or by standardisation organisations.[13]

5.2.33 This policy option would address the risk of counterfeits directly. As the March consultation paper noted, in order to trace counterfeit products it may be crucial to identify who has handled a specific pack in the supply chain; and equally, for the patient to be sure that his or her medicine is authentic, it is essential that the individual pack can be identified.

5.2.34 It is not inconceivable that a 2D barcode itself could be counterfeited, and this possibility implies that it may be necessary to seal the packet with a tamper-evident seal. It is important to note that for this policy option the cost of including a tamper evident seal is not quantified, only of printing a 2D barcode onto the packet, although the Product Security Director at AstraZeneca has stated:[14]

> "Unless we seal the carton with a tamper-evident seal, all we've accomplished with the 2D bar code on the carton is authentication of the folding carton. The tamper evident seal helps us guarantee that what's inside the carton is genuine. The seal has a hologram on it, which is an overt layer of authentication that pharmacists or hospital personnel can see. It also has hidden security features that can't be copied, including a unique 2D bar code printed in ink that is not visible to the naked eye."

5.2.35 Another concern may be that a valid 2D barcode could itself be copied by counterfeiters. It has been argued, however, that the authenticating barcode will detect this activity since each time a barcode is scanned, a record is retained and each new record is compared to all the others in the memory. Therefore, if the new record is a duplicate of one already in the memory it is immediately flagged up as a counterfeit.[15]

5.2.36 The potential benefits of this option are only really apparent when the broad range of other effects is considered. An industry study has found that serialisation could result in a reduction of cost to the firm of €120,000 per line or about €3.6bn per year for 30,000 lines. The majority of this cost reduction is the result of more efficient handling of returns from pharmacies that have a surplus of stock but savings can also occur if a product is recalled. In addition there are potential gains from reduced administration and fraud for national reimbursement schemes. Fraud was the main reason for national regulatory action in many EU Member States.

5.2.37 A 2D barcode is assumed for the purpose of the impact assessment since this would allow room for future expansion of the information on the barcode and allow scope for transition with both current national serialisation numbers and the proposed EU wide

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[13] March consultation paper, p.9.
[14] http://www.healthcare-packaging.com/archives/2007/05/anticounterfeiting_strategies.php
[15] Assure Digitax Inc., "A New Track and Trace, Counterfeit-Proof, Information-Based Cigarette Tax Indicia System" Prepared for the State of California, January 2002

codes being supported with the same barcode for a period. Transition could also apply to any implementation at pharmacy level.

5.2.38 As with batch e-pedigree, parallel traders are keen to stress the importance of keeping the data secret and not allowing manufactures to learn the destination of specific batches (but, as at present, they could be informed of overall market sales). AESGP stresses that these costs are far too high for over-the-counter (OTC) products and no stakeholder seems to suggest that OTC drugs should be subject to these costs.

5.2.39 The cost estimates for this policy relied heavily on information provided by EFPIA initially but these estimates were subsequently circulated to other stakeholders who challenged them (especially EGA who felt that the original numbers were a significant underestimate). Estimates were re-evaluated on the basis of this feedback.

5.2.40 It is assumed that 30 per cent of packaging lines are for patented/branded products and 70 per cent for generics. Generics firms are generally smaller than those that produce patented products and may produce a wider range of products on a greater number of sites. Therefore, the ratio of pharmaceutical packs to packaging lines is greater for producers of patented/branded products and the proportion of packaging lines for generics firms exceeds their proportion of total pharmaceutical production.

5.2.41 The estimated one-off cost of serialisation is given by the costs of the database plus the cost of modifying each packaging line multiplied by the number of lines. Annual costs are line running costs multiplied by number of lines. Both of these could be reduced to focus on patented medicines (rather than all reimbursed medicines), and further reduced to take account of potential industry implementation even in the absence of the implementation of this policy.

5.2.42 There are two alternatives for where authentication could occur — at the last wholesaler or at the retailer.

5.2.43 For wholesaler authentication it is important to draw a distinction between mechanised full-line wholesalers and other wholesalers (e.g. non-mechanised short-line and full-line wholesalers). Mechanised (probably full-line) wholesalers will incur one-off costs of authentication since they must modify their capital so as to enable authentication to occur automatically. This capital will also lead such wholesalers to incur annual running costs. Non-mechanised wholesalers, however, will incur only ongoing labour costs as packs are authenticated manually.

5.2.44 An estimate is used of 20,000 sites of short-line and full-line wholesalers in the EU. This is based on information received from GIRP that there are 1,458 sites of full-line wholesalers in the EU, of which around half are mechanised, and approximately 19,000 short-line wholesalers, each of whom is assumed to have one site on the basis that such

wholesalers are generally small and stock a limited number of pharmaceutical products, sometimes less than 1 per cent of those stocked by full-line wholesalers.[16]

5.2.45 The one-off cost of wholesaler-level authentication would be the cost of mechanised equipment multiplied by the number of mechanised full-line warehouses. Annual costs would be the labour cost to short-line and non-mechanised full-line wholesalers (required hours per site multiplied by wage multiplied by the number sites) plus the running costs at mechanised sites multiplied by the number of mechanised sites.

5.2.46 For the alternative of pharmacist level authentication the capital cost of the scanners has been converted into an annual cost using an industry equipment lifetime of five years. For this option the labour cost of scanning the products is not considered because it would be done while the customer is being served and the delay is not significant. The pharmacist gains useful information from the process and critically pharmacists may already scan individual pack barcodes when dispensing.

5.2.47 Annual pharmacy costs are calculated as the cost of a pharmacy system (scanner cost multiplied by scanners per pharmacy plus extra software costs) divided by the lifetime of the system and finally multiplied by the number of pharmacies in the EU that would need to install a scanner system. Some pharmacies, including those located in Germany, can already read 2D barcodes or will be able to without this policy and hence the number of pharmacies that require this system is not equal to the total number of pharmacies in the EU.

5.2.48 The total cost of this policy option is the sum of the costs of putting barcodes onto the product and one of the authentication alternatives (wholesale or retail).

5.2.49 Serialisation is an expensive policy but potentially most effective against counterfeits. Serialisation ensures that for every packet (and hence serialisation code) produced by manufacturers, only one packet can be dispensed.

5.2.50 The cost estimates in the table below show first the costs of the database and the costs that would be needed per packaging line. These are common whether the final authentication is at retail or last wholesaler level; these costs are then also shown.

[16] Eurostat states that there are approximately 30,000 wholesalers in the EU but discussion at the Pharmaceutical Packaging and Labelling Innovations Conference 2008 indicated that for the UK that approximately 40 per cent of firms that have GDP certificates have not been active for a decade. Therefore, it is likely that if this policy were implemented the total number of wholesalers that would incur the costs would be significantly fewer than 30,000.

Table 5.7: Estimated cost of 4.1.5

Pack based mass serialisation		
Cost category	**Value**	**Source(s)**
Cost of database (including on-going running costs)	€ 120m	EFPIA, Industry, Technology firm
Number of packaging lines	15,000	EFPIA, EGA, Industry, Packaging equipment supplier
Proportion of packaging lines for patented products	30%	EGA, Industry, US Generic Pharmaceutical Association
One-off cost per packaging line	€ 150,000	AESGP, EFPIA, US firm, Industry, Packaging equipment supplier, Technology firm
Running cost per packaging line	€ 30,000	AESGP, EGA, Industry sources, Technology firm
POLICY COST ESTIMATES		
Total gross cost (one off)	**€ 2,370.00m**	
Total gross cost (annual)	**€ 450.00m**	
Total cost (one off) assuming patented products would install system without new regulation	**€ 1,659.00m**	
Total cost (annual) assuming patented products would install system without new regulation	**€ 315.00m**	
Total cost (one off) (risk-based, regulation restricted to patented/branded products, assuming zero implementation without regulation)	**€ 711.00m**	
Total cost (annual) (risk-based, regulation restricted to patented/branded products, assuming zero implementation without regulation)	**€ 135.00m**	
Total cost (one off) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	**€ 0**	
Total cost (annual) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	**€ 0**	
Net Present Value – gross cost	**€ 6,165.90m**	
Net Present Value (assuming patented products would install system without regulation)	**€ 4,316.13m**	
Net Present value (risk-based,	**€ 1,849.77m**	

Pack based mass serialisation		
Cost category	**Value**	**Source(s)**
restricted to patented/branded products, assuming zero implementation without regulation)		
Net Present value (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	**€ 0**	
Last wholesaler level authentication		
Cost category	**Value**	**Source(s)**
Cost of (2D) Scanner	€ 400	Barcode Warehouse, EFPIA, GIRP, Industry, Technology firm
Number of scanners required by short-line wholesaler	3	EE assumption
Number of hours per firm required for scanning at short-line wholesaler	2,000	Industry sources
Wage	€ 14	EE assumption
Lifetime of scanner (years)	5	Technology firm
Average annual cost for short-line wholesaler (or non-mechanised warehouse)	€ 28,240	EE calculation
Number of short-line and non-mechanised full-line warehouses	20,000	GIRP
One-off cost for full-line wholesaler (mechanised warehouse)	€ 500,000	California Board of Pharmacy meeting
Annual cost for full-line wholesaler	€ 50,000	EE assumption
Number of warehouses of full-line wholesalers (mechanised warehouse)	600	EAEPC, GIRP
POLICY COST ESTIMATES		
Total cost (one off)	**€ 300.00m**	
Total cost (annual)	**€ 594.80m**	
Net present value	**€ 5,317.34m**	
Retail level authentication		
Cost category	**Value**	**Source(s)**
Cost of (2D) Scanner	€ 400	Barcode Warehouse, EFPIA, GIRP, Industry, Technology firm
Lifetime of scanner (years)	5	Technology firm
Number of scanners per shop	4	EFPIA, GIRP, PGEU

Pack based mass serialisation		
Cost category	**Value**	**Source(s)**
Extra cost of scanner system per shop	€ 150	GIRP, Technology firm
Number of pharmacies in EU, excluding those that already have a scanner system	130,000	EFPIA, EGA, GIRP, PGEU
POLICY COST ESTIMATES		
Total cost (annual)	**€ 45.5m**	
Net present value	**€ 383.8m**	

5.2.51 As noted above, to calculate the total cost of this policy it is necessary to add the cost of either wholesale or retail authentication to the cost of building the database and installing equipment on packaging lines. The final costs are not immediately clear from Table 5.7 and hence Table 5.8 presents a summary of the one-off annual and total costs of the policy and clearly illustrates the substantial increase in costs if authentication is required at wholesale level.

5.2.52 For clarity of exposition the summary table omits the costs incurred if a risk-based approach were to be taken and EFPIA did not implement the policy without additional regulation. DG Enterprise has strongly suggested that EFPIA will in fact proceed with pack serialisation in the absence of new regulation and it is prudent to focus on the costs associated with more-likely scenarios. Nonetheless, it would be unwise to omit the gross cost of this policy option.

Table 5.8: Cost summary for policy 4.1.5

	Last wholesaler authentication	Retail authentication
Total gross cost (one off)	€ 2,670.00m	€ 2,370.00m
Total gross cost (annual)	€ 1,044.80m	€ 495.50m
Total cost (one off) assuming patented products would install system without new regulation	€ 1,959.00m	€ 1,659.00m
Total cost (annual) assuming patented products would install system without new regulation	€ 909.80m	€ 360.50m
Total cost (one off) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	€ 300.00m	€ 0
Total cost (annual) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	€ 594.80m	€ 45.50m
Net Present Value – gross cost	€ 11,483.23m	€ 6,549.71m
Net Present Value (assuming patented products would install system without regulation)	€ 9,633.46m	€ 4,699.94m
Net Present value (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	€ 5,317.34m	€ 383.81m

Downstream impacts

5.2.53 The downstream effects of this policy may be limited as wholesalers may potentially be unaffected when retail authentication is used. Small generics firms may see costs rise but may be able to recover these costs since generic medicines are often 20-80 per cent cheaper than patented alternatives. The option would create greater demand for technology companies and associated research which, in turn, creates skilled employment.

Synergies between Reference 4.1.4 and 4.1.5

5.2.54 There are some clear synergies between policy options 4.1.4 and 4.1.5. The cost estimates above have assumed that each policy option is introduced independently, but if both policies were to be implemented the total costs would be lower than the sum of the independent costs. The cost of jointly introducing the policy options and find that such a

strategy eliminates the majority of costs associated with policy option 4.1.4 is now assessed.

5.2.55 With joint implementation, there should only be one database in which both the batch number and the pack serialisation number would be entered. The starting point for the total cost of the database is that of the pack serialisation database. It is unlikely that there would be additional costs on top of this to enable the entry of a batch number onto this database and hence assume that the cost of this combined database would be the same as the cost of the pack serialisation database.

5.2.56 It is unlikely that the cost of policy option 4.1.5 would be substantially reduced through joint implementation, but the choice of authentication level for pack serialisation can affect the cost of policy option 4.1.4.

5.2.57 If serial numbers were to be authenticated at retail level and the 2D barcode were to contain both batch number and serial number, a single scan would be capable of entering both the batch number and serial number onto the database. Therefore, the cost of batch authentication at retail level, as may be required in policy option 4.1.4, is eliminated. Given this, the only scenario in which the cost of retail entry of batch numbers can apply is if pack authentication is at last wholesaler level whilst retail authentication is required for batches.

5.2.58 Below, a summary of the cost of jointly implementing these policies is presented. Costs that are eliminated through joint implementation do not appear in the table. Please see the individual sections above and in Annex 1 for an explanation of the methodology for calculating total annual and one-off costs.

Table 5.9: Estimated cost of joint implementation of 4.1.4 and 4.1.5

Batch traceability and mass pack serialisation		
Cost category	**Last wholesaler authentication of 4.1.5**	**Retailer authentication of 4.1.5**
4.1.4		
Total annual cost for pharmacies (if retail authentication is required)	€ 4.69m	€ 0
4.1.5		
Total gross cost (one off)	€ 2,670.00m	€ 2,370.00m
Total gross cost (annual)	€ 1,044.80m	€ 495.50m
Total cost (one off) assuming patented products would install system without new regulation	€ 1,959.00m	€ 1,659.00m
Total cost (annual) assuming patented products would install system without new regulation	€ 909.80m	€ 360.50m
Total cost (one off) (risk-based, regulation restricted to patented/branded products, assuming zero implementation without regulation)	€ 1,011.00m	€ 711.00m
Total cost (annual) (risk-based, regulation restricted to patented/branded products, assuming zero implementation without regulation)	€ 729.80m	€ 180.50m
Total cost (one off) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	€ 300.00m	€ 0
Total cost (annual) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	€ 594.80m	€ 45.50m
JOINT IMPLEMENTATION COST		
Total gross cost (one off)	**€ 2,670.00m**	**€ 2,370.00m**
Total gross cost (annual)	**€ 1,049.49m**	**€ 495.50m**
Total cost (one off) assuming patented products would install system without new regulation	**€ 1,959.00m**	**€ 1,659.00m**
Total cost (annual) assuming patented products would install system without new regulation	**€ 914.49m**	**€ 360.50m**
Total cost (one off) (risk-based, regulation restricted to patented/branded products, assuming zero implementation without regulation)	**€ 1,011.00m**	**€ 711.00m**
Total cost (annual) (risk-based, regulation restricted to patented/branded products, assuming zero implementation without regulation)	**€ 734.49m**	**€ 180.50m**
Total cost (one off) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	**€ 300.00m**	**€ 0**

Total cost (annual) (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	**€ 599.49m**	**€ 45.50m**
NET PRESENT VALUES		
Net Present Value – gross cost	**€ 11,522.80m**	**€ 6,549.71m**
Net Present Value (assuming patented products would install system without regulation)	**€ 9,673.03m**	**€ 4,699.94m**
Net Present value (risk-based, restricted to patented/branded products, assuming zero implementation without regulation)	**€ 7,206.67m**	**€ 2,233.58m**
Net Present value (risk-based, restricted to patented/branded products, assuming patented products would install system without new regulation)	**€ 5,356.90m**	**€ 383.81m**

Increasing transparency concerning authorised wholesalers through a Community database (Reference 4.1.6)

5.2.59 A database of authorisations and GDP certificates should reduce the cost of checking that a firm has a GDP certificate. If the database lists all authorised wholesalers and GDP certificates as well as entries on GDP non-compliance then this should provide re-assurance to wholesalers about the sources they purchase from. A coherent system would require a functioning inspection system of wholesalers with a cycle of at least every three years. The effect on counterfeiters may be moderate because, as noted in the policy options on inspections, these activities are not designed to catch criminals but merely sub-standard practice.

5.2.60 The main source of information for our cost estimates for this policy option was EMEA, who would be primarily responsible for the database as an extension of the EudraGMP database. It is assumed that there are 20,600 GDP certificates to be entered on the basis of the number of full-line and short-line wholesalers used in calculations above.

5.2.61 One-off costs are calculated as the development cost of the database plus the certificates to be entered (adjusted for the number not kept electronically at present) multiplied by the cost for entering the certificate (wage multiplied by time for each entry). Annual costs are the cost of running the database plus the same adjustment for the cost of entering certificates using the annual inspection number as the number of new certificates (note this number is for current practice, not for following CoCP). The cost of actually issuing the certificates was felt to be negligible (a paper certificate would not have to be given out for the system to work).

Downstream impacts

5.2.62 The only real downstream effects are that the database may make it easier to contact and contract with firms in other Member States so as to increase cross-border trade.

Table 5.10: Estimated cost of 4.1.6

Cost category	Value	Source(s)
Cost of building GDP database	€1,000,000	EMEA
Database running costs	€100,000	EE estimate
Total GDP certificates in EU	20,000	EMEA
New certificates each year	4,000	EE assumption
Proportion of GDP certificates not already being entered	40%	EMEA
Cost of issuing certificates	0	EC proposed assumption
Time to insert one certificate (hours)	0.25	EE assumption
Wage	€ 23.45	Eurostat
POLICY COST ESTIMATES		
Total cost (one off)	**€ 1.05m**	
Total cost (annual)	**€ 109,000**	
Net present value	**€ 1.97m**	

5.2.63 A summary of the costs associated with section 4.1 is provided in Table 5.11. It is important to note that, for clarity of exposition, the summary does not account for potential synergies between policies 4.1.4 and 4.1.5. We discussed the possible effects of joint implementation above (see paragraph 5.2.54). However, given that the Public Consultation of 11/03/2008 presented each policy separately, the summary table includes the cost of each policy if implemented independently of all other policies.

Table 5.11: Estimated Total Cost of Option 4.1

Policy Option	Notes	One-off cost (€ m)	Annual cost (€ m)	Net Present Value with 10-year horizon (€ m)
4.1.1(a)		2.33	1.21	12.57
4.1.1(b)i	Accept third-party audits (audit firm conducts audits)		26.45	223.15
	Accept third-party audits (manufacturer conducts audits)		27.52	232.15
	Do not accept third-party audits		1,376.05	11,607.41
4.1.1(b)ii	Accept third-party audits (audit firm conducts audits)		9.14	77.09
	Accept third-party audits (manufacturer conducts audits)		13.34	112.52
	Do not accept third-party audits		1,407.97	11,876.70
4.1.2(a)			19.33	163.08
4.1.2(b)			18.70	157.71
4.1.3	All prescriptions		522.00	4,403.24
	Risk-based		232.00	1,957.00
4.1.4	No retail authentication	20.00	0.00	20.00
	Retail authentication	20.00	4.69	59.56
4.1.5	Total cost for all manufacturers	2,370.00	450.00	6,165.90
	Total cost if full-EFPIA implementation to cover all patented/branded products without regulation	1,659.00	315.00	4,316.13
	Total cost if risk-based, restricted to patented/branded products, zero implementation without regulation	711.00	135.00	1,849.77
	Total cost if risk-based, restricted to patented/branded products, full implementation to cover all patented/branded products without regulation	0.00	0.00	0.00
4.1.5(a)		300.00	594.80	5,317.34

Policy Option	Notes	One-off cost (€ m)	Annual cost (€ m)	Net Present Value with 10-year horizon (€ m)
4.1.5(b)			45.50	383.81
4.1.6		1.05	0.11	1.97
Total	**Minimum**			**€3,036m**
	Maximum			**€39,765m**

5.3 Tightening requirements for the import/export/transit of medicinal products

5.3.1 Two policies are proposed for this purpose. The first outlines a very strict regime for the import of medicinal products into the EU, requiring all medicinal products to have a marketing authorisation for the EU and meet all import requirements. The second policy is more moderate, and aims to clarify the existing import regime with regards to those medicinal products in transit or imported for the purpose of re-export.

Prohibit the import of medicinal products not fulfilling EU requirements into the EU territory (Reference 4.2.1)

5.3.2 This policy option would require all medicinal products passing through the EU *en route* to other parts of the world to meet the same requirements as those for medicinal products intended to be placed on the EU market. This would primarily involve those importing having an EU marketing authorisation for the products concerned.

5.3.3 This would result in a *de facto* ban on the transit and import for export trade in pharmaceuticals as it would almost certainly not be feasible for such products to obtain a marketing authorisation just for this purpose. Importers of these products for the purpose of re-export are unlikely to have the resources or knowledge to apply for an EU marketing authorisation, and it would probably be commercially unviable for manufacturers to apply for one given the time and costs involved.

5.3.4 The main costs to be estimated are therefore the employment and revenue losses resulting from an effective ban on this trade. There are no direct business costs that would result from the implementation of this policy option.

5.3.5 The costs of this policy are separated into those resulting from the loss of transit trade and those resulting from the loss of import-for-export trade. Transit trade refers to medicinal products originating from and destined for countries outside the EU, transited (or transhipped) through EU countries for logistical or other purposes. Import-for-export is when medicines are imported from outside the EU purely for the purpose of being re-exported to other non-EU countries. These medicines often undergo minor processing or

repackaging. In neither case are the medicines destined for the EU market, and thus are not currently required to meet EU marketing authorisation requirements.

5.3.6 The former costs include the loss of revenue for airports and seaports, couriers, airlines and shipping companies; the latter include the loss of revenue and employment for unauthorised importers,[17] the losses to the transport industry, and losses to free areas and bonded warehouses.

5.3.7 The total volume and value of pharmaceutical products that are transhipped through the EU is not recorded in official statistics and is difficult to estimate. Extrapolations based on six major air and seaport transit countries in the EU yield the volume of transhipped pharmaceuticals used in the following calculations. Further extrapolations based on industry opinion and case studies yield the estimates of revenue generated by this trade. The extent of the import-for-export trade (number of unlicensed importers and the value added by the sector) is estimated using evidence from the UK, extra-EU import volumes and data on pharmaceutical wholesalers.[18]

5.3.8 The calculations of the losses resulting from the policy are separated into three tables for air transit, sea transit and import-for-export. Full details of all the steps involved in calculating these losses are included in the Transit Calculations Annex; only the main figures are included in the tables here. The final costs are presented in both annual costs and net present value[19] over ten years.

Table 5.12: Loss of Transit and 'Import for Export' Trade in Pharmaceuticals for Policy 4.2.1

A. Sea Transit[20]		
Figure	**Five main EU Ports**	**Source**
PT: estimated weight of pharmaceuticals transhipped through from outside the EU (1,000 tons)[21]	710	EE estimate based on evidence from Hamburg, applied to Rotterdam, Antwerp, Hamburg, Amsterdam, Le Havre[22]
AR: average revenue per shipment of 10 tons[23]	€4,500	Typical sea route (Laos to Brazil) via EU of transited pharmaceuticals; opinion of Quality Director for EMEA: DHL Excel Supply Chain Cost from TransGlobal Express and

17 It is assumed that an EU-based importer without a Competent Authority-issued license to import licensed medicinal products is engaged in the import for export trade. See Transit Calculations Annex for more details.
18 See Transit Calculations Annex for details of these difficulties and all estimations and extrapolations.
19 See Transit Calculations Annex for full explanation of NPV
20 See Table 1 in Transit Calculations Annex for full estimation details.
21 Across the five main ports. See Transit Calculations Annex for estimation methodology
22 Choice based on Rotterdam Port Authority: Industry and Bulk Cargo; TransGlobal Express; Global Shipping; Antwerp Port Authority
23 Average weight of shipment: 24 pallets at 417kg each

		PharmaExport Includes total revenue to all stakeholders (couriers, shipping lines, seaports) which would be lost.
Total revenue generated across all ports [PT/10*AR]	€319m	

B. Air transit[24]		
Figure	**Six main EU airports**	**Source**
PT: estimated number of transit movements of pharmaceuticals[25]	14,193	EE estimate based on evidence from UK, applied to Frankfurt, Schiphol, Heathrow, Charles de Gaulle, Luxembourg, Milan[26]
AR: average revenue per movement[27]	€39,963	Typical route from India to Nigeria, based on evidence from MHRA[28] Average weight of 4,170kg per movement[29]
Total revenue generated across all airports [PT*AR]	€567m	

C. Import-for-export[30]		
Figure	**Whole EU**	**Source**
NI = number of unauthorised importers	3,336	MHRA consulting with HMRC[31]
TC = total transport costs per firm per year	€408,150	Average of 45 transport movements of 5 pallets each per year per firm; 60% by air and 40% by sea. Details in Transit Calculations Annex
BW = bonded warehouse storage	€3,673	Total of €12,252,794 revenue lost

24 See Table 2 in Transit Calculations Annex for full estimation details

25 Across the six main airports. See Transit Calculations Annex for estimation methodology

26 Choice based on: De La Fuente Layos (2005) "Statistics in Focus: Transport", Eurostat publications; and opinion of Quality Director for EMEA: DHL Excel Supply Chain.

27 This is the total revenue generated by the movment. It is based on quotes from couriers (DHL; TransGlobal Express) and transport industry experts (PharmaExport; EMEA Supply Chain) and consists of all revenue to couriers, forwarding agents, airlines and airports (including handling and processing charges). It was not possible to separate the figure into these various components, but it is sufficient to represent the total loss of transport revenue resulting from the policy.

28 Medicines and Healthcare products Regulatory Agency, UK

29 10 pallets at average 417kg each. More than 10 pallets not likely to travel by air

30 See Table 3 in Transit Calculations Annex for full estimation details.

31 Her Majesty's Revenue and Customs, UK

revenue per firm per year		across all 3,336 firms, based on 53% of all import-for-export pharmaceuticals being stored in warehouses.[32] Costs from DTZ Consulting and Research (2005) "Benchmark study: Antwerp, Le Havre, Rotterdam"
VA = value-added per firm[33]	€716,578	60% of European wholesaler industry average.[34]
EF = employment per firm	16	60% of industry average: Annual Business Inquiry (2007)
Total revenue generated across all importers	€3,764m	[TC+BW+VA]*NI
Total employment lost[35]	53,376	[EF*NI]

Total for Policy	
Total revenue lost from policy per year [A + B + C]	**€4,651m**
NPV over ten years[36]	**€39,233m**

5.3.9 Memorandum items:

(a) The net present value assumes that volumes and prices remain constant. This may be an oversimplification, particularly if volumes of pharmaceuticals are increasing.

(b) The reduction in transport, particularly air and sea, would be beneficial to the environment. Although the transit of pharmaceuticals makes up only a fraction of the total international movement of goods, the ceasing of this would have the effect of saving an estimated 82,302 tons of carbon emissions per year.[37]

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32 Based on transport industry opinion: see Transit Calculations Annex.
33 Contribution to GNP. Made up of net profit and wages
34 See Transit Calculations Annex for further details
35 It is assumed that only employment will be lost among importers, not at ports or airports given small ratios of pharmaceuticals to all other cargo
36 Assuming volumes remain constant
37 See Transit Calculations Annex for calculations.

Make existing requirements for wholesale distribution and manufacturing applicable for medicinal products imported for the purpose of re-export (through free-harbours, transit and bonded warehouses). (Reference 4.2.2)

5.3.10 This policy would require regulations for medicinal products imported in the normal way for use in the EU to be applicable to goods imported for the purpose of re-export. (Unlike policy 4.2.1 however the importer would not be required to hold a full marketing authorization.) Many of these requirements should already be in place; the purpose of this policy would be to clarify and if necessary extend the application of the import provisions.

5.3.11 Those affected by the policy would be importers of medicinal products into the EU who do not have correct authorisation. The requirements they would have to meet include the presence of a qualified person (QP) at all manufacturing or importing sites, staff who comply with the legal requirements concerning manufacture and controls; the use of suitable premises; and the quantitative and qualitative analysis of the imported products (a responsibility of the QP).

5.3.12 The direct business costs of meeting the requirements of this policy would fall upon unauthorised importers who do not comply with existing EU import provisions in pharmaceutical legislation. This number of importers has been estimated for the EU based on a figure for the UK, in the same manner as for policy 4.2.1. All other costs are based on quotes and opinions from industry and relevant experts. Full details of all extrapolations are in the Transit Calculations Annex.

Table 5.13: Direct Business Costs to Importers of Policy 4.2.2

	EU	Estimates
NI = number of unlicensed importers	3,336	Same estimation as for Table 4.2.1 C. See Transit Calculations Annex for details
QP = full-time employment of Qualified Person (annual salary)	€75,180	Based on industry opinion, given qualifications and experience needed
RP = full-time employment of Responsible Person	€35,084	Based on industry opinion, given qualifications and experience needed
WD = wage differential	€40,096	Some importers may already have Responsible Person, in which case their compliance costs would just be the wage differential
SP = GDP inspection for suitable premises (/3)	€878	Only if not current practice MHRA fee, due to lack of EU-wide fee from EMEA Includes expenses[38]; inspection every three years.
IL = importer licence (once off)	€3,368	Based on MHRA 'Manufacturer and Importer Licence' which contains all provisions outlined in Policy Option
LF = administrative cost of licence form per firm AC[39]	€70.35	Time: estimate from importer (3h). Wage: €18.76[40] 25% added for overheads, as per ACM[41]
BI = administrative cost of being inspected AC	€164.15	Wage of importer: €18.76 25% added for overheads, as per ACM 1 day inspection (7h)
QA = quantitative and qualitative analysis per firm[42]	€146,601	Average of €325.78 per batch[43] Estimate of 450 batches per importer per year [44]
Total one-off costs	**€11m**	[IL + LF]* NI
Total annual costs [QP+SP+BI+QA]*NI - [WD+SP+BI+QA]*NI	**€627m - €744m[45]**	With RP – without RP[46]
NPV over 10 years	**€5,296m - €6,284m**	With RP – without RP

38 Evidence from other European regulators: expenses of €400 per inspection

39 AC = administrative costs imposed by legislation as defined in EC IA Guidelines Annex 10. These are incorporated into the Standard Administrative Cost Model spreadsheet in the Annex.

40 Average EU27 wage for industry and services (Eurostat 2005), uplifted to 2007 prices

41 Standard Administrative Cost Model, as outlined in EC Impact Assessment Guidelines Annex 10

42 This will be contracted out, under the responsibility of the QP. See Transit Calculations Annex for more details.

43 Eclipse Scientific Group

44 Two batches per pallet, five pallets a week, 45 working weeks a year. See Transit Calculations Annex.

45 The greatest component of these costs is that of the Qualitative analysis, a total of €489,060,936.

46 The range given takes into account the possibility that some importers will already have a Responsible Person (RP) and therefore will only have to incur the cost of upgrading to a Qualified Person. Other importers will have to incur the full cost of a Qualified Person.

Downstream effects

5.3.13 The annual costs to each firm of meeting the new requirements range from €187,949 (for the company with a Responsible Person) to €223,021 (for the company without a Responsible Person). It must be noted that the biggest driver of these costs is the requirement for qualitative batch testing, which, at an estimated annual cost of €146,601 per firm, accounts for between 66 and 78 per cent of the annual costs.

(a) These costs are equivalent to an average of 25 per cent of gross profit[47] and would represent a significant burden on firms. This is likely to have a displacement effect among the importer firms, in particular the smaller firms with smaller profits.

(b) It is estimated that, as a result of these additional costs, 5 per cent of the import-for-export industry will either not be able to continue operating, or will take their business outside of the EU.[48] The resulting revenue and employment losses have been calculated as a percentage of the losses obtained in policy 4.2.1 where the whole import-for-export industry went out of business. These losses would not be an initial impact of the policy, but a downstream effect.

Table 5.14: Employment and Revenue Loss Resulting from Policy 4.2.2

Figure	EU	Estimates
% of importers leaving EU or going out of business	5%	Industry opinion and EE estimation[49]
Loss of revenue[50]	€188m	5% of total loss of import-for-export revenue from policy 4.2.1
Loss of jobs	2,669	5% of total loss of import-for-export employment from policy 4.2.1

5.4 Tighter requirements for manufacture, placing on the market of active substances and requirements for inspections

5.4.1 Three policies are proposed for this purpose.

[47] Total turnover less total purchases and employment costs. Annual Business Enquiry (2007) "Wholesale of pharmaceutical goods" www.statistics.gov.uk

[48] There has been some indication from industry that if such regulations were passed they may take their business outside the EU.

[49] See Transit Calculations Annex

[50] Total revenue generated by import for export trade

Requirement of a mandatory notification procedure for manufacturers / importers of active substances (Reference 4.3.1)

5.4.2 This policy option states:

> Submit the manufacturing/import of active ingredients to a mandatory notification procedure.
>
> >Render information on notified parties available in a Community database. This could be achieved via extension of the EudraGMP database.

5.4.3 The policy is a complement, indeed, possibly, a precondition to the success of further regulatory initiatives in this area. It is necessary to know who is operating in the EU API chain, as is currently not the case, before other initiatives, such as inspections or audit, can be expected to take full effect.

5.4.4 The precise details of the information to be included on the notification will be worked out at a later stage but would include, at a minimum: site (address, country etc.) of manufacture (both for manufacturers and importers), name of active substances, total or partial manufacture, authorisation/ license under local provision.

5.4.5 The direct business cost here is equal to the number of firms (i.e. manufacturers, not plants) that would be required to complete the notification multiplied by the business cost of submitting this notification (i.e. the wage cost for the time it takes to complete the notification).

Table 5.15: Direct Business Cost of Policy 4.3.1.

	In the EU	Information source and/or equation	Supplying to the EU from outside	Information source and/or equation
API manufacturers	500-700 estimated by CEFIC. 810 basic pharmaceutical product manufacturers are recorded under the NACE category of dg2441. It seems reasonable to assume that while not all of these basic pharmaceutical product manufacturers will be API manufacturers the majority will be so. 600, therefore, seems a reasonable figure for this calculation.	Estimations by Market Experts from the CEFIC membership/Eurostat	15,000	Estimations by Market Experts from the CEFIC membership
API traders	500	Estimations by Market Experts from the CEFIC membership	5,000	Estimations by Market Experts from the CEFIC membership
API brokers	5,000	Estimations by Market Experts from the CEFIC membership	25,000	Estimations by Market Experts from the CEFIC membership
Average hourly wage + Standard Overhead (25%)	€ 23.45	Eurostat	€1.25 - Based on the average Chinese wage rate	YDL Management Consultants
Time taken to complete notification form	1 to 3 hours - the median figure of 2 hours is used for purposes of this quantification	Europe Economics estimation	1 to 3 hours - The median figure of 2 hours is used for purposes of this quantification	Europe Economics estimation
Direct business cost - Fixed	**€ 286,090**	€(600+500+5000)*23.45*2	€ 112,500	€(15,000+5000+25,000)*1.25*2

Direct business cost - Running	**€ 28,609**	Assuming new entrants enter at a rate of 10% of the market per year	€ 11,250	Assuming new entrants enter at a rate of 10% of the market per year
NPV	**€ 527,416**		€ 207,397	

5.4.6 Note that this is a one off cost for firms that remain in the sector. After the first year of policy implementation this cost will only fall on new entrants. The calculations assume that 10 per cent of the market is made up of new entrants and the costs that they face in terms of completing the notification constitute the running costs.

5.4.7 This reasonably small business cost would be classified as an administrative burden under the EC's Standard Administrative Cost model.

5.4.8 The cost would be equally spread across the sector and amount to a relatively small additional burden for each firm so that no major downstream effects are likely.

5.4.9 Note, however, that the EMEA will require resources to run the website. It has been estimated that a EudraGDP database (i.e. GDP certificates and Wholesale licences) would cost approximately €1m, if the format and procedure for issuing GDPc and WL are similar to GMPc and MIA. EMEA will require resources of a similar magnitude to establish the website that is proposed here. If the cost of this were recovered from business, it would add to the direct business costs (but not the administrative costs as per the SACM).

Enhancing audit and enforceability of GMP (Reference 4.3.2)

Policy 4.3.2(a)

5.4.10 There are three policy options considered under 4.3.2. The first of these states:

> "Make regular audits of active substance suppliers on GMP compliance by manufacturers and importers of medicinal products mandatory. Auditors should be sufficiently qualified".

5.4.11 This policy option requires that finished pharmaceutical product manufacturers in the EU audit their API suppliers to ensure that their facilities meet EU GMP standards. It is also required that importers into the EU of finished pharmaceutical products ensure that the non-EU finished pharmaceutical product manufacturers who are supplying to them audit the API manufacturing facilities used in the production of these products to ensure that these API manufacturing facilities meet EU GMP standards. Importers, thus, would not directly carry out API audits themselves but have a responsibility to ensure that their suppliers do.

5.4.12 The direct business cost of this policy is the cost per audit multiplied by the number of finished pharmaceutical product manufacturers in the EU and multiplied again by the average number of API suppliers per finished product manufacturer. There are different possibilities in terms of auditing with different associated costs and benefits. These are considered in the table of costs below.

5.4.13 A 'third party audit' involves an audit team external to the finished pharmaceutical product manufacturers or importers conducting the audit on their behalf, while a 'shared third party audit' involves the sharing of such audit information between manufacturers or importers who use the same API supplier. The 'self-assessment audit' option involves the API manufacturers auditing themselves but this is unlikely to be wholly satisfactory. Further details of such auditing options, including on the scope that they offer for cost reductions to businesses can be found in APIC literature.[51]

5.4.14 Importers of finished pharmaceutical products would be required to ensure that finished pharmaceutical product manufacturers outside the EU from whom they are buying product have conducted such API audits. It is assumed here that the costs of these audits would be passed on to importers of finished pharmaceutical products into the EU.

5.4.15 Details of the sources and calculation summarised in the table below are provided in the Active Ingredients Annex.

[51] http://www.api-compliance.org/APIC_Audit_Programme.pdf

Table 5.16: Direct Business Cost of API Audit Policy Option under 4.3.2.

	In the EU	Information source
Number of pharmaceutical manufacturers and importers	15,000	EMEA
Cost of audit - If conducted by pharmaceutical manufacturers themselves	€ 10,000	AESGP, EAEPC, EGA
Cost of being audited – the wage cost of 2 people for 2 days (+ 25% uplift)	€ 704	Eurostat
Average number of API suppliers per pharmaceutical manufacturer	Estimates range from 25 to 200 for this figure, so the median between these two figures of 112.5 is used for this calculation	Consultation with industry
Direct business cost (if compliance achieved entirely by Third Party Audit) - All manufacturers audit all suppliers themselves	€ 18,062,156,250	
Cost per Third Party APIC audit	€ 8,400	APIC
Direct business cost (if compliance achieved entirely by Third Party Audit) - All manufacturers audit all suppliers by Third Party audit	€ 15,362,156,250	
Shared Third Party APIC audit	€ 2,300	APIC
Direct business cost (if compliance achieved entirely by Shared Third Party audit) - Auditors share information about suppliers amongst manufacturers	€ 5,068,406,250	
Self Assessment APIC audit	€ 4,200	APIC
Direct business cost (if compliance achieved entirely by Self Assessment audit)	€ 8,274,656,250	
Gross direct business cost (based on Third Party Audit and Shared Third Party Audit making up 1% each of total audits)	€ 17,905,218,750	Assumption on incidence of Third Party Audit and Shared Third Party Audit based on industry consultation
High estimate of net direct business cost (gross direct business cost minus proportion of these costs suspected as already being met) - Rolling Annual Cost	€2,395,598,901	High estimate of current compliance based on estimate of volume of EU pharmaceuticals produced by SMEs in generic and OTC sectors.

	In the EU	Information source
Low estimate of net direct business cost (gross direct business cost minus proportion of these costs suspected as already being met) - Rolling Annual Cost	Zero	Low estimate of current compliance based on full current compliance (as claimed by some in industry)
Direct Business Cost (Median between low and high estimate)	**€ 1,197,799,450**	
NPV - based on a median direct business cost between the low and high estimates	**€10,103,835,566**	

5.4.16 There is a view that current non-compliance with this policy is most prevalent amongst SMEs in the generic sectors of the pharmaceutical finished product manufacturing industry. This view is reflected in the high estimate of the net direct business cost shown above. There is an opposing view that holds that current compliance is already almost universal and this view is reflected in the low estimate of net direct business cost. Clearly the extent of business cost that would be faced in reality if this policy were to be introduced depends upon which of these views is the more accurate.

5.4.17 If it is the case that SMEs in generic sectors of the pharmaceutical finished product manufacturing industry are often currently non-compliant, then these firms would face significant additional costs, as the table above clearly illustrates. Costs of this magnitude might be expected to have not inconsiderable downstream effects.

5.4.18 Eurostat indicates that there are 3700 finished pharmaceutical product manufacturers in the EU. This would suggest that of 15,000 importers and manufacturers of finished pharmaceutical product recorded on the EudraGMP, 11,300 are importers of finished pharmaceutical product. Thus, the direct business cost to EU business here may fall proportionately upon importers of finished pharmaceutical product. The Annex explains how these costs may break down between manufacturers based in the EU and importers.

Policy 4.3.2(b)

5.4.19 The second of the policy options to be considered under 4.3.2 states:

> Require, where scientifically feasible, control of active substances via sufficiently discriminating analytical techniques, such as fingerprint technologies, Near Infrared Spectroscopy (NIR), as a mandatory method for identification by the manufacturer of the medicinal product. Such a testing is meant to identify deviations of the manufacturing process and manufacturing site for each batch.

5.4.20 This policy requires that finished pharmaceutical product manufacturers conduct a sufficiently discriminating inspection on each batch of API that arrives at their production facilities to ensure that this API has been produced where the finished pharmaceutical product manufacturers understood that it would be.[52] This policy guards against impurities entering the API via an unexpected change in its location of manufacture, and is thus directly relevant to detecting possible counterfeits. It would be possible to comply with this policy with technologies other than NIR but the costs here have been calculated on the basis that all firms use NIR technology to become compliant.

5.4.21 The fixed cost below is equal to the number of finished pharmaceutical product production sites multiplied by the cost of the NIR technology. Testing would go down to the API batch level, so the running cost is equal to the number of API batches in the EU each year multiplied by the wage cost for the amount of time it takes to apply each NIR test.

5.4.22 If the policy were introduced on a risk-based basis then captive supplies (from API manufacturers directly owned or controlled by pharmaceutical manufacturers) may expect to be exempt from the policy and this is considered below. It may also be that net costs can be reduced further if NIR testing can supersede testing that is currently done. The extent to which this is the case may depend upon what testing is required by regulation and which testing method has been approved in the marketing authorisation.

5.4.23 This net cost below, thus, assumes that captive supplies will be exempt from this policy. However, it is assumed in this net cost calculation that all manufacturers will make at least some purchases on the merchant API market and so will have to meet the fixed cost (i.e. the cost of the NIR technology itself). The net cost (with captive supplies exempt) is only net, therefore, of running costs that are associated with the total volume of API that is accounted for by the captive market.

5.4.24 Net costs here are not insignificant as NIR technology would not seem to be widely used presently and it may even be that the industry is not as alive to the issue which this policy option (and the use of NIR technology) seeks to address as they might be.

[52] For an illustration of the problems that can be associated with this, please see Frank Wienen et al, "Composition and Impurity Profile of Multisource Raw Material of Gentamicin – a Comparison", *Pharmeuropa*, Vol. 15, No. 2, April 2003

Table 5.17: Direct Business Cost of NIR Policy Option under 4.3.2.

	In the EU	Information source
Cost of NIR technology	Price quotations of €25,000 - €200,000 have been given. A figure of €100,000 is used here.	Consultation with industry
Number of finished pharmaceutical product production sites	7,000	EMEA
Number of batches of API (per year)	800,000	Europe Economics analysis of past report by Chemical Pharmaceutical Generic Association
Number of batches of API (per year) - Net of captive supplies	345,000	Europe Economics analysis of past report by Chemical Pharmaceutical Generic Association
Cost per NIR testing (i.e. one hour of average hourly wage)	€ 23.45	Eurostat
Gross Direct Business Cost - Fixed	€ 700,000,000	
Gross Direct Business Cost - Running	€ 18,760,000	
Direct Business Cost - Net of captive supplies - Fixed	**€ 700,000,000**	
Direct Business Cost - Net of captive supplies - Running	**€ 8,090,250**	
NPV - Based on Direct Business Cost - Net of captive supplies	**€ 768,243,942**	

5.4.25 One downstream effect may be an increase in employment in firms that produce NIR technologies but pharmaceutical manufacturers may switch into captive supplies to avoid the costs that are associated with becoming compliant with this policy. This switch would do nothing to reduce the total size of the API sector in the EU but may result in some churn within the sector to the effect that the merchant sector is smaller than it otherwise would be.

Policy 4.3.2 9 (c)

5.4.26 The third policy to be considered under 4.3.2 states:

> Turn principles of good manufacturing practice for active substances placed on the Community market into a legal act of Community law (e.g. a Commission Directive) in order to enhance enforceability.

5.4.27 EU GMP standards on API currently only have the legal force of EC guidance. The legal and policy approach of Member States to guidance is variable. This policy option would increase the legal status of GMP standards on API into an EC Directive.

5.4.28 The calculations below are based on information that has come into Europe Economics on the proportion of an API manufacturers costs that are made up of costs associated with becoming GMP compliant, the size of the EU API market in value terms and what proportion of this market is known to be serviced by EU manufacturers and non-EU manufacturers, as well as analysis of EDQM inspection results and assumptions about the profit margins held by EU and non-EU based API manufacturers.

Table 5.18: Direct Business Cost of giving EU GMP standards on API the legal force of an EC Directive under Policy Option 4.3.2.

API manufacturers	In the EU	Information source	Supplying to the EU from outside	Information source
Number	500-700 estimated by CEFIC. 810 basic pharmaceutical product manufacturers are recorded under the NACE category of dg2441. It seems reasonable to assume that while not all of these basic pharmaceutical product manufacturers will be API manufacturers the majority will be so. 600, therefore, seems a reasonable figure for this calculation.	Estimations by Market Experts from the CEFIC membership/Eurostat	15,000	Estimations by Market Experts from the CEFIC membership
Market Non-compliance measure (estimated addition to total costs in sector for full compliance)	0%	Europe Economics analysis of EDQM inspection reports	15%	Europe Economics analysis of EDQM inspection reports and IBM research
Gross direct business cost	€0.36bn		€0.81bn	
Net direct business cost (gross direct business cost minus proportion of these costs suspected as already being met) - Rolling Annual Cost	**Zero**		**€0.48bn**	Current level of compliance estimated based on Europe Economics analysis of EDQM inspection reports and IBM research
NPV - Based on net direct business cost	**Zero**		**€4.01bn**	

5.4.29 EDQM inspection results suggest a striking difference in GMP compliance between API manufacturers based in the EU and those based outside. Consequently, EU based API manufacturers have found it hard to compete with non-EU based API manufacturers for market share in EU. Indeed, it is claimed by industry representatives that EU API manufacturers often find it easier to gain market share in the USA where regulation makes it harder for non-GMP compliant API manufacturers to undercut them. The USA has, therefore, created a “level playing field” for GMP compliant API manufacturers and

the effect of this policy would be to create such a “level playing field” in the EU. This can be expected to increase jobs and growth amongst the EU API manufacturing sector.

5.4.30 This effect would be compounded by the removal of the current disadvantage that EU API manufacturers (assuming that they are GMP compliant) face relative to non-EU API manufacturers (assuming that they are less GMP compliant than their EU competitors) in terms of compliance with “variation regulations”.

Enhancing GMP inspections (Reference 4.3.3).

5.4.31 There are three policy options under 4.3.3. These are:

(a) The competent authority may carry out announced or unannounced inspections of active substance manufacturers in order to verify compliance with the principles of good manufacturing practice for active substances placed on the Community market.

(b) The competent authority shall carry out these inspections if there is suspected noncompliance with GMP.

(c) The competent authority shall carry out repeated inspections in the exporting country if the third country applies standards of good manufacturing practice not at least equivalent to those laid down by the Community or if mechanisms for supervision and inspections are not at least equivalent to those applied in the Community. To this end, a Member State, the Commission or the Agency shall require a manufacturer established in a third country to undergo an inspection.

5.4.32 As these policy options are understood, they have exactly the same cost implications for business and are, therefore, all captured in the table below. The net cost for inspections outside the EU acknowledges that to some degree such inspections are already taking place but considers the policy options to constitute an extension of such inspections beyond what is presently done.

Table 5.19: Direct Business Cost of 4.3.3.

	In the EU	Information source	Supplying to the EU from outside - Based on EU inspectors inspecting outside EU	Information source	Supplying to the EU from outside - Based on non-EU inspectors inspecting in their home countries
API manufacturers	500-700 estimated by CEFIC. 810 basic pharmaceutical product manufacturers are recorded under the nace category of dg2441. We think it reasonable to assume that while not all of these basic pharmaceutical product manufacturers will be API manufacturers the majority will be so. 600, therefore, seems a reasonable figure for this calculation.	Estimations by Market Experts from the CEFIC membership/Eurostat	15,000	Estimations by Market Experts from the CEFIC membership	15,000
Cost of inspection	800 –1200 € /day/inspector - A figure of €1000 is used for purposes of this quantification	Based on consultation with EU regulators	800 –1200 € /day/inspector – A figure of €1000 is used for purposes of this quantification	Based on consultation with EU regulators	Assume €50 per inspector per day
Average expense for inspector per inspection (travel, accommodation, food)	€ 400	Based on consultation with EU regulators	€ 5,000	Based on consultation with EU regulators	Assume €20
Cost of being inspected – The wage cost of 2 people for 2 days (+ 25% uplift)	€ 704	Eurostat	Assume $38		Assume $38
Frequency of inspection	At least once every three years		At least once every		At least once

	In the EU	**Information source**	**Supplying to the EU from outside - Based on EU inspectors inspecting outside EU**	**Information source**	**Supplying to the EU from outside - Based on non-EU inspectors inspecting in their home countries**
			three years		every three years
Gross Direct Business Cost (based on 2 man inspection days per inspection)	€ 700,800		€ 60,190,000		€ 890,000
Net Direct Business Cost	**Zero**		**€ 54,171,000**		€ 801,000
NPV	**Zero**		**€ 456,950,349**		€ 6,756,701

5.5 The initial impact cost of the package as a whole

Table 5.20: Initial impact cost summary

Policy proposal	Notes	Direct business cost - Fixed - To EU business - In €millions to one decimal place	Direct business cost - Running - To EU business - In €millions to one decimal place	NPV in €bn to one decimal place -high	NPV in €bn to one decimal place - low
4.1.1					
(a) Apply wholesaler obligations to all parties in the distribution chain		2.3	1.2	0.0	0.0
b(i) Mandatory GMP audit of contract manufacturers	Accept third party audits (Audit firm)	Zero	26.5		0.2
	Accept third party audits (Manufacturer)	Zero	27.5		
	Do not accept third party audits	Zero	1376.0	11.6	
b(ii) Mandatory GDP supplier audit	Accept third party audits (Audit firm)	Zero	9.1		0.0
	Accept third party audits (Manufacturer)	Zero	13.3		
	Do not accept third party audits	Zero	1408.0	11.9	
4.1.2					
(a) Apply compilation of Community procedures to all		Zero	19.3	0.2	0.2

Policy proposal	Notes	Direct business cost - Fixed - To EU business - In €millions to one decimal place	Direct business cost - Running - To EU business - In €millions to one decimal place	NPV in €bn to one decimal place -high	NPV in €bn to one decimal place - low
GMP and GDP inspections					
(b) GMP FP Inspections in third countries		Zero	18.7	0.2	0.2
4.1.3					
Seal packs with a ban on repackaging	All prescriptions	Zero	522.0	4.4	
	Risk-based	Zero	232.0		2.0
4.1.4					
Batch tracking e-pedigree	No retail authentication	20.0	Zero		0.0
	Retail authentication	20.0	4.7	0.1	
4.1.5					
Pack based mass serialisation	Total	2370.0	450.0	6.2	
	Total assuming full roll-out by patented pharmaceutical manufacturers in base case	1659.0	315.0		
	Risk-based	711.0	135.0		
	Risk-based assuming full roll-out by patented	Zero	Zero		0.0

Policy proposal	Notes	Direct business cost - Fixed - To EU business - In €millions to one decimal place	Direct business cost - Running - To EU business - In €millions to one decimal place	NPV in €bn to one decimal place -high	NPV in €bn to one decimal place - low
	pharmaceutical manufacturers in base case				
(a) Last wholesaler level authentication		300.0	594.8	5.3	
(b) Retail level authentication		Zero	45.5		0.4
4.1.6					
Community database of wholesalers		1.0	0.1	0.0	0.0
Sub-total: Traceability (4.1.1. - 4.1.6.)				39.8	2.9
4.2.1					
Prohibit all transit trade (revenue and employment costs, not direct business)		Zero	4,651.0	*	
4.2.2					
Apply import regulations		11.2	626.5 - 743.5	6.3	5.3
Transit total (4.2.2)				6.3	5.3
4.3.1.					
Notification procedure		0.3	<0.1	0	0
4.3.2					
Mandatory Audit		1,198 each year	1,198 each year	10	10
Control of API - NIR		700	8	0.8	0.8
GMP as Directive		Zero	Zero		
4.3.3.					
Inspections		Zero	Zero		

Policy proposal	Notes	Direct business cost - Fixed - To EU business - In €millions to one decimal place	Direct business cost - Running - To EU business - In €millions to one decimal place	NPV in €bn to one decimal place -high	NPV in €bn to one decimal place - low
API total (4.3.1. - 4.3.3)				10.8	10.8
TOTAL				**€51**	**€19**

** = cost not considered in total*
The final costs consolidated in this table appear in bold throughout the individual cost tables for each policy option

5.6 Second round effects

5.6.1 We turn now to the second round effects of those policy measures that bear upon the supply chain of medicines to EU consumers (i.e. all except measure 4.2.2, whose second round effects have already been discussed.) This section reports on some analysis that has been carried out in order to estimate:

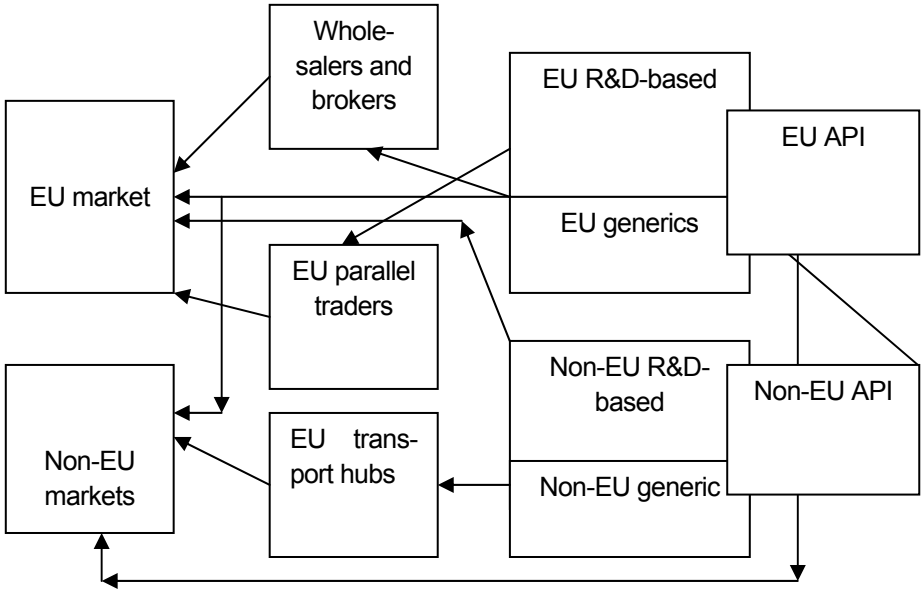
(a) whether, and to what extent, the policies would affect the competitive position of EU producers[53]

(b) how they might be expected to affect the price of medicines in the EU.

5.6.2 Some relevant linkages in the pharmaceutical supply chain are shown below. The focus of interest here are the interactions between the EU and non-EU producers: in active pharmaceutical ingredients (APIs), in R&D-based medicines and in generic medicines.

[53] European Commission, *Impact assessment guidelines*, 15 June 2005, with March 2006 update), SEC(2005)791.

Chart 5.1



5.6.3 A profile of the EU pharmaceutical industry is shown in Table 5.21. The API producers fall within NACE 24.41, Basic pharmaceutical products. The R&D-based and generic producers are included within NACE 24.42, Pharmaceutical preparations.

Table 5.21: Turnover, value added and employment in the medicines supply chain, EU-27, 2005

NACE	Description	Turnover	Value added at factor cost	Employees
		€ million	€ million	
24.41	Basic pharmaceutical products *	10,000	5,000	66,000
24.42	Pharmaceutical preparations	170,000	60,000	524,000
51.46	Wholesale of pharmaceutical goods	259,000	35,000	439,000
52.31	Dispensing chemists	138,000	31,000	666,000
Source: Eurostat. * Derived by subtracting 24.42 from 24.4, Pharmaceutical products				

5.6.4 The points of interest here are:

(a) Where along the supply chain (API manufacturers, finished product manufacturers, wholesalers, and pharmacists) would the costs fall?

(b) How would these costs affect the competitiveness of the EU's industries, and hence the numbers of people they employ? Insofar as the costs would bear unequally as between EU producers and their foreign counterparts, there would be changes in market shares.

(c) What would we expect the supply chain to *do* with these costs: would they pass them all though to the users (the national healthcare organisations that bear most of the costs of medicines), or would they be forced, by competitive pressures from outside the EU, to absorb them to some degree?

(d) To what extent would the increase in the price of medicines affect the EU's use of medicines?

5.6.5 The additional costs that would be borne by non-EU producers have relevance, too. Although of no *direct* concern to the EU, they would push up the price of medicines in the EU market, reducing the welfare of EU consumers.

5.6.6 The table 5.22 calculates the total annual costs of the policies (converting the one-off costs into an equivalent annual cost), and apportions them along the supply chain. It also notes whether they bear on EU or on non-EU producers.

Table 5.22: Total cost to the EU supply chain (€ million)

		One-off costs	Annual costs	Annuitised one-off costs *	Total annual costs
API manufacturers					
EU		0	0	0	0
Non-EU		0	530	0	530
Finished product manufacturers:					
EU	Minimum	700	1,780	110	1,890
	Maximum	3,070	5,270	500	5,760
Non-EU		0	850	0	850
Wholesalers, brokers and traders	Minimum	0	0	0	0
	Maximum	300	600	50	650
Retailers	Minimum	40	50	10	60
	Maximum	20	0	0	10
General: EU		0	20	0	20
General: non-EU		0	20	0	20
Total	Minimum	740	3,250	120	3,370
	Maximum	3,390	7,280	550	7,840
Total costs falling on EU producers	Minimum	740	1,850	120	1,970
	Maximum	3,390	5,890	550	6,430

* 16 per cent of the one-off costs. This would be the cost of an equivalent ten-year annuity, at an interest rate of 10 per cent (industry's estimated weighted average cost of equity and debt).

5.6.7 Three important features of this picture are that:

(a) most of the costs of the policies would fall on the finished product manufacturers;

(b) in the API sector, the policies would impose costs on non-EU API manufacturers but not on their EU competitors;

(c) in finished products, the policies would impose greater costs on the EU manufacturers than on their non-EU competitors.

5.6.8 The costs that would fall directly on the EU's supply chain would be equivalent to between 1.0 per cent and 3.3 per cent of the EU's estimated expenditure on medicines.

Table 5.23: Total costs of measures falling on EU supply chain, as a proportion of the EU's estimated expenditure on medicines

	One-off costs	Annual costs	Annuitised one-off costs	Total annual costs
	€ million	€ million	€ million	€ million
Minimum	700	1,800	100	2,000
Maximum	3,400	5,900	600	6,400
Estimated EU expenditure on medicines (at retail prices), 2007				196,000
Total costs of measures, as proportion of this expenditure				
Minimum				1.0%
Maximum				3.3%

5.6.9 This does not necessarily mean that retail prices in the EU would increase by this amount. They could rise by *more* than this. As already noted, some of the additional costs that would be borne by non-EU producers would be passed through into higher prices in the EU market; and gross profit would also be added in the supply chain. Wholesalers and pharmacists enjoy a natural protection from international competition, due to their advantages of location. They would therefore be able to pass through increases in ex-factory prices, as well as the costs of the policies that fall directly on them, plus their usual profit margins.

5.6.10 On the other hand, competition from non-EU producers could be expected to limit the extent to which EU manufacturers would pass on the additional costs. To understand these price impacts, as well as the employment consequences for the EU, some simulations were undertaken.

Simulating competitive outcomes

5.6.11 The simulations make a distinction between, on the one hand, the producers of differentiated products (the in-patent medicines), and on the other, the producers of homogeneous products (APIs and generics).

5.6.12 The producers of in-patent medicines have much higher overheads, and need higher gross margins to cover them. Prices are between four and five times the cost of goods. Their markets are highly segmented into narrowly defined therapeutic categories, within which there are comparatively few competing producers. For example, in a study of competition in the supply of the first-generation anti-infective drug called cephalosporin, there were just four suppliers, offering close therapeutic substitutes [54]. We assume that there are four producers per therapeutic category. The simulations suggest that their market shares are not hugely sensitive to changes in their unit costs of production, relative to those of their foreign competitors.

5.6.13 The modelling suggests that the policies would have the following impacts:

(a) The price of in-patent medicines in the EU would be pushed upwards very slightly, by between 0.4 and 1.6 per cent;

(b) Employment in the innovative sector would fall by between 0.3 and 1.5 per cent, or by between 1,300 and 6,500.

5.6.14 In the API market, there are many more suppliers of each product category. We assume 30 (but the outcomes are not very sensitive to this). The measures directed at APIs (4.3.2(b) and 4.3.3) would together raise the unit operating cost of non-compliant API producers by about 17 per cent. We estimate that one-sixth of the non-EU suppliers to the EU market are currently wholly non-compliant and we assume that the other five-sixths are compliant to varying degrees, ranging up to fully compliant. Thus, the measures would force up the costs of the wholly non-compliant one-sixth by 17 per cent, and of the rest by between zero and 17 per cent – an average of 9 per cent. These producers are understood to account for a major share of the EU market, so these additional costs would push up prices in the EU API market.

5.6.15 Our simulations of the interplay between the EU and non-EU producers suggest that prices would rise by about four per cent, adding €700 million a year to the costs of the EU finished product manufacturers.

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[54] Sara Ellison, Iain Cockburn, Zvi Grilliches and Jerry Hausman, *Characteristics of demand for pharmaceutical products: an examination of four cephalosporins*, Rand Journal of Economics, Vol. 28, No. 3, Autumn 1997, pp. 426-446.

5.6.16 The additional costs falling on the non-EU API manufacturers would, of course, improve the competitive position of the EU API producers. Indeed, it is precisely that source of competition that would discourage the non-EU producers from passing on more than about one-half of the increase in their costs. We estimate that the EU API producers would increase production by 7 per cent, taking on 3,600 employees.[55]

5.6.17 In generics, imports are assumed to account for 25 per cent of the EU market (the estimated average for all Finished Products). In this case, we set up the model with 24 producers, of which 18 are EU producers. Policy 4.3.2 (a) would push up the unit cost both of the EU generic producers and of the non-EU producers supplying the EU, by 14 per cent. The other measures would add to the costs of the EU generic producers by between two and twelve per cent to their unit costs, without affecting the non-EU producers at all.

5.6.18 The effect on prices of the competitive interactions in these three markets are shown in Table 5.24: the retail price of medicines as a whole would rise by between 1.5 per cent and 3.4 per cent – an amount that is not very different to the crude cost comparison in Table 5.25.

Table 5.24: Impact of measures on the price of medicines in the EU

APIs		3.7%
In-patent medicines	Minimum	0.4%
	Maximum	1.6%
Generics	Minimum	7.6%
	Maximum	11.1%
All medicines, ex-factory	Minimum	1.6%
	Maximum	3.2%
All medicines, retailed	Minimum	1.5%
	Maximum	3.4%

5.6.19 The employment effects are brought together in Table A5. The EU would lose between 13,000 and 25,000 jobs. They include the expected loss of 2,800 EU jobs that would result from measures to deal with the transit and import-export trades in medicines, and the loss of jobs in parallel trading.

[55] Assuming that three-quarters of those who are employed in NACE 24.41 (70,000 in 2004) were engaged in API production.

Table 5.25: Impacts on EU employment

	EU employment (2005)	Change in volume		Implied change in employment	
		Minimum costs	Maximum costs	Minimum costs	Maximum costs
Basic pharmaceutical products (NACE 24.41)(1)	66,000				
of which API manufacture	49,500	7.3%	7.3%	3,600	3,600
Pharmaceutical preparations (NACE 24.42)	524,000	-0.5%	-1.9%	-2,400	-10,100
of which:					
innovative sector	434,900	-0.3%	-1.5%	-1,300	-6,500
generic sector	89,100	-1.3%	-4.0%	-1,200	-3,600
Wholesale of pharmaceutical goods (NACE 51.46)	439,000				
of which estimated to be in EU supply chain (1)	259,200	-0.2%	-0.6%	-500	-1,500
Import-export				-2,800	-2,800
Parallel trading				-10,000	-10,000
Pharmacists (NACE 52.31)	666,000	-0.2%	-0.6%	-1,200	-3,800
Net impact on employment				-13,400	-24,600

5.6.20 The impact of the policies on the demand for medicines is shown in Table 5.26.

Table 5.26: Impact of the policies on the demand for medicines in the EU

	Minimum	**Maximum**
Impact on prices	1.5%	3.4%
Price elasticity of demand		
-0.2	-0.3%	-0.7%
-0.5	-0.8%	-1.7%
-1.0	-1.5%	-3.4%

5.6.21 The implication of this is that, if the demand for medicines is not sensitive to price (i.e. a price elasticity of demand of -0.2 - see discussion in Section 5 of the value of the benefits to health - the policies would lead to a reduction in the use of medicines in the EU of about one-half of a per cent. The simulation results were consistent with a price elasticity of demand for medicines of -0.2

5.7 The Commission's Standard Administrative Cost Model

5.7.1 The following table presents estimates of the incremental administrative costs that would result from the package of policies under consideration. The definition of administrative costs used in this model does not include the costs for business or consumers of complying with any new policies but only the cost of providing information about them to the authorities.

Table 5.27: The EC's Standard Administrative Cost Model

Additional administrative costs of Policy Options designed to tackle counterfeit medicines in the legitimate supply chain.				**Tariff (€ per hour)**		**Time (hour)**		**Price (per action or equip)**	**Freq (per year)**	**Nbr of entities**	**Total nbr of actions**	**Total cost**	**Regulatory origin (%)**				**Notes**
Policy option in IA	**Type of obligation**	**Description of required action**	**Target group**	**i**	**e**	**i**	**e**						**Int**	**EU**	**Nat**	**Reg**	
4.1.1(a)	GDP inspection by competent authorities	Familiarising with the information obligation, completing application form(s) and accompanying inspectors during initial inspection (**existing firms**)	Brokers, agents and traders not licenced or inspected at present	23.45		15.25		357.61	*1.00*	1000	1,000	357,613		100%			
4.1.1(a)	GDP inspection by competent authorities	Familiarising with the information obligation, completing application form(s) and accompanying inspectors during initial inspection (**new entrants**)	Brokers, agents and traders not licenced or inspected at present	23.45		15.25		357.61	1.00	200	200	71,523		100%			
4.1.1(a)	GDP inspection by competent authorities	Familiarising with the information obligation, completing form(s) and accompanying inspectors during inspection	Brokers, agents and traders not licenced or inspected at present	23.45		11.25		263.81	0.33	1,000	333	87,937		100%			
4.1.1(b)i	GMP audit of contract manufacturers (accept third-party audits)	Familiarising with the information obligation, completing forms and accompanying auditors	Contract manufacturers	23.45		30.00		703.50	0.13	2,000	267	187,600		100%			
4.1.1(b)i	GMP audit of contract manufacturers (do not accept third-party audits)	Familiarising with the information obligation, completing forms and accompanying auditors	Contract manufacturers	23.45		30.00		703.50	0.13	100,000	13,333	9,380,000		100%			

Additional administrative costs of Policy Options designed to tackle counterfeit medicines in the legitimate supply chain.				**Tariff (€ per hour)**		**Time (hour)**		**Price (per action or equip)**	**Freq (per year)**	**Nbr of entities**	**Total nbr of actions**	**Total cost**	**Regulatory origin (%)**				**Notes**
Policy option in IA	**Type of obligation**	**Description of required action**	**Target group**	**i**	**e**	**i**	**e**						**Int**	**EU**	**Nat**	**Reg**	
4.1.1(b)ii	GDP audit of suppliers (accept third-party audits)	Familiarising with the information obligation, completing forms and accompanying auditors	Suppliers	23.45		15.00		351.75	0.33	6,300	2,100	738,675		100%			
4.1.1(b)ii	GDP audit of suppliers (do not accept third-party audits)	Familiarising with the information obligation, completing forms and accompanying auditors	Suppliers	23.45		15.00		351.75	0.33	665,000	221,667	77,971,249		100%			
4.1.2(a)	Apply CoCP to all GMP and GDP inspections (new GDP inspections)	Familiarising with the information obligation, completing form(s) and accompanying inspectors during inspection	Suppliers	23.45		22.50		527.63	1.00	3,000	3,000	1,582,875		100%			
4.1.2(a)	Apply CoCP to all GMP and GDP inspections (existing GDP inspections)	Familiarising with the information obligation, completing form(s) and accompanying inspectors during inspection	Suppliers	23.45		7.50		175.88	1.00	3,200	3,200	562,800		100%			
4.1.2(a)	Apply CoCP to all GMP and GDP inspections	Familiarising with the information obligation, completing form(s) and accompanying inspectors during inspection	Brokers, agents and traders not licenced or inspected at present	23.45		16.88		395.72	1.00	333	333	131906		100%			
4.1.2(b)	GMP inspection in third countries	Familiarising with the information obligation, completing form(s) and accompanying inspectors during inspection	Non-EU finished product manufacturers	1.25		45.00		56.25	0.33	1,600	533	30,000		100%			

Additional administrative costs of Policy Options designed to tackle counterfeit medicines in the legitimate supply chain.				**Tariff (€ per hour)**		**Time (hour)**		**Price (per action or equip)**	**Freq (per year)**	**Nbr of entities**	**Total nbr of actions**	**Total cost**	**Regulatory origin (%)**				**Notes**
Policy option in IA	**Type of obligation**	**Description of required action**	**Target group**	**i**	**e**	**i**	**e**						**Int**	**EU**	**Nat**	**Reg**	
4.2.2	GDP inspection for suitable premises	Familiarising with the information obligation, completing form(s) and accompanying inspectors during inspection	Importers for re-export	23.45		7.00		164.15	0.30	3,336	1,112	182,535		100%			
4.2.2	Obtain licence to import medicines from third countries	Familiarising with the information obligation and completing form	Importers for re-export	23.45		3.00		70.35	*1.00*	3,336	3,336	234,688		100%			Notification of (specific) activities Familiarising with the information obligation
4.3.1	Requirement of mandatory notification procedure for manufacturers/importers of active substances	Completing form	API manufacturers and importers	23.45		2.00		46.9	*1.00*	6,100	6,100	286,090		100%			
4.3.2.(a)	GMP audit of API manufacturers	Familiarising with the information obligation, completing forms and accompanying auditors	Finished product manufacturers and importers	23.45		30.00		703.5	1.00	15,000	1,687,500	1,187,156,250		100%			Number of actions is the number of pharmaceutical manufacturers and importers (15,000) multiplied by the average number of API suppliers each (112.5)
4.3.3.	GMP inspection of API manufacturers	Familiarising with the information obligation, completing application form(s) and accompanying inspectors during	API manufacturers	23.45		30.00		703.5	0.33	600	600	422,100		100%			Non-labelling information for third parties Adjusting existing data

Additional administrative costs of Policy Options designed to tackle counterfeit medicines in the legitimate supply chain.				**Tariff (€ per hour)**		**Time (hour)**		**Price (per action or equip)**	**Freq (per year)**	**Nbr of entities**	**Total nbr of actions**	**Total cost**	**Regulatory origin (%)**				**Notes**
Policy option in IA	**Type of obligation**	**Description of required action**	**Target group**	**i**	**e**	**i**	**e**						**Int**	**EU**	**Nat**	**Reg**	
		initial inspection															

Total administrative costs (€) **1,279,383,840**

Administrative costs by origin (€) EU 100%

Regulatory act refers to legislative and statutory acts

For the reference of the proposal / act, use EU-Lex format (‘cut and paste’ of the reference given by http://europa.eu.int/eur-lex/lex/RECH_menu.do?ihmlang=en).

No. = gives a number for each action.

Ass. Art.= article and § detailing the obligation assessed on that line.

Orig. Art. = if the act assessed is the transposition of an act adopted at another level, insert here the article and § of the 'original' act corresponding to the obligation assessed on that line (for ex., article of the EC directive at the origin of one specific obligation imposed by national law)

i = internal tariff (administrative action carried by the enterprise itself). e = external tariff (administrative action contracted out).

Price per action = (TAi*TIi) + (TAe*TIe). Total Nbr of actions = Frequency * Number of entities. Total cost per action = P*Q.

For equipment, yearly cost based on the depreciation period must be put in the ‘price’ column; the ‘tariff’ and ‘time’ columns must be left empty column

For one-off costs, put '1' in the frequency column in italics

When the act amends existing provisions and diminishes the number of hours or frequency, negative figures corresponding to the burden reduction should be typed in the corresponding columns

5.8 The possible benefits of the package as a whole

Valuing the benefits of health treatments

An approach based on possible loss of life

5.8.1 With regard to the potential benefits from the possible new policies, as far as is known there have been no reported cases of fatalities in the EU/EEA as a result of counterfeit medicines.

5.8.2 In order to quantify potential benefits for the purpose of the Impact Assessment a pessimistic view might be taken of what might happen if incidents such as those reported in less developed parts of the world were to occur in the EU, and the values for a statistical life suggested in the EC IA guidelines are assumed.

5.8.3 The most pessimistic scenario considered was one in which counterfeit medicines that would have been prevented by the new policies results in 10,000 deaths in the EU. Other scenarios had smaller numbers of deaths.

5.8.4 The computed values for benefits are shown in Table 5.25 below, under alternative values of a statistical life.

Table 5.28: Benefits (€m p.a.)

Scenarios	Assumed value of statistical life:		
	€0.65m	**€1m**	**€2.5m**
50 people affected	32.5	50	125
100 people affected	65	100	250
300 people affected	195	300	750
3000 people affected	1,950	3,000	7,500
10,000 people affected	6,500	10,000	25,000

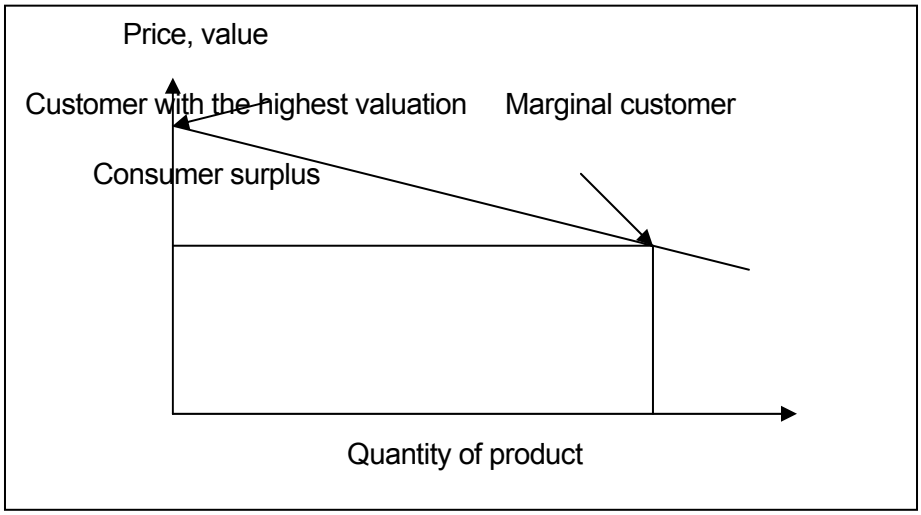
Valuing the benefits of health treatments

5.8.5 An expenditure approach, based on consumer surplus

5.8.6 An alternative approach to valuing the benefits appeals to the concept of "consumer surplus". At the time at which customers buy a product or service, the value that they place on it is *greater* than the price that they pay for them. If this were not so, it would not be rational on their part to buy the product. In economists' language, customers enjoy a "consumer surplus". Only the "marginal customer" – the customer who is only just persuaded to the buy a product at the price that it is offered – does not do so. If one were to rank customers in descending order of the value that they place on a product – highest

first – the relationship between value and quantity is known as a "demand curve" may be illustrated as follows:

Chart 5.2: Consumer Surplus



5.8.7 In this chart the rectangle represents the expenditure on a product (equal to the price at which it is offered times the quantity purchased). The customer with the highest valuation is located at the extreme left of the diagram: the marginal customer is on the right; he values the product at no more, and at no less than its price. In this example, all customers pay the same price i.e. there is no price discrimination on the basis of willingness, or ability, to pay. The sum of the values placed by the consumers on this product is the area beneath the demand curve. This area, less their total expenditure, is the triangle that represents their combined consumer surplus. This is an ancient idea in economics, going back to the French economist, Dupuit,[56] who first addressed in an analytical way, in 1844, the question of whether a public works project – a bridge – should be built and how it should be charged for.[57] The concept has been used before in the

[56] Jules Dupuit, *On the measurement of the utility of public works*, translated and reprinted in J K Arrow and T Scitovsky, eds. Readings in welfare economics, Vol. 12, Homewood 1969.

[57] There is theoretical weakness in the concept, namely, that its measuring rod – the marginal utility of money – would itself change as the price of the product changes, because a price change has "income effects" i.e. it makes consumers richer or poorer. Hence it would not be strictly valid to sum the consumer surplus over a range of prices, as is done below, without compensating for these income effects. This is of relevance to products which account for a significant share of incomes is: this the case here? The relevant test for an individual consumer was proposed by Willig (Robert D Willig, Consumer's surplus without Apology, The American Economic Review, Vol 66, No. 4, September 1976, pp589-597) : income elasticity*consumer surplus/2*income<0.05. Medicines in the EU comfortably pass that test.

context of medicines, for example, to evaluate alternative drug price control regimes in the U.S.[58]

5.8.8 It is possible – by indirect means – to estimate the EU's expenditure on medicines. The consumers in this case are, for the most part, the health authorities that prescribe and largely pay for medicines on citizens' behalf. The size of the consumer surplus, relative to this expenditure, depends on the gradient of the demand curve. If the buyers of medicines are *in*sensitive to price, the demand curve would be quite steep, and the consumer surplus that derived from the consumption of medicines would be correspondingly large in relation to the total expenditure on them. (For so-called 'lifestyle medicines' seen by many consumers as discretionary purchases and paid for directly, the demand curve would be flatter, reflecting market conditions more like those for (other) consumer goods. There is still consumer surplus, but the amount is different.)

5.8.9 Because many medicines are so essential to health, and health is valued highly, the demand for prescription medicines is quite insensitive to price. Economists refer to this sensitivity as the "price elasticity of demand", which is defined as the proportional change in the quantity demanded in response to a change in the price, divided by the proportional change in the price. It is usually a negative number, because an increase in the price usually prompts a fall in the quantity demanded. An acknowledged difficulty here is dealing with an unknown bundle of counterfeit medicines that is likely to include a spectrum of medicines, ranging from the life-saving to the "lifestyle" varieties, whose demands would be, respectively, price-insensitive and price-sensitive. The price elasticity of demand for medicines has been found in the US to lie between – 0.1 and – 0.2. For the UK, Hughes and McGuire estimated the long-run price elasticity to be at the lower end of this range, – 0.09.[59] On the other hand, a study of the demand for medicines in seven advanced countries (U.S., France, Germany, Italy, Spain, the UK and Japan) from 1980-1987,[60] found that the demand for medicines was quite sensitive to the average retail price (the net out-of-pocket price to the consumer after reimbursement by private or public insurance schemes) for a basket of ethical pharmaceutical drugs (a price elasticity of -2.8 for the seven countries as a whole, -0.6 in France, -2.0 for Germany, -2.8 (but not statistically significant) for Italy, Spain and the UK). It is also relevant that health authorities, and the Finance Ministries that seek to cap their expenditures, are notably price-resistant. Fixed budgets for medicines, for example, would imply a price elasticity of minus one. In view of these uncertainties, surrounding both the composition of counterfeit medicines, and the price-sensitivity of the demand for medicines in general, it seems prudent to consider a range of price elasticities, ranging from – 0.2 to – 1.0. On this basis, the value of medicines to their users would lie between three-and-a-half and one-and-a-

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58 Rexford E Santerre and John A Vernon, *Assessing consumer gains from a drug price control policy in the U.S.*, National Bureau of Economics Reseach, Working Paper No. W11139, February 2005.

59 David Hughes and Alistair McGuire, Patient charges and the utilisation of NHS prescription medicines: Some estimates using a cointegration procedure, Health Economics, Volume 4, Issue 3, pp. 213-220, 1995.

60 Donald Alexander, Joseph Flynn and Linda Linkins, *Estimates of the demand for ethical pharmaceutical drugs across countries and through time*, Applied Economics, 1994, 26, 821-826.

half times the amount spent on them.[61] Notice that it is the *value* of medicines to the user, not just the consumer surplus, that is relevant here. What counterfeit medicines do, in this conceptual framework, is to offer something worthless in return for the market price of the genuine medicine, as well as depriving the user of the consumer surplus that he/she would have derived from the genuine product.

[61] If the demand curve intercepts the price axis at P_0, the price is P_1 and the quantity demanded is Q_1, the ratio between consumers' valuation of the products they buy and their expenditure on them is $[(P_0 - P_1) Q_1/2 + P_1 Q_1]/ P_1 Q_1 = 1 + (P_0 - P_1) /2P_1$. The elasticity of demand, $E = \Delta Q/ \Delta P * (P/Q) = Q_1/ (P_1 – P_0) *(P_1/Q_1) = P_1/ (P_1 – P_0)$. Thus ratio between consumers' valuation and their expenditure is $1 – 1/ (2E)$.

Table 5.29: Estimated value of medicines to the EU population, and of potential losses of value due to counterfeits

Estimated EU-27 expenditure on medicines					
	2005	**2007**			
EU market	**€ million**	**€ million**			
1. At ex-factory prices (1)	125,500	174,100			
2. At retail prices (2)		196,200			
			Assumed incidence of counterfeit medicines in EU		
Value to consumers			0.1%	0.5%	1%
Price elasticity of demand assumptions	Implied value/expenditure	Implied value of medicines to EU users	Losses of this value due to counterfeit medicines in 2007		
		€ million	€ million	€ million	€ million
-1	1.5	294,300	300	1,500	2,900
-0.5	2	392,400	400	2,000	3,900
-0.2	3.5	686,700	700	3,400	6,900
(1) EFPIA, The Pharmaceutical Industry in Figures, Key Data, 2007 update. Page 3. Data for EU-27.					
(2) Noting average gross margins in the EU wholesale and pharmacy sectors, and assuming that the hospital segment (assumed to be 14% of the market by volume - the UK level) is supplied at ex-factory prices. The 2007 figure is derived using Index of Turnover, Chemicals and chemical products, Eurostat April 2008.					

5.8.10 In order to estimate the EU-27 expenditure on medicines the starting point taken is the EFPIA market sales at ex-factory prices (€129.5 billion), and add wholesale and retail margins, derived from the cost structure of these activities. In the EU-27, the purchases of goods and services (approximated as turnover less value added) are equal to 88 per cent of the turnover of the pharmaceutical wholesalers, and hence of the wholesale price of medicines. Similarly, goods and services are equal to 79 per cent of the turnover of the pharmacists, and hence of the retail price of medicines. These two estimates indicate that the ex-factory cost of medicines accounts for 69 per cent of the retail price, or to put it another way, the retail value of medicines is about 145 per cent of their ex-factory value. Allowance is also made for the fact that hospitals and healthcare organisations (assumed to be 14 per cent of the market by volume - the UK level) are probably supplied at or not much above ex-factory prices.

5.8.11 On this basis, the retail value of the medicines consumed in the EU in 2007 was probably of the order of €196 billion.

5.8.12 Medicines' value to EU consumers (and more relevantly, to the health care providers which prescribe and order two-thirds of these medicines on patients' behalf) would have

been some multiple of this - probably between three-and-a-half and six – indicating a value in 2007 of between €800 billion and €1,350 billion.

5.9 Valuing the benefits of health treatments: an outcomes approach, based on medicines' contributions to longevity

5.9.1 An alternative approach to valuing the benefits derived from medicines is to consider the contributions which healthcare in general, and medicines in particular, have made to extending human lives, and to enhancing the quality of these lives. Studies in the US by Murphy and Topel[62] have shown that, for example:

(a) In 1970 the life-expectancy of an average American male infant was 62; in 2000 it had risen to 74.

(b) In 1970, an average 50-year-old man could expect to live another 23 years. By 2000, a 50-year-old man could expect to live another 28 years. A 50-year-old man in 2000 was 5 years "younger" than his equivalent in 1970.

Table 5.30: Life expectancy in the US, at birth and at age 50, 1970-2000

	Life expectancy at birth	Life expectancy at age 50
Men		
1970	62	23
2000	74	28
Women		
1970	75	30
2000	79	32

Source, Murphy & Topel, using US Government, National Vital Statistics Reports, February 2004, Table 12.

5.9.2 Murphy and Topel place values on these gains in longevity, using US wage rates. They estimate that during the 20th Century, gains in life expectancy were worth over $1.2 million per person to the current population. Between 1970 and 2000, increased longevity has added about $3.2 trillion *per year* to the national wealth of the US, with half of these due to progress against heart disease alone.

5.9.3 For this study, the relevant question concerns the identifiable contribution to these life enhancements that is made by pharmaceutical products. In a series of studies on the contribution of consumption of these products on life expectancy in 20 OECD countries, Frech and Miller concluded that pharmaceutical consumption is "measurably productive" in the sense that has "positive and statistically significant relationships with life

[62] Kevin M. Murphy and Robert H. Topel, *The value of health and longevity*, NBER Working Paper No. 11405 June 2005.

expectancies".[63] They estimated that the lifetime cost of extending a life in OECD countries by the use of pharmaceuticals was $28,000 at 1990 prices. This provides a basis for estimating the additional years of life that are being secured by the EU's current spending on pharmaceuticals.

Table 5.31: Longevity benefits attributable to pharmaceutical products, 2007

European expenditure on pharmaceuticals [a]	€ billion	227		
European expenditure on pharmaceuticals/person [b]	€	460		
Lifetime costs of extending life by one year in OECD countries by spending on pharmaceuticals [c]	$ 1990	28,069		
	$ 2007	56,980		
	€ 2,007	43,218		
Longevity benefit per person achieved by each year's expenditure [d]	days	3.9		
QALY/DALY (€ 2007)		40,000	60,000	80,000
Longevity benefits per person	€	425	638	851
Total longevity benefits to EU population	€ billion	210	315	420
Total longevity benefits to EU population expressed as a ration of proportion of the EU's expenditure		93%	139%	185%
Exchange rate $/€, 2007: 0.76				
[a] Source: calculated from H. E. Frech III and Richard D. Miller Jr.,The Productivity of Health Care and Pharmaceuticals: Quality of Life, Cause of Death and the Role of Obesity, July 2002.2002, Tables 10 and 11.				
[b] See Table XX. The EU-27 population in 2007 was 494 million in 2007. [c] Producer price index for medicines in US (1990 = 100) was 203. [d] Equal to 517 / 43,218 * 364				

5.9.4 Each *year's* expenditure on pharmaceutical products is extending the life of the average EU citizen by *3.9 days*, and total lifetimes of the EU population by 5.3 million years. These estimates suggest that the *additional* longevity benefits, and the improved quality of life that are now associated with them, that are being secured each year in the EU through the use of pharmaceutical products are worth between 90 per cent and 180 per cent of the EU's annual expenditure on them. Noting that a high proportion of the medicines that are prescribed are for conditions other than the life threatening, this

[63] H. E. Frech III and Richard D. Miller Jr., *The Productivity of Health Care and Pharmaceuticals: An International Comparison*, The American Enterprise Institute Press, 1999.
H. E. Frech III and Richard D. Miller Jr.,The Productivity of Health Care and Pharmaceuticals: Quality of Life, Cause of Death and the Role of Obesity, July 2002.

conclusion adds weight to the argument that the *total* benefits that are derived from medicines greatly exceed the sums spent on spent on them.

The direct benefits to be derived from eliminating counterfeit medicines

5.9.5 Counterfeit medicines are depriving some EU patients of some of the benefits from medicines. The "market share" of counterfeit medicines in the EU is not known. A share of "up to 1 per cent" in developed country markets has been suggested by the WHO, and this has been taken as the basis for some of the scenarios explored. However, there is – naturally enough – no solid basis for this figure from the WHO, and it may be an over-estimate for medicines supplied through the legal supply chain in the EU. Nobody can be sure.

5.9.6 Counterfeit medicines appear to be representative of the medicines that are prescribed – some of them address serious, life-threatening conditions, others deal with less serious ones. It seems reasonable to assume, then, that counterfeit medicines deprive patients of the benefits conferred by the genuine medicines, in proportion to their market share. If that market share is one-half percent, the EU's patients are deprived of one-half percent of the health benefits that can be attributed to medicines. On the basis of the consumer surplus valuation (see Table 5.27), those health benefits would be worth *€1.5 - €3.4 billion* a year.

5.9.7 If counterfeit medicines in the EU were progressively eliminated by 2015, commencing in 2011, the health benefits would increase to and then continue at this level.

5.9.8 In addition, some counterfeit medicines inflict harm (as has been proven the case in other parts of the world).

An illustration

5.9.9 A recent incident involved a counterfeit consignment of 6,000 packets of a prescription medicine. The price which was paid by the relevant healthcare authority for this consignment was probably of the order of €180,000 (6,000 times the average price of €30 per prescription). The health benefits that would have been delivered by this consignment, and that will now be lost, would probably be of the order of six times this figure - €1,080,000.

5.9.10 A University of Liverpool study[64] of 18,820 patients admitted at two large general hospitals in Merseyside, England, concluded that 6.5 per cent of admissions related to an adverse drug reaction (ADR), with the ADR directly leading to the admission in 80 per cent of cases. The median bed stay was eight days, accounting for 4 per cent of the hospital bed capacity. The burden of ADRs on the NHS includes morbidity, mortality, and extra costs. The projected annual cost of such admissions to the NHS was estimated to be £466 million (€580 million at 2008 exchange rates).

Indirect benefits: protecting public confidence in the EU's healthcare systems

5.9.11 An alternative approach to assessing the value of the maintenance of public confidence in the EU's healthcare systems is to consider how much the EU and Member States *already* spend in order to reduce/eliminate the risks posed by new medicines. The EU's social planners have already reached judgements on the importance of reducing/eliminating the risks posed by new medicines in these areas; they are implicit in the policies in place.[65] One might then consider whether the measures which would be required to eliminate imports of counterfeit medicines are likely to be more, or less, cost-effective than these expenditures.

5.9.12 The broad scale of the costs of complying with these policies can be derived by considering the cost of introducing a new medicine. The average pre-approval costs of developing a drug have been estimated to lie between $800 million and $880 million.

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[64] Munir Pirmohamed et.al, Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients, British Medical Journal 2004;329:15-19 (3 July).

[65] This is not to say that these judgements are beyond dispute. For example, there are those who argue that the regulations of new medicines has become excessively cautious, in that the healthcare benefits of greater certainty about safety are outweighed by the long delays in the benefits from new medicines.

Table 5.32: Pre-approval costs of drug development

Pre-approval costs of drug development				
	Boston Consulting Group [a]		DiMasi et al.[b]	
Component	**US $ million**	**Percentage**	**US $ million**	**Percentage**
Biology	370	42%		
Chemistry	160	18%		
Pre-clinical safety	90	10%		
Total pre-clinical	620	70%	335	42%
Clinical	260	30%	467	58%
Total	**880**	**100%**	**802**	**100%**
A Revolution in R&D: How Genomics and Genetics are transforming the Biopharmaceutical Industry, Boston Consulting Group, 2001.				
The Price of innovation: new estimates of drug development costs, J. DiMasi, R.W.Hansen & H.G. Grabowski, Journal of Health Economics, 22, 151-185, 2003. Average out-of-pocket costs were $400 million (2000 dollars). Capitalising these at 11% yielded a total pre-approval of $802 million (2000 dollars).				

5.9.13 Between 30 per cent and 58 per cent of these costs were accounted for by the "clinical stage" i.e. testing drugs' efficacy and safety. According to the Boston study, pre-clinical safety studies accounted for another 10 per cent of the development costs.

5.9.14 In 2005 the UK pharmaceutical industry spent 21per cent of its 2005 turnover on R&D (£3,308 million).[66] If 58 per cent of this was accounted for by clinical trials (the DiMasi figure),[67] these trials accounted for 12 per cent of the industry's turnover. Expressed in another way, they represented a 14 per cent premium over all *non*-clinical costs of the innovative sector of the pharmaceutical industry. This is the financial cost of ensuring that the industry's products are safe.[68]

5.9.15 The "stock" of these expenditures is a minimum measure of the value of public confidence in medicines, which is being put at risk by counterfeit medicines.

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66 ABPI figure, based on ONS data.

67 Arguably more applicable than the Boston Consulting Group's 30%, because the latter applied only to biopharmaceutical products.

68 There are, in addition, the operating costs of the regulatory agencies of the Member States. To judge by the UK's experience, these costs are quite modest compared to the costs of clinical trials to the pharmaceutical industry. The MHRA's operating costs in respect to medicines in 2004-05 were £56.7 million (MHRA Annual Report and Accounts 2004-05, page 81), equivalent to 3% of the UK pharmaceutical industry's estimated clinical stage expenditure in 2004. (These are recouped from the industry, and may in fact be included in its expenditure on R&D).

Industrial policy aspects

5.9.16 The pharmaceutical industry is one of Europe's outstandingly successful industries. During the ten years up to 2006 its output grew by an average of 6.1 per cent a year - almost three times as fast as Europe's manufacturing sector (2.1 per cent a year).

5.9.17 Whereas the total trade in goods of the EU-27 was in deficit in 2006, with exports covering only 86 per cent of imports, exports of pharmaceutical products were 191 per cent of the EU's imports.

Table 5.33: Comparative trade performance, EU-27, 2006

	Exports	Imports	Balance	Coverage ratio
	€ million	€ million	€ million	
All products (SITC 0-9)	1,165,000	1,361,000	-195,000	86%
Manufactured products (SITC 5-8)	988,000	861,000	127,000	115%
Pharmaceutical products (SITC 54)	67,000	35,000	32,000	191%

Source: Eurostat, External and intra-European trade, Statistical Yearbook - Data 1958-2006, 2008 edition.

5.9.18 The EU's pharmaceutical industry is more productive than the EU's non-financial business economy, and manufacturing as a whole. In 2004 it was over twice as productive as these sectors in terms of value added per employee. Part of this would have been due to the fact that it employed higher quality, and hence more expensive people, but after adjusting for that, its wage-adjusted productivity was significantly higher than that in the rest of the non-financial economy. The industry was also more profitable.

Table 5.34: The comparative performance of the EU pharmaceutical industry, 2004

	Value added	**Employment**	**Value added per person**	**Wage-adjusted product-ivity[a]**	**Gross operating rate[b]**
	(€ billion)	**(thousands)**	**(€ 000)**		
Non-financial business economy	5,100	125,000	41	148%	11%
Manufacturing industry	1,800	37,500	48	153%	11%
Pharmaceutical industry (NACE 24.4)	60	590	101	192%	16%
[a] Value added divided by personnel costs: expenditure on labour inputs it is more relevant for comparisons across activities with very different incidences of part-time employment.					
[b] Gross operating surplus less personnel costs divided by turnover: it is one measure of profitability.					

Source: European Business - Facts and Figures, 2007 Edition

5.9.19 These considerations by themselves would justify concerns about counterfeit medicines, since they threaten the reputation and competitiveness of an industry which is important to the EU economy.

5.10 Conclusions

5.10.1 This discussion began by describing two plausible baseline scenarios, assuming that the policies to counter counterfeit medicines come into force in 2011:

(a) An "optimistic" base case: the EU market share of counterfeit medicines was *one-half percent* in 2005, and would remain at that level;

(b) A "pessimistic" base case: the EU market share of counterfeit medicines was one-half percent in 2005, and is growing by 10 per cent a year.[69]

5.10.2 In the "optimistic" case, a realistic target would be to eradicate counterfeit medicines from the legitimate supply chain by 2015. In the "pessimistic" base case, it would be more realistic to consider containment at 2011 levels.

5.10.3 The annual health benefits associated with the use of medicines in the EU are estimated to lie in the range of €290 billion - €690 billion (see Table 5.2.1). If counterfeit medicines reduce those benefits by one-half percent, or by €1.5 billion - €3.4 billion, the benefits that could be expected in the two illustrative scenarios are as follows:

- "optimistic-eradication" net present value between €8 billion and €19 billion;
- "pessimistic-containment" net present values respectively of between €12 billion and €30 billion.

[69] Far more pessimistic scenarios are easily imagined.

6 COMPARING THE OPTIONS

6.1 The costs of the package as a whole in relation to the potential benefits

6.1.1 In the light of this analysis, in what circumstances would the policies be beneficial, in cost benefit terms? In the first place, the costs that the policies would add to the EU supply chain – between € 2,000 million and € 6,400 million a year – would reduce, by that amount, the consumer surplus that Europeans currently derive from using medicines. This *loss* of benefits would be greater than the benefits from eliminating a 0.5 per cent counterfeit share of the EU market, estimated at Table 5.21 to be between €1,500 million and €3,400 million a year.

6.1.2 There would be another, second order loss, because, by pushing up the price of medicines, the policies would - at the *margin* - discourage their use. That is to say, patients, and their healthcare providers, would choose to do without their *least valued* medicines. However, only a small part of this – less than €100 million - would represent an economic loss, because the resources that would be released from the supply chain in this process could find alternative uses. The economic loss is the difference between the valuation that users place on this marginal tranche of medicines and the cost of the resources that are currently used to produce it.

6.1.3 On the benefit side, the policy options would remove (in one scenario), or contain (in another), a tranche of counterfeit medicines. If, as assumed, on the evidence to date, the counterfeit medicines are a representative "bundle" of medicines, then the benefits from using the genuine version, and hence from removing or limiting the counterfeit version, would probably outweigh the loss of some of the most marginal medicines as a result of the increase in their cost resulting from the package of policy options under consideration. This would not be the case if, on the other hand, counterfeit medicines account for a very minute share of the EU market (say, 0.1 per cent rather than the assumed 0.5 per cent), and/or they are targeted predominantly at the clinically less significant medicines. In these cases, the increase in costs of all medicines would be more likely to outweigh the (smaller) benefits of removing or reducing the supply of counterfeits.

6.2 Other likely consequences of the proposed policies

Rest of world

Table 6.1: Major likely effects in other parts of the world (not quantifiable)

Costs	Benefits
Increased costs and reduced output and jobs in less developed countries	Reduced risk of supplies of counterfeits through EU entrepot trade (but assume displaced to other routes)

Parallel trade in the EU

6.2.1 It is likely that 80 per cent or more of parallel trade business would be lost if there were a seal on original packages and measures to ensure that packages could be securely traced through the distribution chain. The trade remaining would be between Member States using the same language, and any parallel trade in generic medicines

Table 6.2: Major reduction in parallel trade

Costs	**Benefits**
Social cost of loss of jobs and profits in parallel trade firms (c. 10,000 jobs)	Value added to EU economy of resources no longer absorbed in parallel trade
Social cost of possible higher prices paid by healthcare systems in importing (generally higher income) Member States (e.g the German Government states that it saves €380 m p.a. from parallel imports)	Social benefits to healthcare systems in lower-income Member States of lower prices for patented medicines. The sums involved are likely to easily outweigh any savings in the richer countries.
NB No significant cost or other disadvantage to patients	Benefits to patients from: > Safer medicines > More accurate package leaflets > More efficient recalls > Reduced risk of counterfeits > Fewer supply shortages > Reduced delays in launching new products in lower income Member States > Increased access to medicines in lower income Member States

6.3 Comments on ways in which package might be made more cost-effective

6.3.1 There is considerable scope for a more cost-effective set of policies to be designed (note that the package proposed in the subsequent Commission Staff Working Document on this subject did differ significantly from that reviewed here).