ANNEX 1: Calculations

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1 PRODUCT INTEGRITY AND TRACEABILITY COST CALCULATIONS

Lack of Data

1.1 Much of the information required for estimation of the costs associated with the policy options contained within Section 4.1 was not available from public sources. We therefore relied substantially on the knowledge of industry experts, including firms operating within the pharmaceutical industry and associations representing the various sections of the supply chain.

1.2 In the majority of instances, little information was available and that which was provided to us sometimes varied widely. Therefore, we were frequently required to make a judgement of the most likely cost for a particular category based on the information we had received. The purpose of this Annex is to explain for each category of cost associated with each policy option the reasons behind the figures we use in our calculations.

Prices, Wages and Net Present Values (NPV)

1.3 Much of the information we received on costs was expressed in 2007 prices. There were instances, however, in which the most recent available cost information was from earlier years. In these cases it was necessary to adjust for inflation between the year of cost estimation and 2007 using harmonised index of consumer prices (HICP) data for the EU-27 obtained from Eurostat.

1.4 An important element of the cost analysis for several policy options is the wage of a worker undertaking a specified type of work. In some cases we obtained information on the wage directly, in other cases we considered that using the average EU wage would be appropriate.

1.5 The average EU wage used in our calculations is based on average gross annual earnings in industry and services for the EU-27. This information was obtained from Eurostat and we expressed it in hourly terms based on an assumption of 7.5 hours per day and 225 working days per year. The most recent year for which wage data are available is 2005 and hence it was necessary to adjust the raw data so as to express the wage in 2007 terms. Since the rate of price inflation differs significantly from wage inflation, it would be inappropriate to use HICP for this adjustment.

1.6 Information on a Europe-wide wage index is available only to 2005. Therefore, to convert the 2005 wage to 2007 terms we assumed 4.5 per cent nominal growth in wages per annum, which is roughly equivalent to 2 per cent inflation and 2.5 per cent real growth in wages. Once wages were expressed in 2007 terms, we applied a 25 per cent mark-up to account for overhead costs, as per the EC's standard administrative cost model (SACM).

1.7 Some policy options require an estimate of Chinese wage levels. Research has suggested that the average Chinese wage is one-twentieth of that in the EU and this is an assumption we employ.[1]

1.8 Our cost estimates are expressed in terms of one-off costs, annual costs and net present values. 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:

$$NPV = C_1 + \sum_{t=2}^{T} \frac{C_t}{(1+r)^t}$$

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.

1.9 In this case, we express net-present values for a ten year horizon. We assume 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, we utilise a discount rate of 4 per cent. Therefore, the expression used in our NPV calculations is:

$$NPV = C_1 + \sum_{t=2}^{10} \frac{C_t}{(1+0.04)^t}$$

Calculation of Costs

1.10 The remainder of this Annex explains the methodology for calculating each of the individual costs that are subsequently used in the calculation of total one-off and annual costs for each policy option.

Policy option 4.1.1 — Subject all actors of the distribution chain to pharmaceutical legislation

Part a

1.11 Table 1.1 presents a summary of the central estimates of costs for this policy option of subjecting all actors in the pharmaceutical distribution chain to legislation and Table 1.2 provides the sources of these cost estimates. In our calculations, we include all brokers, traders and agents as wholesalers that require GDP licences and would be subject to inspections. No allowance is made for any investigative or policing work that the authorities might undertake to try to identify currently unlicensed brokers etc.

[1] YDL Management Consultants, "China: the Untapped Freighter Market"

Table 1.1: Cost Summary for Policy Option 4.1.1(a)

	COST CATEGORY	**Value**
A	Number of currently unlicensed finished products brokers/traders etc. in EU	1,000
B	Proportion of new entrants per year	20%
C	Administration hours for wholesaler application (one-off cost)	4.00
D	GDP inspection fees for these (non-complex) firms (3/4 of day)	€ 1,976
E	Frequency of GDP inspection (current) (years between)	-
F	Frequency of GDP inspection (required) (years between)	3
G	Administration hours for inspection (2 people, 3/4 day)	11.25
H	Wage	€ 23.45
	POLICY COST ESTIMATES	
	Administrative cost (one-off)	**€ 0.36m**
	Administrative cost (annual)	**€ 0.16m**
	One-off cost total	**€ 2.33m**
	Annual cost total	**€ 1.21m**
	Net present value	**€ 12.57m**

1.12 As illustrated in Table 1.2 below, the information we received with regard to the number of currently unlicensed finished products brokers/traders etc. in EU was limited, but informative. On the basis of this information, we considered it reasonable to assume that there are around 1,000 such businesses within the EU and, given that such businesses are likely to be small, we assume that each has one only site. Noting the fluidity of the market and low barriers to entry led us to conclude that around 20 per cent of firms would enter each year.

1.13 Quantitative information on inspection fees in the UK was provided by MHRA. Due to the relative simplicity of the activities of brokers and the lesser complexity of GDP audits compared to GMP, we assumed that an inspection would last for three-quarters of one day and that inspection costs would be relatively constant across the EU. Therefore, we converted the MHRA inspection fee into euros (at current exchange rate of £1=€1.2475) and added an additional €400 to account for expenses charged by MHRA.

1.14 The trade association AESGP informed us that internal costs for GMP and GDP audits are in the region of €2,000. Using the SACM we calculated internal administration costs for inspections of unlicensed brokers to be less significant than this.

1.15 The number of hours required for administration includes the time spent developing familiarity with the regulations, completing forms and accompanying inspectors throughout the inspection. The estimates we received from industry exclude the time taken for accompanying inspectors and we therefore assume that total administration time would be 11.25 hours, or three-quarters of a day for two individuals. Of this,

completing forms would take two man-hours. The wage of each of the individuals undertaking administrative tasks is assumed to be the average EU wage.

1.16 Using the letters in the left-hand column of Table 1.1, one-off and annual administrative costs are calculated as follows:

One-off administrative cost = (a*(c+g)*h)

Annual administrative cost = ((a*g*h) / f) + (a*b*(c+g)*h)

1.17 The total one-off and annual cost of a subjecting all actors in the pharmaceutical distribution chain to legislation is calculated as follows:

Total one-off cost = (a*(c+g)*h) + (a*d)

Total annual cost = (a*b*(d+(c+g)*h))+(a*(d+(g*h))/f)

Table 1.2: Source of Information

Category	**Sources**		
A. Number of currently unlicensed finished products brokers/traders etc. in EU	EC – expect far more than 400, given 30,000 wholesalers in EU	MHRA – Do exist in the UK	
B. Proportion of new entrants per year	Industry sources consider this to be a liquid market with low barriers to entry and so there may be significant entry each year.		
C. Administration hours for wholesaler application (one-off cost)	EE estimate based on time taken to complete application form		
D. GDP inspection fees for these (non-complex) firms (3/4 of day)	MHRA: GDP inspection fee: £1,792 for whole day, reduced rate: £896. Reduced rate fee will be payable by wholesale dealers who handle general sales list (GSL) products only and for registered retail pharmacies and small wholesale dealers where wholesaling of licensed products does not exceed 15% or £35,000 of total turnover only where an inspector spends less than 3.5 hours on site.		
E. Frequency of GDP inspection (current) (years between)	Regulators – Not currently inspected		
F. Frequency of GDP inspection (required)	EE assumption - same as for the rest of the supply chain		

(years between)			
G. Administration hours for inspection	EMEA - 2 man hours for GDP, double if CoCP.	GIRP - 1 man day for GDP.	EE – assume 2 people, 3/4 day
H. Wage	Eurostat - Average 2005 EU wage adjusted as described above		

Part b(i)

1.18 Table 1.3 presents a summary of the costs for this policy option of mandating GMP audits of finished product contract manufacturers and Table 1.4 illustrates the sources of these cost estimates.

Table 1.3: Cost Summary for Policy Option 4.1.1(b)i

	Cost category	**Value**
A	Total number of audits of contract manufacturers supplying the EU if third-party audits are not accepted	500,000
B	Number of sites of contract manufacturers supplying to the EU (including non-EU sites)	10,000
C	Total third-country (i.e. non-EU) audits of contract manufacturers if third-party audits are not accepted	300,000
D	Number of sites of contract manufacturers supplying to the EU based outside EU	6,000
E	Cost of travel to these non-EU sites, expenses etc.	€ 30,000
F	Proportion not being adequately audited (every 3 years)	20%
G	Target frequency of audit (years between audit)	3
H	Current frequency of audit of those below target (years between audit)	5
I	Cost of audit firm carrying out audit	€ 8,500
J	Cost of manufacturer carrying out the audit themselves	€ 12,500
K	Administration hours (2 people, 2 days)	30.00
L	Wage	€ 23.45
	Annual administrative cost (accept third-party audits)	**€ 0.19m**
	Annual administrative cost (do not accept third-party audits)	**€ 9.38m**
	Annual cost total (accept third-party audits, conducted by audit firm)	**€ 26.45m**
	Annual cost total (accept third-party audits, conducted by manufacturer)	**€ 27.52m**
	Annual cost total (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**

1.19 On the basis of information from various industry sources, we assumed that there are 7,000 sites of finished product manufacturers (including both rights-holders and contract manufacturers) located within the EU and 8,000 outside, giving a total of 15,000 finished products sites supplying the EU.

1.20 Industry sources indicated that the number of sites of contract manufacturers supplying the EU is more than 7,000 and could be far more than 20,000. We considered that an assumption of 10,000 contract manufacturer sites is appropriate, 6000 of which are based outside the EU. It seems reasonable to assume that the number of contract manufacturers supplying to the EU would be double the number of rights-holders.

1.21 AESGP informed us that each rights-holder has 100 contract manufacturers, on average. On this basis, since there are some 5000 rights holders if each contract giver had to audit each of their contract manufacturers, the total number of audits of contract manufacturers supplying the EU would be 500,000. Of this, 300,000 audits would be conducted in third countries, given that 60 per cent of sites of contract manufacturers are located outside the EU.

1.22 Inspections in third countries incur costs that do not apply to those conducted within the EU, namely significant greater travel costs and expenses for auditors. We did not receive any information on travel costs and expenses for audits conducted in countries outside the EU but did receive estimates for inspections in such countries. We considered that there should not be a significant difference between inspections and audits for travel costs and expenses. On the basis of the information provided we considered it appropriate to assume an additional cost of €30,000 for audits outside the EU. This assumes that two auditors travel on a long-haul flight to Asia and that the whole audit would take approximately five days including travelling time.

1.23 Varied estimates were given by industry sources of the proportion of contract manufacturers that are not currently audited at least once every three years. Several trade bodies believe that in excess of 90 per cent of contract manufacturers are audited at least once in every three years, but EMEA stated that possibly 50 per cent of contract manufacturers are not audited so frequently at present. Striking a balance between these views, we assumed that the interval between audits exceeds three years for 20 per cent of contract manufacturers and (reflecting a view from EMEA) that the frequency of audit for these firms is 5 years.

1.24 The estimates of costs for audits conducted by manufacturers ranged from approximately €10,000-€15,000 as an EU average, and for our calculations we took the mid-point of this range. For audits conducted by specialist audit firms, costs were estimated at approximately €8,500. We assume that the audit would take two days to complete and that all administrative tasks could be completed within four man-days.

1.25 Using the letters in the left-hand column of Table 1.3, the annual administrative costs of mandating GMP audits of finished product contract manufacturers are calculated using the following formulae:

Annual administrative cost (accept third-party audits) = ((b*f*k*l)/g)-((b*f*k*l)/h)

Annual administrative cost (do not accept third-party audits) = ((a*f*k*l)/g)-((a*f*k*l)/h)

Total annual costs are calculated as follows:

Annual cost total (accept third-party audits, audit firm) = (b*f*(i+(k*l))/g)-(b*f*(i+(k*l))/h)

Annual cost total (accept third-party audits, other manufacturer audits) = (b*f*(j+(k*l))/g)-(b*f*(j+(k*l))/h)

Annual cost total (do not accept third party) = (a*f*(j+(k*l))/g)-(a*f*(j+(k*l))/h)

Table 1.4: Source of Information

Category	Sources				
A. Total number of audits of contract manufacturers supplying the EU if third-party audits are not accepted	EGA – A large manufacturer has 800-1,000 suppliers and a medium manufacturer has 150-400 suppliers.	AESGP - Every contract manufacturer has on average 100 contract givers (=purchasers). Each contract manufacturer will therefore be audited every two weeks.	EAEPC - Maybe 8,000 finished products manufacturers based outside EU supplying to EU.	EMEA - 7,000 GMP certificates for finished product manufacturer sites/importers, with 3,000 inspections a year	
B. Number of contract manufacturers supplying EU (sites)	EAEPC - Maybe 8,000 finished products manufacturers based outside EU supplying to EU.	570 for one large EFPIA firm	EMEA - 7,000 GMP certificates for finished product manufacturer sites/importers, with 3,000 inspections a year	EGA – There are 20,000 sites in India and China supplying EU.	
C. Total third-country (i.e. non-EU) audits of contract manufacturers if third-party audits are not accepted	EGA – A large manufacturer has 800-1,000 suppliers and a medium manufacturer has 150-400 suppliers.	AESGP - Every contract manufacturer has on average 100 contract givers (=purchasers). Each contract manufacturer will therefore be audited every two weeks.			
D. Number of sites of contract manufacturers supplying to the EU based outside EU	EAEPC - Maybe 8,000 finished products manufacturers based outside EU supplying to EU.	EGA – There are 20,000 sites in India and China supplying EU.	570 for one large EFPIA firm		
E. Cost of travel to these non-EU sites, expenses etc.	German inspector for Nordrhein-Westfalen: flights can be €4,000 return, €400 – 25500.norm local (800 – 1200 €), - also about 6 days time including travelling (2 inspectors) plus €8,000 to €20,000 expenses i.e. total possible €40,000.	EMEA - €6,000 + normal cost, parallel trade GMP costs £10,000.	EGA – €15,000-20,000 may be near the mark if one inspector or about €40,000 for two inspectors.		

F. Proportion not being adequately audited (every 3 years)	AESGP - Usually happen every three years. Usually, due to the high amount of audits to be performed, companies carry out an audit together or the audit report is made available to other concerned companies.	EAEPC - most i.e. 90-95% audited every three years.	EMEA - possibly 50% not audited every three years.	Audit firm - most manufacturers audit their contract manufacturers every 12 months.	EGA - only 5% do not audit properly.
G. Target frequency of audit (years between audit)	EE assumption				
H. Current frequency of audit of those below target (years between)	EMEA – maximum time between audits 5 years, average 3 years (for all firms).				
I. Cost of audit firm carrying out audit	AESGP - €10,000 possibly lower limit. Many medicine manufacturers experience costs amounting to €25,000-€30,000.	EAEPC - 1 day of €100,000 QP plus preparation (€2,000).	EGA- Third-party audit can cost €8,500 but needs some preparation from firm hiring them.	Audit firm: contract manufacturer audit 2 people over 4 days, cost £1500 per person per day. Total cost: £12,000 exclusive of transport costs etc. Audit of a packaging plant would take three man-days: Total cost £4500.	Audit firm - cost £5,000+expenses GMP and bit less GDP
J. Cost of manufacturer carrying out the audit themselves	AESGP - €10,000 possibly lower limit. Many medicine manufacturers experience costs amounting to 25,000-30,000 euro.	EGA - €8,000	EFPIA - member cost €600 to €2500 per auditor in Europe, or €5,000 in China, average may be €3,000 per audit.	EGA - cost of audit of supplier/contract manufacturer €10,000-15,000,	
K. Administration hours (2 people, 2 days)	EE estimate – Assume a two-day inspection. One person spends two hours completing forms etc. Remaining hours are spent with inspectors.				
L. Wage	Eurostat				

Part b(ii)

1.26 Table 1.5 presents a summary of the costs for this policy option of mandating GDP audits of finished product suppliers and Table 1.6 illustrates the sources of these cost estimates.

Table 1.5: Cost Summary for Policy Option 4.1.1(b)ii

	Cost category	**Value**
A	Total number of supplier audits (independent audits)	700,000
B	Total number of supplier audits (if third party audits are accepted)	7,000
C	Target frequency of audit (years between audit)	3
D	Proportion not being adequately audited (independent)	95%
E	Proportion not being adequately audited (joint)	90%
F	Current frequency of audit of these firms	-
G	Cost of audit firm conducting audit	€ 4,000
H	Costs of carrying out the audit themselves	€ 6,000
I	Hours required for administration (2 people, 1 day)	15.00
J	Wage	€ 23.45
	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**

1.27 We assume that this policy option would take a risk-based approach and hence our cost estimates assume that audits between suppliers will occur only in cases of suspicion of non-compliance with GMP and/or GDP. It should be noted that with independent audits, suspicion of one supplier's lack of compliance would generally lead to several audits being conducted since one supplier is likely to have numerous clients.

1.28 EMEA states that there are 20,000 GDP certificates in the EU and we estimated for policy option 4.1.1(b)i that there are 15,000 sites of finished product manufacturers/contract manufacturers supplying the EU.[2] We were informed by DG Enterprise that GDP licences would only be issued to those based in the EU, and hence wholesalers based in third countries would not be affected by this policy option. Therefore, our estimate of the number of sites of suppliers that may need to be audited is 35,000.

1.29 It is obviously not reasonable to assume that each site would be suspected of non-compliance each year and so we assume that 20 per cent of firms would be audited each year. This implies a total of 7,000 audits if third-party audits are accepted. Given industry information that each supplier may have 100 customers, the number of independent audits would be 700,000.

1.30 Industry sources had little information on the proportion of suppliers not being adequately audited at present. However, there was a general feeling that few such audits are currently undertaken and on this basis we assumed that, if each purchaser must independently audit their supplier, 95 per cent of potential audits do not currently take place. If third-party audits are accepted, we assumed that 90 per cent of potential supplier audits do not currently take place.

1.31 The cost of and administration time required for a GDP audit was estimated on the basis of the information provided to us regarding GMP audits due to a lack of alternative information. GDP audits should be less time-consuming than GMP audits and hence fewer costs should be incurred. We assumed that the administration time and fees for GDP audits would be approximately 50 per cent of those for GMP audits. It was assumed that the individual completing administrative tasks earns the average EU wage.

1.32 Using the letters in the left-hand column of Table 1.3, annual administrative costs of mandating GMP audits of finished product contract manufacturers are calculated using the following formulae:

Annual administrative cost (accept third-party audits) = (b*e*i*j)/c

Annual administrative cost (do not accept third-party audits) = (a*d*i*j)/c

Total annual costs are calculated as follows:

Annual cost total (accept third party audits, audit firm audits) = b*e*(g+(i*j)) /c

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[2] We note that Eurostat states that there are approximately 30,000 wholesalers in the EU but we have also received information 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.

Annual cost total (accept third party audits, other manufacturer audits) = b*e*(h+(i*j)) /c

Annual cost total (do not accept third party) = a*d*(h+(i*j)) /c

Table 1.6: Source of Information

Category	**Sources**				
A. Total number of supplier audits (independent audits)	EAEPC - For 40 firms and 100 suppliers per firm = 4,000 independent supplier audits (about 80% of audits involve different firms auditing the same suppliers)	EAEPC - some co-operation (i.e. a quarter of no co-operation)	AESGP - Every contract manufacturer has on average 100 contract givers (purchasers).		
B. Total number of supplier audits (if third party audits are accepted)	EMEA - 20,000 GDP licenses (although some may only supply pharmacies)	Eurostat - for 2005 says there are 30,848 registered firms for "g5146 Wholesale of pharmaceutical goods" in the EU27			
C. Target frequency of audit (years between audit)	EE assumption				
D. Proportion not being adequately audited (independent)	Industry group - less than 1% of potential audits currently happening,	Other industry groups point to higher proportions			
E. Proportion not being adequately audited (joint)	Industry group -only 1/6 firms do supplier audits	Other industry groups point to higher proportions			
F. Current frequency of audit of these firms	No audit done where no program				
G. Cost of audit firm	AESGP - €10,000 possibly lower	EAEPC - 1 day of €100,000 qualified	EGA- Third party audit can cost	Audit firm: contract manufacturer	Audit firm - cost £5,000+expenses GMP and bit less

conducting audit	limit. Many medicine manufacturers experience costs amounting to €25,000-30,000.	person (QP) plus preparation (€2,000).	€8,500 but needs some preparation from firm hiring them.	audit 2 people over 4 days, cost £1500 per person per day. Total cost: £12,000 exclusive of transport costs etc. Audit of a packaging plant would take three man-days: Total cost £4500.	GDP
H. Costs of carrying out the audit themselves	AESGP - €10,000 possibly lower limit. Many medicine manufacturers experience costs amounting to 25,000-30,000 euro.	EGA - €8,000	EFPIA - member cost €600 to €2500 per auditor in Europe, or €5,000 in China, average may be €3,000 per audit.	EGA - cost of audit of supplier/ contract manufacturer €10,000-15,000,	
I. Hours required for administration (2 people, 1 day)	EE estimate – 1 day inspection due to reduced complexity relative to GMP audit				
J. Wage	Eurostat				

Policy option 4.1.2 — Subject all actors of the distribution chain to pharmaceutical legislation

Part a

1.33 Table 1.7 presents a summary of the costs for this policy option of applying Compilation of Community Procedures (CoCP) to all GMP and GDP inspections and Table 1.8 illustrates the sources of these cost estimates.

Table 1.7: Cost Summary for Policy Option 4.1.2(a)

	Cost category	Value
A	Proportion of non-CoCP GMP inspections	0%
B	Extra cost for GMP inspections to apply CoCP(fee)	€ 0.00
C	Extra administration hours for CoCP GMP inspections	0.00
D	Number of GMP inspections by EU authorities (annual)	3,500
E	Extra number of GMP inspections required	0
F	Proportion of GDP inspections following simplified standards in the absence of harmonised CoCP	80%
G	Total cost of CoCP GDP inspection (fee for 1 day)	€ 3,951
H	Total administration hours for CoCP GDP inspections	22.50
I	Extra cost for current GDP inspections to apply CoCP (fee)	€ 1,317
J	Extra administration hours for current GDP inspections	7.50
K	Number of GDP inspections by EU authorities at present (annual)	4,000
L	Extra number of GDP inspections by EU authorities if follow CoCP in the future	3,000
M	Proportion of GDP inspections following simplified standards in the absence of harmonised CoCP for unlicensed brokers/traders	100%
N	Total cost of CoCP GDP broker/trader inspection (fee- ¾ of a day)	€ 2,964
O	Total administration hours for CoCP GDP broker/trader inspections	16.875
P	Number of unlicensed broker/trader inspections required (annual)	333
Q	Wage	€ 23.45
	Total annual administrative cost	**€ 2.28m**
	Total annual cost	**€ 19.33m**
	Net present value	**€ 163.08m**

1.34 DG Enterprise suggested we assume that all GMP inspections currently apply CoCP. Therefore, the additional cost of applying CoCP to these inspections is zero and it will not be necessary to allocate any extra time for administrative tasks. EMEA informed us that all firms have GMP inspections at least once every three years and hence the number of GMP inspections would not increase as a result of this policy option.

1.35 In summary, mandating all GMP inspections to apply CoCP would not involve any costs, given that all inspections follow CoCP at present. By the same token, it would not contribute much to policy objectives.

1.36 In contrast to our assumption that all GMP inspections apply CoCP at present, industry sources indicated that the proportion of GDP inspections that would meet such standards at present is far smaller. We assumed that CoCP is applied to a fifth of current GDP inspections.

1.37 The full cost of a non-CoCP GDP inspection is based on information from MHRA. The extra cost for GDP inspections refers to the additional cost of moving from a non-CoCP GDP inspection to one that applies CoCP. We received little quantitative information from industry of the likely costs of moving towards applying CoCP, although some sources indicated that they would not be surprised if costs were to at least double. We considered that whilst this is likely to be true for some regions, there would be others in which the current inspection regime would be closer to that which would result from the application of CoCP. We therefore assumed that the extra cost of inspections and extra administration time would be approximately 50 per cent of the total cost of a non-CoCP inspection.

1.38 EMEA informed us that 20,000 GDP certificates have been issued. Given that the current inspection frequency is likely to be less than the target of once every three years, we assumed that the current annual number of GDP inspections is 4,000. For all 20,000 GDP certificates to be re-issued in this period it would be necessary to conduct 7,000 inspections per annum, i.e. 3,000 more than at present.

1.39 It was noted in policy option 4.1.1(a) that we assume there are 1,000 currently unlicensed broker and traders in the EU and none of these are subject to a GDP inspection at present. To meet the target inspection frequency of 3 years, it would be necessary to conduct 333 inspections of unlicensed brokers each year, incurring full costs of the inspection. In common with the assumption made for policy option 4.1.1(a) we assume that inspection costs for currently unlicensed brokers and traders are 75 per cent of the figure quoted by MHRA because of the relatively small size and non-complexity of these firms.

1.40 The costs for this policy option are given by the following formulae:

Total administrative costs= a*(c*q)*d+f*(j*q)*k+(h*q)*l+m*(o*q)*p

Total annual cost =a*(b+(c*q))*d+f*(i+(j*q))*k+(g+(h*q))*l+m*(n+(o*q))*p

Table 1.8: Source of Information

Category	Sources		
A. Proportion of non-CoCP GMP inspections	EC – assume all in EU currently apply CoCP		
B. Extra cost for GMP inspections to apply CoCP(fee)	EE assumption due to all current inspections applying CoCP		
C. Extra administration hours for CoCP GMP inspections	EE assumption due to all current inspections applying CoCP		
D. Number of GMP inspections by EU authorities (annual)	EudraGMP contains 15,000 manufacturers and importers, done at least every 3 years, but often more regularly, quoted on EMEA website.	EMEA thinks this is high- real number is: 7,000 GMP certificates for finished product manufacturer sites/importers, with 3,000 inspections a year	
E. Extra number of GMP inspections required	All done at least every three years		
F. Proportion of GDP inspections following simplified standards in the absence of harmonised CoCP	EE assumption based on industry information that fewer GDP inspections apply CoCP than GMP		
G. Total cost of CoCP GDP inspection (fee for 1 day)	MHRA: reduced rate GDP inspection £896, (full £1,792 per day)	MHRA/EAEPC €6,000 for GDP with CoCP	GIRP (€ 3000 - 4000 in the UK plus licensing or 9,000 for new site),
H. Total administration hours for CoCP GDP inspections	EE estimate based on assumption that 50% greater than for non-CoCP inspections		
I. Extra cost for current GDP inspections to apply CoCP (fee)	AESGP - cost possibly rise (fees+internal) to €10,000 (bit less than GMP), time-consuming inspections.	German inspector for Nordrhein-Westfalen: The fees have to increase in order to be able to cover the costs of the inspectorates for more in depth and more time	EMEA - GDP is quite simple therefore there is not much room for significant variation in practice and would not expect a significant increase in costs

J. Extra administration hours for current GDP inspections	EE estimate based on assumption that 50% of non-CoCP		
K. Number of GDP inspections by EU authorities at present (annual)	EMEA - 20,000 GDP certificates possibly done every 4 years, some firms in UK not been audited for many years.		
L. Extra number of GDP inspections by EU authorities if follow CoCP in the future	For all 20,000 to have a GDP inspection in a three year period requires approx 7,000 inspections each year		
M. Proportion of GDP inspections following simplified standards in the absence of harmonised CoCP for unlicensed brokers/traders	None currently inspected		
N. Total cost of CoCP GDP broker/trader inspection (fee- ¾ of a day)	EE estimate based on full cost of CoCP GDP inspection		
O. Total administration hours for CoCP GDP broker/trader inspections	EE estimate based on assumption that 50% greater than non-CoCP		
P. Number of unlicensed broker/trader inspections required (annual)	EE calculation so all brokers inspected in a three-year period		
Q. Wage	EMEA: GDP 2 man hours double CoCP,	GIRP: 1 man day for GDP.	

Part b

1.41 Table 1.9 presents a summary of the costs for this policy option of mandating GMP inspections of finished product manufacturers based in third countries that supply the EU and Table 1.10 illustrates the sources of these cost estimates.

Table 1.9: Cost Summary for Policy Option 4.1.2(b)

	Cost category	Value
A	Number of sites of pharmaceutical manufacturers supplying EU based outside EU	8,000
B	Proportion of firms being inspected	80%
C	Target inspection frequency (years between inspection)	3
D	Cost (fees + expenses) of GMP inspection in third countries	€ 35,000
E	Administration hours of audited firm (2 people, 3 days due to language, unfamiliarity etc.)	45
F	Administrative wage in non-EU countries not currently inspected	€ 1.25
	Annual administrative cost	**€ 0.03m**
	Annual cost total	**€ 18.70m**
	Net present value	**€ 157.71m**

1.42 It was estimated for policy option 4.1.1(b)i that there are 7,000 sites of finished product manufacturers located within the EU and 8,000 outside. Estimates from industry sources ranged from 200 to more than 20,000 and, given this, our estimate of 8,000 is appropriate.

1.43 On the basis of information provided to us by various industry sources, we assume that 80 per cent of non-EU pharmaceutical sites that supply to the EU are inspected at present. AESGP indicated that all firms are inspected at least every 5 years and EMEA stated that they would be surprised if more than 100 are not inspected properly. It should be noted, however, that EMEA does not inspect suppliers located in the USA or other countries in which it believes the inspection regime to be adequate. Therefore, the total number and proportion of sites in countries that are not inspected to European standards or by European inspectors is likely be far greater than 100. As a conservative estimate, we assumed that 20 per cent are not properly inspected at present and that these firms are located in developing countries such as China and India rather than the USA.

1.44 The cost of conducting inspections in third countries is far greater than that of conducting inspections in the EU. There are several reasons for this. First, transport costs are significantly greater and could be approximately €10,000 in total if two inspectors were to fly to China, for example. The number of man-days required per inspection is also greater since travel could be one day each way and partly as a result of this, expenses are also greater than those in the EU. The estimates of EGA and a German pharmaceutical body were broadly similar whereas that of EMEA was far below this. We considered that the total cost — including fees — of conducting a non-EU inspection would be far greater than the estimate of EMEA and believe €35,000 to be a reasonable estimate.

1.45 We had initially believed that the administration costs of a GMP inspection in third countries would be below those in the EU as a result of lower wages in those countries that do not currently inspect. However, EGA stated that our initial estimate

underestimated the true cost because the purchaser of the products often accompanies the inspector for inspections in third countries and so there are significant costs of travel and time for EU personnel. Whilst this may be true, the cost of an EU employee accompanying an inspector to the third country should not be treated as an incremental cost of the policy since the action is not a requirement of the policy but a business decision of the EU importer.

1.46 We assumed that administrative tasks would be undertaken by non-EU based employees and hence the time required for administrative tasks for inspections in third countries exceeds the time required for inspections in the EU. There are several reasons for this, including a lack of familiarity with the forms to be completed and potential language difficulties. On this basis, we assume that administrative tasks would take six man-days (i.e. 50 per cent greater than for inspections in the EU).

1.47 The wage for those conducting administrative tasks is assumed to be €1.25 on the basis of an average Chinese wage of €1 per hour and a 25 per cent adjustment to account for overheads as per the ACM. We base the non-EU wage on Chinese wages because more developed countries such as the USA already inspect all those that supply to the EU. Therefore, incremental administration costs occur in less-developed countries such as China.

1.48 Using the letters in the left-hand column of Table 1.9, annual administrative costs are given by the formula:

Annual administrative costs = a*(1-b)*e*f / c

Annual costs total = a*(1-b)*(d+(e*f)) / c

Table 1.10: Source of Information

Category	Sources		
A. Number of sites of pharmaceutical manufacturers supplying EU based outside EU	AESGP - About 200 (very roughly estimated) finished products suppliers are located outside EEA.	EGA – 20,000 generics sites in India and China alone	EMEA – 4000 sites including both API and finished products
B. Proportion of firms being inspected	AESGP - inspected every 3 to 5 years and audited several times a year by different purchasers.	EMEA - total of 100 not inspected properly. Note that the EMEA does not inspect any firms in the US or other countries that it feel are already adequately inspected so the total may be much higher	
C. Target inspection frequency (years between inspection)	EE assumption		
D. Cost (fees + expenses) of GMP inspection in third countries	German inspector for Nordrhein-Westfalen: flights can be €4,000 return, €400 – 25500.norm local (800 – 1200 €), - also about 6 days time including travelling (2 inspectors) plus €8,000 to €20,000 expenses i.e. total possible €40,000.	EMEA - €6,000 + normal cost, parallel trade GMP costs £10,000.	EGA – €15,000-20,000 may be near the mark if one inspector or about €40,000 for two inspectors.
E. Administration hours of audited firm	EE estimate - 2 people, 3 days due to language, unfamiliarity etc.		
F. Administrative wage in non-EU countries not currently inspected	YDL Management Consultants, "China: the Untapped Freighter Market": wage in China €0.96 (plus 25 per cent for overheads)		

Policy option 4.1.3 — Seal packs with a ban on repackaging

1.49 Table 1.11 presents a summary of the costs for this policy option of introducing seal packs and banning repackaging and Table 1.12 illustrates the sources of these cost estimates.

Table 1.11: Cost Summary for Policy Option 4.1.3

	Cost category	Value
A	Number of packs in EU (all prescriptions)	29bn
B	Number of packs in EU (non-generic)	14.5bn
C	Cost of a seal or hologram	€ 0.02
D	Proportion of non-generic packs already being sealed	20%
	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**

1.50 AESGP informed us that there are approximately 29 billion packs of pharmaceutical products in the EU each year. Industry was less sure of the proportion of these that are generics and hence would not be subject to risk-based legislation. On the basis of the information we received it is appropriate to assume that 50 per cent of prescriptions are generics.

1.51 The cost of a seal or hologram was estimated by industry sources to be no more than €0.02; we took the upper range of the estimates for our calculations. EFPIA noted that some manufacturers of high-risk products already seal or place a hologram on their packs but did not provide a proportion. We assume that generics are not sealed and that 20 per cent of non-generics are currently sealed.

1.52 Utilising the letters in the left-hand column of Table 1.11, the calculation of total annual costs if all prescriptions must be sealed is:

Total annual cost (all prescriptions)=a*c - (b*c*d)

Total annual cost (non-generics)=b*c*(1-d)

Table 1.12: Source of Information

Category	Sources		
A. Number of packs in EU (all prescriptions)	AESGP – 29 billion packs in the EU (including prescription and non-prescription products)		
B. Number of packs in EU (risk-based)	EGA presentation gives EU generic volume as 37% 2005,	AESGP – around 9bn non-prescription products in EU	EGA says 2007 may be 42% accept 50% for future policy
C. Cost of a seal or hologram	EFPIA - €0.01-0.02 per pack (high risk products only), could be 0.5 cents for label or 5% cost rise for hot melted box (less than 1c each).	EGA - €0.02 is not too low. It notes that this could cost €200,000 per packaging line to introduce (excluding costs of training and ongoing label costs)	AESGP - €0.02 (for basic stickers); €0.04 for more elaborate ones (e.g. with holograms)
D. Proportion of packs already being sealed	EFPIA some manufacturers of high-risk products do this.		

Policy option 4.1.4 — Batch tracking e-pedigree

1.53 Table 1.13 presents a summary of the costs for this policy option of introducing batch tracking e-pedigree and Table 1.14 provides the sources of these cost estimates.

Table 1.13: Cost Summary for Policy Option 4.1.4

	Cost category	Value
A	Database costs (exclusive of the cost of option 4.1.6)	€ 20m
B	Number of batches per pharmacy (annual)	125
C	Time per entry (hours)	0.01
D	Wage	€ 23.45
E	Number of pharmacies in EU	160,000
	Total cost (one off)	**€ 20.00m**
	Total cost (annual, if retail authentication is required)	**€ 4.69m**
	Net present value (no retail authentication)	**€ 20.00m**
	Net present value (with retail authentication)	**€ 59.56m**

1.54 Industry estimates of the database costs differed significantly. Some sources felt that the costs for a batch-tracking database would be far less than the cost of a serialisation database, whilst others disagreed. We initially circulated to the industry a figure of €2 million. This was felt to be a significant underestimate and we took on board the advice of a technology company that the true figure could as much as ten times greater.

1.55 Industry sources indicated that there are approximately 145,000 pharmacies within the EU-22 which we extrapolated to 160,000 for the EU-27. To calculate the number of batches per pharmacy we divided the number of packs in the EU by the multiple of the number of pharmacies and an estimated number of packs per batch (information on which was provided by EAEPC, EFPIA and a manufacturer).

1.56 Using the letters in the left-hand column of Table 1.13, the total one-off and annual cost of batch-tracking e-pedigree is calculated as follows:

Total one-off cost = a

Total annual cost = b*c*d*e

Table 1.14: Source of Information

Category	**Sources**					
A. Database costs (exclude cost of option 4.1.6)	Efpia - database cost €3m to €7.5m (not explained why so much less than for serialisation)	EGA - this database must have fewer entries than the serialisation version but more complex list of wholesalers all through chain so could be about as expensive as the serialisation database.	Technology firm: Depending on the number of batches involved and the need for real time or not €2m for the database could be an underestimate by a factor of 10 or more.			
B. Number of batches per pharmacy	EAEPC – 250 packs per batch	EFPIA - 100s to 1000s packs per batch	Manufacturer- €3400 to €80,000 depending on product			
C. Time per entry (hours)	EE assumption					
D. Wage	Eurostat					
E. Number of pharmacies	PGEU - 140,000 in EU	EFPIA - 144,000	EGA – we should consider hospitals, nursing	GIRP - 147,000 pharmacies in EU22. Germany		

			homes and dispensing doctors	already has scanners and there are 21,000 pharmacies there,		

Policy option 4.1.5 — Pack-based mass-serialisation

1.57 Table 1.15 presents a summary of the costs for this policy option of pack-based mass serialisation and Table 1.16 illustrates the sources of these cost estimates.

Table 1.15: Cost Summary for Policy Option 4.1.5

	Cost category	Value
A	Cost of database (including on-going running)	€ 120m
B	Number of packaging lines	15,000
C	Proportion of packaging lines for branded/patented products	30%
D	Cost per packaging line	€ 150,000
E	Running cost per packaging line	€ 30,000
	Total cost (one off)	**€ 2,370.00m**
	Total cost (annual)	**€ 450.00m**
	Total cost (one off) (full EFPIA implementation to cover all patented/branded products without regulation)	**€ 1,659.00m**
	Total cost (annual) (full-EFPIA implementation to cover all patented/branded products without regulation)	**€ 315.00m**
	Total cost (one off) (risk-based, restricted to patented/branded products, zero implementation without regulation)	**€ 711.00m**
	Total cost (annual) (risk-based, restricted to patented/branded products, zero implementation without regulation)	**€ 135.00m**
	Total cost (one off) (risk-based, restricted to patented/branded products, full implementation to cover all patented/branded products without regulation)	**€ 0**
	Total cost (annual) (risk-based, restricted to patented/branded products, full implementation to cover all patented/branded products without regulation)	**€ 0**
	Net Present Value	**€ 6,165.90m**
	Net Present Value (full-EFPIA implementation to cover all patented/branded products without regulation)	**€ 4,316.13m**
	Net Present value (risk-based, restricted to patented/branded products, zero implementation without regulation)	**€ 1,849.77m**
	Net Present value (risk-based, restricted to patented/branded products, full implementation to cover all patented/branded products without regulation)	**€ 0**

1.58 We received a broad range of estimates for database costs. An EFPIA member believed the cost could be as low as €30m whereas EFPIA has previously estimated that it could cost €0.01- 0.02 per pack, implying a total cost of up to €400m. Based on the various estimates we received we considered an appropriate assumption to be € 120m.

1.59 Numerous industry sources estimated the number of packaging lines.[3] Taking into account all the information we received, an estimate of 15,000 packaging lines in the EU seems appropriate. This implies that there is one packaging line for each finished product site supplying to the EU.

1.60 EFPIA is considering implementing a pilot serialisation scheme and we had received information that, if successful, EFPIA may proceed with a pan-European roll-out of this scheme even in the absence of increased regulation. This is important because it affects the incremental cost of the policy option. If EFPIA proceeds with their pan-European roll-out anyway, the costs of this should not be considered as incremental costs as a result of the policy. We therefore present costs assuming zero EFPIA roll-out in the absence of the implementation of this policy option and assuming 100 per cent EFPIA roll-out.

1.61 We assume that 30 per cent of packaging lines are for patented/branded products and 70 per cent for generics. This may appear inconsistent with our previous assumption that 50 per cent of pharmaceuticals are generics, but the two are reconciled by noting that 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.

1.62 The final costs to be estimated in this section are the implementation cost and running cost per packaging line. The implementation cost estimates of industry sources were varied. Accounting for all these estimates, we considered it appropriate to assume implementation costs of €150,000 per line. Running costs per line were estimated on the basis of industry estimates ranging from €5,000- €80,000. We considered €30,000 to be an appropriate assumption.

1.63 Using the letters in the left-hand column of Table 1.15, total one-off and annual costs assuming zero EFPIA implementation without regulation were calculated using the following formulae:

Total cost (one off)=a+(b*d)

[3] Packaging line refers to the machinery and labour that places pharmaceutical products into boxes or alternative outer packaging prior to being placed into a batch for distribution to pharmacies etc.

Total cost (annual)=b*e

1.64 The formulae for total one-off and annual costs assuming 100 per cent Efpia implementation without regulation are:

Total cost (one off)=(a+(b*d))*(1-c)

Total cost (annual)=(b*e)*(1-c)

1.65 Assuming that the regulation were restricted such that only EFPIA members were required to implement pack-based mass serialisation, the formulae for total one-off and annual costs assuming zero EFPIA implementation without regulation are:

Total cost (one off)=(a+(b*d))*c

Total cost (annual)=b*c*e

1.66 The incremental cost of this policy option is zero if it is restricted to EFPIA members and 100 per cent implementation by EFPIA without additional regulation is assumed.

Table 1.16: Source of Information

Category	**Sources**					
A. Cost of regulatory co-operation and harmonisation for policy	This should not be significant compared to other requirements, but there will be a burden on national competent authorities					
B. Cost of database (including on-going running)	EFPIA firm - €30m - €40m	Industry - €60m over 5 years	EFPIA previously estimated €0.01- 0.02 per pack (preliminary estimate) for running and updating database network	Technology firm €1.5m each for 5 biggest markets for 10-20 firms.		
C. Number of packaging lines	Large generic firm has 40 product lines per packaging line. Applying this to the EU (250,000/40=6250), but probably more packaging lines to account for smaller firms.	Packaging equipment supplier - we get widely varying numbers depending on the definition of Pharma and Europe.	Industry information is that the ratio of product lines to packaging lines is 5:1 (Given estimate of 250,000 product lines, maybe 50,000	EGA say 20,000+ sites supplying EU and 5-10 packaging lines per small company	EFPIA - A top 10 firm may have 60 lines	Based on Industry data of 4 million packs per line and given 20bn packs in the EU there could be 5,000 lines supplying EU.

		Of course many lines supplying Europe are actually outside…but I'd guess it's in the low thousands of lines. France allegedly has around 700 alone.	packaging lines)	so maybe 200,000 packaging lines (may include some OTC).		
D. Proportion of packaging lines for EFPIA (originators)	EGA: Expect that more than half packaging lines would be generic, but this includes generic firms sub-contracting for innovative, which may have to be adapted if the policy applied to all innovative medicines.	EGA claim to have more sites supplying the EU than EFPIA	US Generic Pharmaceutical Association – Approx. 65% of prescriptions are generics	Industry source - EFPIA possibly fifth of market		
E. Cost per packaging line	Technology firm (one-off): Hardware costs per line = £25,000, software costs = £150,000 (RFID)–£100,000 (barcode),regulatory costs = £2,000,	AESGP - €50,000 per packaging line. Most of the OTC manufacturers have three lines and more which would make a total of about €150,000 per manufacturer (€50,000 per line). Such increase of cost would be particularly difficult to bear for the many smaller size companies in the sector.	Large US Generic manufacturer, 68 unique packing lines cost of $35million to install 2D equipment on these lines. Other firms consider this to be a significant overestimate.	Packaging equipment supplier - You can budget from under £10k (just for a simple printer) through to around £100k for a system that tracks random serialised codes at speed.	EFPIA estimates: €50,000 – 100,000 / lines x 3,000 – 6,000 line Altogether ~ €150 - 600 million	AESGP - stickering machine (one per production line): approx. €200,000 per line. Cost of printing 2D barcode on the pack: €0.04 (for the manufacturer);
F. Running cost per packaging line	Technology firm - 0.1 full-time employee per annum, per line QP €100,000 QA	Industry says €80,000 for labelling mostly labour (a label costs	EGA production line staff need to work on three shifts (and the	Industry source – 5 half-time employees (or 2.5 full-	AESGP - additional labour required: approx.	

	€40/h EFPIA, assistant €24/hour, production manager €40/hour or €50K (inc overheads) i.e. 5K total cost.	€0.003 each).	wage estimation may be low), this should include maintenance and may need full time staff (more like €50,000).	time employees)	€50,000 per year per line	

Part a

1.67 Table 1.17 presents a summary of the costs for this policy option of last wholesaler level authentication and Table 1.18 illustrates the sources of these cost estimates.

Table 1.17: Cost Summary for Policy Option 4.1.5(a)

	Cost category	Value
A	Cost of (2D) Scanner	€ 400
B	Number of scanners required by short-line wholesaler	3
C	Number of hours per firm required for scanning at short-line wholesaler	2,000
D	Wage	€ 14
E	Lifetime of scanner (years)	5
F	Number of short-line and non-mechanised full-line warehouses	20,000
G	One-off cost for full-line wholesaler (mechanised warehouse)	€ 500,000
H	Annual cost for full-line wholesaler	€ 50,000
I	Number of warehouses of full-line wholesalers (mechanised warehouse)	600
	Total cost (one off)	**€ 300.00m**
	Total cost (annual)	**€ 594.80m**
	Net present value	**€ 5,317.34m**

1.68 The cost of a 2D scanner varies dependent upon the quality, brand and functionality. On the basis of prices on the website of a leading barcode scanner retailer and information provided to us by industry, we assumed a cost of € 400 per scanner and that three scanners would be required per short-line wholesaler. A technology firm informed us that these scanners typically need replacing after five years.

1.69 Calculations based on information provided by industry sources indicated that the number of required hours could be between 5,000 and 20,000 for medium-sized firms. However, the sources also noted that there are many smaller firms for which time requirements could be less than 1 per cent of the figure quoted. We therefore assumed that the time required is 2000 hours per firm.

1.70 The cost for a short-line wholesaler is based on a wage of €14 per hour, including a 25 per cent increment for overheads as per the ACM. This is approximately two-thirds of the

average EU wage and is considered appropriate because scanning packs will require low-skilled labour.

1.71 Our estimate of the number of short-line and full-line wholesalers in the EU was based on a document provided to us by GIRP. We extrapolated to EU level figures for Denmark, Germany, Italy, Hungary, Portugal and the UK, noting that Germany and the UK are relatively large players. For full-line wholesalers we also accounted for further information provided to us by GIRP and EAEPC.

1.72 The cost for a full-line wholesaler is based on a cost estimate provided by GIRP, using US cost estimates as a benchmark, noting that the technology proposed in California is more complicated than that proposed here. The system required would be similar to that for batch e-pedigree and hence the costs to full-line wholesalers are the same for both policy options. We assumed that annual maintenance costs would be 10 per cent of the implementation cost.

1.73 Using the letters in the left-hand column of Table 1.17, the formulae for calculating the total one-off and annual costs of last wholesaler authentication are:

Total one-off cost = g*i

Total annual cost = ((a*b)/e) + (c*d)*f) + (h*i)

Table 1.18: Source of Information

Category	Sources				
A. Cost of (2D) Scanner	Based on Datalogic products at www.thebarcodewarehouse.co.uk	EFPIA - €1,500 per pharmacy (approx €300 - 400 € per reader)	Technology firm - €1,000 each for the first one and €500 for the second and third total.	Industry - €400 scanner	GIRP - €600
B. Requirements at short-line wholesaler (scanners)	EE assumption				
C. Requirements at short-line wholesaler (hours) per firm	Industry source: 150m/75packs-per-hour/100 firms= 20,000 hours but many much smaller (some as low as only 0.5-1%)	Industry and EE calculation - average of 5,000 hours for each of 20,000 manufacturers.			
D. Wage	Low-cost labour				

E. Lifetime of scanner	Technology firm: 5 years				
F. Number of short-line (including non-mechanised full-line warehouses)	GIRP table shows information on the number of wholesale licences and full-line wholesalers in Denmark, Germany, Italy, Hungary, Portugal and the UK				
G. Cost for full-line wholesaler (mechanised warehouse) one-off	California Board of Pharmacy meeting: costs warehouse $1,300,000 or $1.5m to $20m over 5 years per warehouse				
H. Requirements at full-line wholesaler (annual)	EE assumption				
I. Number full-line (mechanised warehouse)	EAEPC half regional UK manual others automatic	GIRP 1,458 full-line warehouses so assume 600 are fully mechanised based on EAEPC.			

Part b

1.74 Table 1.19 presents a summary of the costs for this policy option of retail-level authentication and Table 1.20 illustrates the sources of these cost estimates.

Table 1.19: Cost Summary for Policy Option 4.1.5(b)

	Cost category	**Value**
A	Cost of (2D) Scanner	€ 400
B	Lifetime of scanner (years)	5
C	Number of scanners per shop	4
D	Extra cost of scanner system per shop	€ 150
E	Number of pharmacies in EU, excluding those that already have a scanner system	130,000
	Total cost (annual)	**€ 45.50m**
	Net present value	**€ 383.81m**

1.75 The cost of a 2D scanner varies dependent upon the quality, brand and functionality. On the basis of prices of a leading internet barcode scanner retailer and information provided to us by industry, we assumed a cost of € 400 per scanner and that four scanners would be required per shop. A technology firm informed us that these scanners typically need replacing after five years.

1.76 We asked if there would be extra annual costs associated with the scanner system (e.g. licences, software costs and so on). A technology firm stated that there would be no additional costs whereas GIRP believes such costs would be €150. We considered it unlikely that there would be no additional costs and hence took the upper estimate in our calculations.

1.77 We are aware that pharmacies in Germany generally have scanner systems installed already. Therefore, the number of pharmacies that would require a new scanner system is not equivalent to the number of pharmacies in the EU. The estimates of industry sources generally referred to the number of pharmacies in the EU, although GIRP informed us that there are approximately 21,000 pharmacies in Germany. On this basis, we assume that the number of pharmacies that would require new scanners is 130,000.

1.78 Using the letters in the left-hand column of Table 1.19, the total annual cost of retail-level authentication is calculated as follows:

Total annual cost = (e*((a*c)+d))/b

Table 1.20: Source of Information

Category	Sources				
A. Cost of (2D) Scanner	Based on Datalogic products at www.thebarcodewarehouse.co.uk	EFPIA - €1500 per pharmacy (approx €300 - 400 € per reader)	Technology firm - €1000 each for the first one and €500 for the second and third total.	Industry - €400 scanner	GIRP - €600
B. Lifetime of scanner	Technology firm - 5 years				
C. Number of scanners per shop	EFPIA - 5-10	PGEU - 4 scanners per pharmacy	GIRP - 4 at point-of-sale		
D. Extra cost of scanner system per shop	Technology firm- none software costs constant	GIRP - €150			
E. Number of pharmacies in EU (that need to purchase scanners)	PGEU -140,000 in EU	EFPIA - 144,000	EGA – we should consider hospitals, nursing homes and dispensing doctors	GIRP - EU 22 147,000 but Germany already has these and there are 21,000 there.	

Policy option 4.1.6 — Community database of wholesalers

1.79 Table 1.21 presents a summary of the costs for this policy option of introducing a community database of wholesalers and Table 1.22 illustrates the sources of these cost estimates.

Table 1.21: Cost Summary for Policy Option 4.1.6

	Cost category	**Value**
A	Cost of building GDP database	€1,000,000
B	Database running costs	€100,000
C	Total GDP certificates in EU	20,000
D	New certificates each year	4,000
E	Proportion of GDP certificates not already being entered	40%
F	Cost of issuing certificates	0
G	Time to insert one certificate (hours)	0.25
H	Wage	€ 23.45
	Total cost (one off)	**€ 1.05m**
	Total cost (annual)	**€ 0.11m**
	Net present value	**€ 1.97m**

1.80 We received relatively little information regarding the costs associated with this policy option. Indeed, as Table 1.22 illustrates, we received only one industry estimate for each cost category and so in contrast to previous sections, an explanation of the derivation of the costs used in our calculations is not required. It should be noted that the costs of this policy option would be borne by the regulator but are likely to be passed on to industry as fees charged by the regulator.

1.81 Using the letters in the left-hand column of Table 1.21, the total one-off and annual costs of a Community database of wholesalers is calculated as follows:

Total one-off cost=a + (c*e*g*h)

Total annual cost =b + (d*e*g*h)

Table 1.22: Source of Information

Category	Sources
A. Cost of building GDP database	EMEA - €1m if format and procedure for issuing GDPc and WL are similar to GMPc and MIA.
B. Database running costs	EE estimate based on assumption of 2 skilled full-time employees to manage database
C. Total GDP certificates in EU	EMEA - 20,000 GDP certificates
D. New Certificates each year	EE assumption that firms inspected slightly less frequently than every 3 years
E. Proportion of GDP certificates not already being entered	EMEA: 8 NCAs represent the biggest countries in terms of GMPc and MIAs. They developed national databases due to the high volume of data they own and it could represent more than 50% of the total volume of the EU (EMEA think it is 60%).
F. Cost of issuing certificates	EC - certificate itself is not really costly
G. Time to insert one certificate (hours)	EE assumption
H. Wage	Eurostat - Average 2005 EU wage adjusted as described above

2 TRANSIT CALCULATIONS

Introduction

2.1 The nature of trade in transhipped goods makes it very difficult to estimate what proportion are pharmaceuticals, especially those travelling by air or sea. Transhipped goods do not enter into circulation in the EU and often pass right through with minimal customs control (for example, goods moving from one aeroplane to another are seldom monitored). They do not require a customs declaration and therefore are not recorded according to their product type.[4] They are also not recorded in official trade statistics.[5]

2.2 Goods travelling under customs control (between free areas or through the EU) require a T1 form, which is filled out both upon entry to and exit from the EU area to ensure the goods leave the EU. However, records of these forms and, in particular, the products they relate to are poorly maintained; any reliable past data in this regard have been obtained via specific Member State questionnaires, none of which relate to pharmaceutical products.[6]

2.3 For these reasons, estimations and extrapolations have been used to estimate the volume of pharmaceuticals products transhipped and transited through the EU, and the revenue generated by this practice.

Basis for estimation and extrapolation

2.4 While the majority of general cargo is transported by sea, the transport of finished pharmaceuticals likely to be more evenly distributed between sea and air. This is due to the fact that many pharmaceutical products are relatively light and sensitive to storage conditions (relating to temperature) and time spent in transit, for which air travel is better suited. Pharmaceuticals are also high-value goods and insurance while in transit issues may be less costly if they are transported by air. In addition (this is particularly applicable to individual importers), shipping cargo requires a minimum weight which makes it competitive to transport smaller consignments by air. Land transport makes up an almost negligible percentage of the transit of pharmaceuticals between non-EU countries through the EU.[7]

2.5 For this reason it is assumed that for the large-scale transit of pharmaceuticals, 50 per cent travel by air and 50 per cent by sea. For transport relating to individual importers for

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4 Evidence from customs expert, HMRC
5 WTO 'Definitions and Methods': http://www.wto.org/english/res_e/statis_e/its2003_e/technotes_e.htm
6 Report to the European Parliament by the Committee of Inquiry into the Community Transit system (1997); section 3.2.2.1
7 Opinion of Quality Director for EMEA: DHL Excel Supply Chain. It is competitive to transport a consignment of under 12 pallets by air.

export, who are more likely to move smaller amounts, 60 per cent is assumed to travel by air and 40 per cent by sea.[8]

2.6 Transit volumes and revenues have been estimated separately for air and sea for the main hub air and seaports in the EU. The tables below are more detailed than those in the main report (where just the key figures are presented) and show all stages of the calculations.

2.7 The revenue figures for both shipping and flying include all revenue generated by the movements: for forwarding agencies, airlines, airports, shipping lines and sea ports.

Sea

Table 2.1: Revenue from pharmaceuticals transhipped via sea

Major ports in EU:	**Rotterdam**	**Antwerp**	***Hamburg***	**Amsterdam**	**Le Havre**	**Total**
TP: throughput of all goods in 2007 (1,000 tons)[9]	406,812	182,897	*140,381*	87,480	78,885	896,455
R: ratio to Hamburg $[TP_O / TP_H]$[10]	2.898	1.303	*1*	0.623	0.562	
PT: estimated weight of pharmaceuticals transited through from outside the EU (1,000 tons)[11] $[R*PT_H]$	322	145	*111*	69	62	*** 710**
AR: average revenue from transit shipment from Laos to Brazil,[12] per 10 tons[13]: *** €4,500**[14]						
RP: revenue per port (€ millions): [AR*PT/10]	145	65	50	31	28	*** 319**
Total revenue from pharmaceuticals transhipped by sea: €319,454,170						

Notes:

Figures may not add up accurately due to rounding

Figures with stars appear in Table 1A in main report

8 Opinion of Quality Director for EMEA: DHL Excel Supply Chain
9 Rotterdam Port Authority: Industry and Bulk Cargo
10 Subscript 'H' represents Hamburg; subscript 'O' represents other ports
11 This weight makes up part of the total throughput of all goods
12 Typical sea route via EU of transited pharmaceuticals, provided by opinion of Quality Director for EMEA: DHL Excel Supply Chain
13 Average weight of a shipment: 24 pallets at 417kg each
14 TransGlobal Express; PharmaExport

2.8 Trade and transit statistics from the port of Hamburg (in italics) form the basis of the estimation of the volume of pharmaceuticals transited through five major 'transit-hub' ports: Rotterdam, Antwerp, Hamburg, Amsterdam and Le Havre. These were chosen due to their high volume of trade and their positioning along global transit routes.[15]

2.9 The volume of pharmaceuticals transhipped from outside the EU (PT) was estimated for Hamburg as follows:

- In 2007, the total throughput (imports and exports; not necessarily in transit) of pharmaceuticals[16] through Hamburg was 585,000 tons.
- This formed 0.417 per cent of Hamburg's total throughput (TP) of all goods in 2007.
- The volume of transit traffic via Hamburg in 2003 was 20.2 million tons.[17] A transit traffic statistic was not available for 2007, but was estimated to be 26.7 million tons. This estimate was made by applying the ratio of transit traffic to total throughput in 2003 (19 per cent) to total throughput in 2007.
- It is assumed that the same proportion of total trade made up by pharmaceuticals applies to transit trade.
- This gives **111,167 tons of pharmaceuticals** that were transited through Hamburg in 2007 (0.00417 * 26,676,352).

2.10 Estimates for the other ports shown assume the same relationship between total throughput and pharmaceuticals transited through from outside the EU as in Hamburg.

2.11 The total weight of pharmaceuticals transhipped from outside the EU was calculated as follows:

$$\mathbf{PT_A = PT_H + \sum PT_O}$$

where $\mathbf{PT_A}$ = weight of pharmaceuticals transhipped from outside the EU for all ports (710,000 tons)

$\mathbf{PT_H}$ = weight of pharmaceuticals transhipped from outside the EU though Hamburg

$\mathbf{\sum PT_O}$ = sum of the weight of pharmaceuticals transhipped from outside the EU though each of the other four ports

$= \sum \mathbf{R_O * PT_H}$

where $\mathbf{R_O}$ = ratio of total throughput (TP) of other ports to Hamburg

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15 Rotterdam Port Authority: Industry and Bulk Cargo; TransGlobal Express; Global Shipping www.globalshippingnet.com; Antwerp Port Authority

16 "Pharmaceuticals, including aesthetic oils and cleansing preparations"

17 Hamburg Port Authority

$$= \mathbf{TP_O / TP_H}$$

2.12 The revenue generated from this transit is calculated as follows:

$$\mathbf{TR = \sum RP_A}$$

where **TR** = total revenue from pharmaceuticals transhipped by sea

RP_A = revenue per port for all ports

$$= \mathbf{AR*PT_A/10}$$

where **AR** = average revenue of shipment per 10 tons

2.13 The revenue generated by these movements has been estimated based on a 'case-study' sea route suggested by transport experts, from Laos to Brazil. Due to the distance this assumption is likely to result in an upper bound for shipping costs. The average cost for a shipment of ten tons for this route is € 4,500.

Air

Table 2.2: Revenue from pharmaceuticals transhipped by air

Major airports in EU[18]	**Frankfurt**	**Schiphol**	***Heathrow***[19]	**Charles de Gaulle**	**Luxembourg**	**Milan**	**Total**
TT = total transit movements			*267,552*				
R = ratio to Heathrow (freight volume)[20]	1.26	1.04	*1*	0.918	0.463	0.245	
PT = estimated number of transit movements of pharmaceuticals[21] [$R*PT_H$][22]	3,637	2,995	*2,878*	2,643	1,335	704	***14,193**
AR = average revenue per movement[23]				***** €39,963			
RP = revenue per airport (€million) [AR*PT]	145	120	115	106	53	28	*** 567**
Total revenue from pharmaceuticals transhipped by air: €567,194,859							

Notes:

Figures may not add up accurately due to rounding

Figures with stars appear in Table 1B of main report

2.14 Transit statistics from the United Kingdom form the basis of the estimation of the volume of pharmaceuticals transhipped through six main 'transit-hub' airports: Frankfurt, Schiphol, Heathrow, Charles de Gaulle, Luxembourg and Milan. For each of these airports extra-EU freight was dominant in 2003 (at least 78 per cent of total freight transport), and three of the airports were top for freight transport to and from Africa, Australasia, Asia and America.[24] These airports were also suggested by a pharmaceutical transport industry expert as being among the main transit hubs in the EU.[25]

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18 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.

19 The UK forms the basis for the estimation: related figures in italics.

20 Ratios from De La Fuente Layos (2005) "Statistics in Focus: Transport", Eurostat publications

21 See paragraph 1.5.2 for estimation methodology.

22 Subscript H represents Heathrow.

23 Typical air route from India to Nigeria, based on evidence from MHRA. Costs from Trans Global Express and PharmaExport. Average weight of 4,170kg per movement: 10 pallets at average 417kg each – more than 12 pallets would not go by air.

24 De La Fuente Layos (2005) "Statistics in Focus: Transport", Eurostat publications

25 Opinion of Quality Director for EMEA: DHL Excel Supply Chain.

2.15 The number of transit movements of pharmaceuticals from outside the EU was estimated for the UK as follows:

$$\mathbf{PT_{UK} = (TT*PO*PP) * 0.5}$$

Where $\mathbf{PT_{UK}}$ = number of transit movements of pharmaceuticals through the UK from outside the EU

TT = number of total transit movements through UK

PO = proportion of import quantities (all goods) to the UK that originated from outside the EU in 2007

PP = percentage of pharmaceuticals as a share of total imports for the UK

0.5 = proportion of all pharmaceutical transit movements that go by air

- The number of total transit movements (TT) for 2007 (267,552) was obtained for the UK from HMRC.[26] The proportion of total import quantities to the UK that originated from outside the EU in 2007 (PO = 0.65) was applied to this figure to get an estimate of the transit movements from outside the EU (173,909). The percentage of pharmaceuticals as a share of total imports for the UK (PP = 0.0331) was then applied to this figure, to get an estimate of the transit movements of pharmaceuticals from and to non-EU countries (5,756).[27]

- For the purpose of the general transit of pharmaceuticals, it is assumed that 50 per cent travel by air. The estimated number of transit movements of pharmaceuticals through the UK is therefore decreased by 50 per cent to arrive at the air transit figure in the table (2,878).

2.16 This figure was then extrapolated across the other five main air-transport hubs using ratios obtained from *De La Fuente Layos (2005) "Statistics in Focus: Transport"*[28] to get the average number of transit pharmaceutical movements across the six main hubs.

2.17 Each movement is estimated to be an average of 10 pallets of pharmaceuticals, at a total revenue of €39,963. This is based on evidence and opinions from pharmaceutical transport experts and forwarding companies (couriers).

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[26] Transit movements entered into the New Computerised Transit System. No indication of product, or if originated from outside the EU.

[27] All trade figures obtained from www.uktradeinfo.com, using SITC 54.

[28] Eurostat publications 2005

Estimating costs for EU firms only

2.18 The average revenue for a movement of pharmaceuticals (€39,963 for air and €4,500 for sea) are estimates from two courier agencies[29], and include the total revenue generated by the movement accruing to the courier/forwarding agent who arranges the transport, the airline or shipping company responsible for the actual movement of the goods, and the airport and seaport responsible for handling the goods in transit.

2.19 For the purpose of this study, we are only interested in those lost revenues that accrue to EU firms. In addition, the policy option intends only to prevent pharmaceuticals passing through the EU; not to prevent all transhipment. For these reasons it is possible that the total revenue lost to the EU from the policy options will be less than previously stated.

2.20 However, it is difficult to separate the total cost quoted by the courier agents into the different components i.e. how much would go to the airline/shipping company, and how much to the airport/seaport. Furthermore, it is unclear where exactly EU or non-EU firms will be affected. For example, if an Indian or Nigerian forwarding agent arranged the movement of pharmaceuticals from India to Nigeria, using an Indian or Nigerian airline, then the only cost of the movement accruing to the EU would be the airport handling charges in the EU transit country. However, it may well be the case that an EU airline is used to transport the pharmaceuticals from India to the EU, and then out again, or that an EU forwarding agent is tasked with overseeing the transit. This situation seems relatively common (for example British Airways flying goods from India to Heathrow, and then on to Nigeria) [30], and for this reason we have assumed that mainly EU-based airlines are used.

2.21 In addition, many large pharmaceutical companies engage in major transhipment (such as Pfizer) from their factories outside the EU to other non-EU countries. In this case, as the pharmaceutical company is based in the EU, EU forwarding agents and airlines are typically used.[31] In this case, the total revenue lost would accrue to the EU.

2.22 Furthermore, in some cases the route from non-EU country to non-EU country specified *has* to go through the EU (for example the sea route from Laos to Brazil must pass through Hamburg) for logistical reasons (refuelling etc). In this case, there would be no alternative route avoiding the EU, and the policy option would effectively ban the total transhipment. The total revenue would therefore be lost.

Hypothetical calculations

2.23 However, in the unlikely case that exclusively non-EU airlines and shipping companies were used in the transhipment, then the only revenue losses to the EU of the policy would be from the airports/seaports. I have attempted to estimate these. The majority of the

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29 Costs from Trans Global Express and PharmaExport
30 Opinion of Quality Director for EMEA: DHL Excel Supply Chain
31 Opinion of Pfizer expert in charge of re-export

cost of transport is due to the actual flight/shipment. Air transport is particularly expensive, as the costs are determined by volume, not weight. So a large pack of medicine boxes, even if it is relatively light, will take up a lot of space and therefore be expensive to transport.

Air

2.24 Many airlines employ their own freight handlers and rent storage space from airports. Others use contracted service providers. These will be based in the EU country of transit, and any loss of revenue will therefore affect the EU.

2.25 An idea of the charges involved in moving cargo during a transhipment ("processing and removing freight to other bonded premises to await reloading (on arrival), and processing, handling and warehousing of cargo up to the point of delivery to the aircraft") are:

€350 (inbound) and €397 (outbound) for 4,170kg

Total of €936 per movement.[32]

2.26 This is what would accrue to the contractors. As previously mentioned, large airlines (BA; Virgin etc) include these charges in the original airway bill and it is not possible to separate them out.

Sea

2.27 The situation when shipping goods is slightly different, as here charges for handling cargo are levied by the ports themselves (most likely due to the need for large loading equipment, the ownership of which is not cost effective for individual shipping lines).

2.28 An average obtained from three main EU seaports, Le Havre, Antwerp and Rotterdam, for loading, unloading and temporary storage of 24 pallets[33] is:

€785[34] per shipment of 24 pallets.

2.29 In conclusion, if in all cases only non-EU airlines and couriers are used in the transhipment of goods, then the above two sets of costs per movement (€936 for air and €785 for sea) will be all that is lost to the EU. This works out to a total of €13,284,648 for air transport (€936 * 14,193 movements) and €55,735,000 for sea transport (€785 * 71,000 movements).[35]

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32 Based on information from BA World Cargo
33 Our 'case study' shipment'
34 DTZ Consulting and Research (2005) "Benchmark study: Antwerp, Le Havre, Rotterdam"
35 Using the same figures for number and weight of movements found in tables 1.4 and 1.5 in the Annex

2.30 However, as mentioned before, we think it highly unlikely that only non-EU airlines, shipping companies and couriers will be used, and therefore the revenue losses to the EU have remained as those originally stated.

Estimating revenues from import for export trade

Number of importers

2.31 Medicinal imports intended solely for re-export are included in national import statistics, but are not disaggregated as such.

2.32 It is assumed that importers of medicinal products without a license issued by the Competent Authority authorising the import of licensed medicines into the EU are engaged in the import for export trade. The products they bring into the EU are not intended for the EU market and often remain under customs control (for example in free zones) until they are ready to be re-exported from the EU.

2.33 It is these importers who would not be able to trade should regulations be passed prohibiting the entry of medicines into the EU not fulfilling all EU requirements.

2.34 Evidence from the MHRA[36] and UK customs shows that in 2006, 602 of the 700 importers that recorded imports from non-EU countries under customs code 3003 and 3004[37] did not have a licence granted by the MHRA to import licensed medicines. This figure of 602 unauthorised importers forms the basis for our extrapolation to the EU, bearing in mind the opinion that the UK is a particular 'target' for transit and import for export trade.[38]

2.35 UK figures were extrapolated across the five other main transit countries (Germany, France, the Netherlands, Belgium and Italy) to obtain an estimate of the number of unlicensed importers in the EU. A small allowance is made for other Member States.

2.36 The following table shows the necessary calculations.

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36 Medicines and Healthcare Regulatory Authority, UK

37 Customs codes for medicinal products

38 European Commission Fact Finding Mission Questionnaire (2007) "Studies on distribution channels on patient safety aspects related to counterfeits and parallel trade in medicines and medical devices." UK response

Table 2.3: Calculation of number of unlicensed importers in the EU.

Main transit countries in EU:	**UK**	**France**	**Germany**	**Italy**	**Belgium**	**Netherlands**	**Total**
TI = total non-EU pharmaceutical imports (€million)[39]	4,874	4,102	6,848	4,100	3,529	4,776	28,229
NU = number of unlicensed importers[40]	602						
R = unlicensed/licensed	0.86						
UI_{UK} = extra-EU imports accounted for by unlicensed importers (€million)	4,192						
IPI = imports per importer (€) [UI_{UK}/NU]	6,963,399						
Assume unlicensed importers account for 70% of extra-EU imports in other hubs							
UI = extra-EU imports accounted for by unlicensed importers (€million) [TI*0.7]		2,872	4,794	2,870	2,471	3,343	
Number of importers [UI/IPI]	602	412	688	412	355	480	2,950
For all other states, assume unlicensed importers account for 5% of extra-EU imports.							
Number of unlicensed importers in non transit-hub states							386
Total number of unlicensed importers in EU:							*** 3,336**

Note: Figures with stars appear Table 1C in main report

2.37 Unlicensed importers in the UK represent 86 per cent (602/700) of importers importing pharmaceuticals from outside the EU. It is not expected that unlicensed importers truly account for 86 per cent of the value of imports, as these importers are assumed to be small businesses whose trade is far outweighed by the main pharmaceutical manufacturers and wholesalers. This ratio is merely used as a means of relating the number of importers in the UK to a statistic common across all other EU countries, namely pharmaceutical imports from outside the EU.

[39] Eurostat 2006; SITC 54
[40] MHRA and HMRC expert opinion

- This same logic applies to the 'imports per importer' figure.. As the UK is seen as a main target for this trade, it is assumed that in the other main transit countries unlicensed importers account for 70 per cent of extra-EU imports.

- The value of pharmaceutical imports accounted for by unauthorised importers for the other four countries was calculated by applying 70 per cent to the value of pharmaceutical imports from outside the EU. This was then divided by an average 'value per importer' of €6,963,399 to get the number of unlicensed importers. This assumes firms in the other four countries are the same size as those in the UK (they deal with the average amount of business) but that they form a smaller industry.

- In order to get a representation for other Member States, it was assumed that unlicensed importers accounted for 5 per cent of extra-EU pharmaceutical imports. The same working as above applies.

2.38 All trade figures used were obtained from Eurostat 2006, as this was the year for which the MHRA knew the number of unlicensed importers. However, as the trade data were used for extrapolation purposes only and the MHRA was of the opinion that the number of importers would not change much in one year, the figures have not been updated to 2007 prices.

2.39 As mentioned before, the figure of unauthorised importers is only an estimate, and it is possible that there exist more of these unlicensed firms of whom the authorities have no knowledge.[41] On the other hand, it is possible that the assumption that in non-UK transit countries unauthorised importers account for 70 per cent of extra-EU imports could be too high. We know that this kind of trade is relatively high in the UK, but the extent to which it exceeds other countries is not known, and could be less than 70 per cent.

Transport revenue generated

2.40 The transport costs each importer incurs are based on pharmaceutical industry opinion of the typical volume and frequency of import of small, unauthorised importers. This is a weekly import of five pallets (assuming two batches of medicines per pallet[42]), at an average of 417kg per pallet. This gives a total of 750,600 pallets transported in a year.[43]

2.41 The average cost[44] of transporting a pallet by air of €2,690 and by sea of €500[45] for an India to Brazil route is adjusted to account for the shares in transport of 60 per cent and 40 per cent respectively. Out of the 750,600 pallets transported in a year, it is assumed

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41 Expert opinion from pharmaceutical industry.

42 Larger pharmaceutical companies keep to one batch/product per pallet for safety reasons, but smaller companies who import less may have more than one batch in a pallet.

43 Based on 3,336 importers and 45 working weeks in a year.

44 Costs obtained from TransGlobal Express and PharmaExport

45 This is not a true representation for one pallet as often a minimum weight applies.

450,360 will go by air and 300,240 by sea, giving the total revenue generated of €1,361,588,400. This results in transport costs per firm of €408,150 a year.

2.42 The loss of import for export trade will also result in a downstream loss to warehouse storage and handling revenue, as some importers for export process their goods in warehouses within customs free zones. Although a relatively small proportion of total trade (all goods) goes through these areas, this is thought to be higher for pharmaceuticals imported for the purpose of re-export, mainly because some of the products are not licensed in the EU and cannot leave customs control. Estimates of the proportion of all import-for-export trade in pharmaceuticals that goes through these warehouses range from 45 per cent to 60 per cent.[46]

2.43 The total number of pallets transported across importers is 750,600. An average of 53 per cent (397,818) of these will go through warehouses. An estimate of handling and storage costs for transit through customs warehouse for 5 pallets (a weekly import) is €154,[47] bringing the revenue lost to warehouses to €12,252,794 across the EU.

Value added

2.44 'Value-added' or 'net output' is defined as the difference between the value of the output a firm generates and the value of the inputs purchased from other firms.[48] It is used to describe a firm's contribution to GNP, and is made up of wages and net profit.

2.45 If importers for export are no longer able to carry out their trade in the EU, the value-added they generate will be lost.

2.46 Data from an Institute for Pharmaeconomic Research report "The European Pharmaceutical Wholesale Industry: Structure, Trends, and socio-economic Importance" (2005) provide the basis for estimates of value-added of these import-for-export firms. It is assumed that importers for export undertake similar activities to wholesalers, but to a lesser degree and therefore add less to the economy (case-study evidence from Malta suggests activities are limited to breaking down bulk and assembling smaller packs, and that operations and number of employees are relatively small).[49] Value-added figures for wholesalers have therefore been reduced by 40 per cent to account for this.

2.47 The average direct value-added from pharmaceutical wholesalers in the EU for 2005 was €68,353 per employee,[50] 60 per cent of which is €41,012.

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46 Opinion of Quality Director for EMEA: DHL Excel Supply Chain; and UK free zone manager.
47 DTZ Consulting and Research (2005) "Benchmark study: Antwerp, Le Havre, Rotterdam"
48 Clement et al (2005) "The European Pharmaceutical Wholesale Industry: Structure, Trends, and socio-economic Importance", IPF
49 Malta Medicines Authority
50 Clement et al (2005) "The European Pharmaceutical Wholesale Industry: Structure, Trends, and socio-economic Importance", IPF

2.48 It is assumed that each firm employs an average of 16 employees,[51] bringing total value-added per firm to €656,192. This is adjusted to reflect 2007 wages,[52] giving a final value of €716,578 per firm.

Direct business costs: Policy option 4.2.2

Qualitative analysis

2.49 One of the requirements of policy option 4.2.2 is for importers to subject each batch they receive to qualitative and quantitative analysis. These tests check for, among other things, the presence of and correct amount of active ingredients. It is assumed that such tests would be contracted out by the importer, under the responsibility of the Qualified Person.

2.50 Estimates from a pharmaceutical testing company, Eclipse Scientific Group, place the cost of such tests at an average of €325.78 per batch.[53] As it is estimated that each importer imports 5 pallets a week, at two batches per pallet, this brings to the total number of batches per importer per year to 450, and the costs of testing to €146,601 per firm.

Downstream impacts

2.51 The average annual per-firm costs of meeting the requirements of Policy 4.2.2 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 (testing the quality and quantity of active ingredients in medicinal products), which, at an estimated annual cost of €146,601 per firm, accounts for between 66 and 78 per cent of the annual costs.

2.52 As the closest comparable data, gross profit[54] figures for wholesalers on the UK[55] were used as a base against which to evaluate these costs. The gross profit figures were adjusted slightly downward to take into account the higher transport costs importers for export would incur, as opposed to ordinary wholesalers.

2.53 Additional per-firm costs stemming from the proposed new policies came to an average of 25 per cent of gross profits, and would account for an even larger proportion of net profit (after the inclusion of costs such as capital expenditure and interest). This is likely to have a displacement effect among the importer firms, in particular the smaller firms with less turnover and smaller profits.

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51 60% of industry average: Annual Business Inquiry (2007) "Wholesale of pharmaceutical goods" www.statistics.gov.uk

52 Assuming 4.5 per cent nominal growth in wages per annum, which is roughly equivalent to 2 per cent inflation and 2.5 per cent real growth in wages.

53 Between €210 and €442 per batch, depending on the complexity of the medicine.

54 Total turnover less total expenditures and employment costs

55 Annual Business Inquiry (2007) "Wholesale of pharmaceutical goods" www.statistics.gov.uk

2.54 We therefore assume that many smaller firms, accounting for 10 per cent of the total firms in this trade, may decide that they cannot profitably stay in business with the additional costs, which may be higher in relation to their gross profits than is the case for larger firms. They withdraw. It is very likely that part of their business will be taken up by the larger firms in the industry, who will also be losing competitiveness and some business in the EU as a result of additional costs.

2.55 It is therefore estimated that the policy option will have a downstream effect of pushing just under 5 per cent of the industry out of business (as those firms who go will be smaller than those who stay). Including those firms who may take their re-export business outside the EU as a result of the policy[56] brings the proportion of business lost as a result of this policy to a full 5 per cent. The losses are expressed in terms of total revenue generated (€188m) and employment (2,669 jobs; or 166 firms), calculated as 5 per cent of the total revenue and employment losses stemming from policy 4.2.1, where the whole import-for-export industry goes out of business.

Carbon savings

2.56 The carbon emission of a single-passenger flight from India to Brazil (our case-study route) is estimated at 1.62 tons of CO_2, and trip of a large sea-going bulk carrier via this route emits nearly 16,000 tons.[57] Clearly a small shipment of pharmaceuticals will not contribute much to the overall weight of a large bulk carrier, but this figure gives an idea of the possible saving involved if the transit of medicines did not take place.

2.57 Applying these estimates to the figures for sea and air transit yields the following estimated carbon savings:

- Number of flights (transit movements): 14,193
- Carbon emissions saved: 27,634 tons
- Total weight of sea journeys: 710,000 tons
- Carbon emissions saved: 54,668
- Total carbon emissions saved in one year: 82,302

[56] The possibility of this occurring was suggested by an industry expert.
[57] www.carbonfootprint.com; www.climatecare.org

3 ACTIVE PHARMACEUTICAL INGREDIENTS CALCULATIONS

3.1 This pillar of the proposed package of policies aims for:

> "Tighter requirements for manufacture, placing on the market of active substances and requirements for inspections."

3.2 Three policies are proposed for this purpose. They are referred to under the headings of 4.3.1, 4.3.2 and 4.3.3. There are sub-options within these categories.

Wages and prices

3.3 Much of the information we received on costs was expressed in 2007 prices. There were cases, however, in which the most recent available cost information was from prior to 2007. It was therefore necessary to adjust these prices for inflation between the year of cost estimation and 2007. The adjustment utilised Harmonised Index of Consumer Prices (HICP) data for the EU-27, obtained from Eurostat.

3.4 We obtained data on the average gross annual earnings in industry and services for the EU-27 from Eurostat and expressed this in hourly terms based on an assumption of 7.5 hours per day and 225 working days per year. The most recent year for which data are available is 2005 and hence it was necessary to adjust the raw data so as to express the wage in 2007 terms. Since the rate of price inflation differs significantly from wage inflation, it would be inappropriate to use HICP for this adjustment.

3.5 Information on a Europe-wide wage index is available only to 2005. Therefore, to convert the 2005 wage to 2007 terms we assumed 4.5 per cent nominal growth in wages per annum, which is roughly equivalent to 2 per cent inflation and 2.5 per cent real growth in wages. Once wages were expressed in 2007 terms, we applied a 25 per cent mark-up to account for overhead costs, as per the EC's standard administrative cost model (SACM).

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

3.6 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.

3.7 The policy is a complement, indeed a possible 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.

3.8 We understand that the precise details of the information to be included on the notification will be worked out at a later stage but will 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.

3.9 The direct business cost here is equal to the number of firms (i.e. manufacturers and importers, 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).

3.10 The wages in the table below for non-EU businesses are based on an estimation of Chinese wages as a high proportion of API imported into the EU from outside the EU comes from China. Research suggests that wage costs in China are about around twenty times smaller than those in the EU, and our calculations reflect this.[58]

[58] YDL Management Consultants, "China: The Untapped Freighter Market, A China-USA Perspective",

Table 3.1: Direct Business Cost of 4.3.1.

	In the EU	**Information source or equation**	**Supplying to the EU from outside**	**Information source**
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
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 - We have used the median figure of 2 hours for purposes of this quantification	Europe Economics estimation	1 to 3 hours - We have used the median figure of 2 hours for purposes of this quantification	Europe Economics estimation
Direct business cost – One-off - AC[59]	**€ 286,090**	**2*€23.45*(600+500+5000)**	**€ 112,500**	**2*€1.25*(15,000+5,000+25,000)**

[59] 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.

Direct business cost – Running (p.a.) - AC[60]	**€ 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**	

Other Business Costs

3.11 Note, however, that the EMEA would 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. So EMEA will require resources of a similar magnitude to establish the website that is proposed here. Such a website would not impact directly upon business costs. However it might be such that the business faces an indirect cost as a result of this, either as feepayers or as taxpayers, depending upon how the EMEA's costs are recovered.

Downstream Effects

3.12 This reasonably small business cost will be equally spread across the sector and amount to a small additional burden for each firm so that we do not anticipate any substantial downstream effects.

3.13 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 but does not seem large enough significantly to deter new entry.

Enhancing audit and enforceability of GMP (Policy option 4.3.2)

Policy proposal 4.3.2(a)

3.14 Three policy options are considered under 4.3.2. The first of these (which we will call 4.3.2.(a)) states:

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

3.15 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

[60] 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.

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 so.

Number of Firms Affected

3.16 The direct business cost of this policy is the cost of per audit multiplied by the number of finished pharmaceutical product manufacturers and importers in the EU and multiplied again by the average number of API suppliers per finished pharmaceutical product manufacturer. There may be some economies of scope for companies dealing in many APIs but this is a reasonable basis for estimation.

3.17 Eurostat indicates that there are 3,700 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.

3.18 We received a range of views across the industry on the average number of API suppliers per finished pharmaceutical product manufacturer. The range presented in the table below reflects these views.

Cost per audit

3.19 There are different possibilities in terms of auditing with different associated costs and benefits. These are considered in the table of costs below.

3.20 The Association of the European Self-Medication Industry (AESGP), the European Association of Euro-Pharmaceutical Companies (EAEPC) and the European Generic Medicines Association (EGA) each provided estimates of the cost of a GMP supplier audit. The cost given below if the audit is conducted by the finished pharmaceutical manufacturer themselves reflects these estimates, while bearing on the lower end of these estimates to reflect the possibility that API audits may be more straight-forward to conduct than the other supplier audits.

3.21 The cost of being audited is calculated by the wage cost of the time that those who are receiving the audit have to take away from business activities that they would otherwise be doing.

3.22 Note that 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 share an API supplier. (A self-assessment audit option would involve 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.[61]

Incremental Cost of the Policy

3.23 In order to estimate the costs resulting from this new policy proposal, allowance needs to be made for the extent to which API audits are already being carried out and would continue to be carried out under the continuation of current policies.

3.24 There is a view that current non-compliance with this policy is most prevalent amongst SMEs supplying generic pharmaceuticals to either the prescription medicines sector or the over-the-counter (OTC) sector. This view is reflected in the high estimate of the net direct business cost shown in the table. There is an opposing view that holds that current compliance is already nearly 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 more accurate.

3.25 Considering that fraction of the cost that will fall on manufacturers, the EGA has indicated that it will use a figure of 50 per cent for the market share held by generics in the EU medicines market in coming years. The EGA also considers approximately 70 per cent of its members to be small enterprises (SMEs). Multiplying the number of finished pharmaceutical manufacturers in the EU (3,700) by 50 per cent and again by 70 per cent thus gives an estimate of the possible number of non-compliant manufacturing firms. This calculation gives a figure of 1,295. Dividing 1,295 by the total number of firms impacted (manufacturers and importers) of 15,000 gives the fraction of the net business cost that can be attributed to manufacturers, rather than importers. This cost would fall entirely upon SMEs manufacturing generic pharmaceutical products. This means that this sector of European industry faces an annual cost of approximately €1,500m. (Please see row M. in table 2 below).

3.26 From this we can conclude that if it is the case that SMEs in generic and over-the-counter (OTC) sectors of the pharmaceutical finished product manufacturing industry are currently non-compliant, then these firms face significant additional costs, as the table below clearly illustrates. Costs of this magnitude might be expected to have not inconsiderable downstream effects.

3.27 Turning to the incremental cost that falls upon importers, 82 per cent of the EU's pharmaceutical imports come from the US and Switzerland.[62] Regulatory regimes and market structures in both of these jurisdictions reassure us that manufacturers in these jurisdictions will generally already be compliant with this policy. This means that 18 per cent of imports may derive from non-EU manufacturers who are non-compliant. It is

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61 http://www.api-compliance.org/APIC_Audit_Programme.pdf

62 Eurostat, External and intra-European Trade, Statistical Yearbook – Data 1958-2006, 2008 Edition

assumed that the market share held by SME generic manufacturers within this 18 per cent is consistent with the EGA figures above (i.e. the market share held by generics is 50 per cent with 70 per cent of generic firms being small enterprises).

3.28 Dividing 11,300 by 15,000 gives the proportion of the gross cost (please, see Row L) that falls upon importers to the EU of finished pharmaceutical product. This figure (roughly €13,500m) might be considered as the importer's gross cost. Multiplying this figure by 18 per cent, by 50 per cent and by 70 per cent gives the net cost that such importers can be expected to face. This calculation gives a figure of roughly €850m. (See row M). This cost would take the form of ensuring that the non-EU finished product manufacturers who are supplying to them have undertaken audits of their API suppliers as per the requirement of this policy. It is assumed that non-EU finished product manufacturers pass this auditing cost on to the importers into the EU who they are supplying.

3.29 In terms of downstream effects, these processes might be expected to reduce business opportunities that are presently enjoyed by some importers to the EU of finished pharmaceutical products but this effect might be expected to be counterbalanced by an improvement in the competitive position of EU generic manufacturers relative to some competitors, i.e. placing the responsibility on the importer to ensure that non-EU manufacturers who are supplying to them are conducting API audits undermines any potentiality for EU generic manufacturers to lose market share (as a consequence of an incremental cost increase due to this policy) to non-EU generic manufacturers.

3.30 It may be, however, that within the generic manufacturing sector, both within the EU and externally, SMEs are disadvantaged relative to non-SMEs, as this policy creates an incremental cost for SMEs but does not likewise for non-SMEs. This would seem to be the case if non-SMEs are currently compliant with the policy but SMEs are not.

Table 3.2: Direct Business Cost of API Audit Policy Option under 4.3.2.

	In the EU	Information source and/or equation
A. Number of pharmaceutical manufacturers and importers	15,000	EMEA
B. Cost of audit - If conducted by pharmaceutical manufacturers themselves	€ 10,000	AESGP, EAEPC, EGA
C. Cost of being audited – The wage cost of 2 people for 2 days (+ 25% uplift) - AC[63]	€ 704	Eurostat 2*7.5*2*€23.45
D. Average number of API suppliers per pharmaceutical manufacturer	We have seen estimates range from 25 to 200 for this figure, so will use the median between these two figures of 112.5 for this calculation	Consultation with industry
E. Direct business cost (if compliance achieved entirely by Third Party Audit) - All manufacturers audit all suppliers themselves	€ 18,062,156,250	(€10,000+€704)*15,000*112.5
F. Cost per Third Party APIC audit	€ 8,400	APIC
G. Direct business cost (if compliance achieved entirely by Third Party Audit) - All manufacturers audit all suppliers by Third Party audit	€ 15,362,156,250	(€8,400+€704)*15,000*112.5
H. Shared Third Party APIC audit	€ 2,300	APIC
I. Direct business cost (if compliance achieved entirely by Shared Third Party audit) - Auditors share information about suppliers amongst manufacturers	€ 5,068,406,250	(€2,300+€704)*15,000*112.5
J. Self Assessment APIC audit	€ 4,200	APIC
K. Direct business cost (if compliance achieved entirely by Self Assessment audit)	€ 8,274,656,250	(€4,200+€704)*15,000*112.5
L. 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

[63] 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.

	In the EU	Information source and/or equation
M. 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 (=€1,500m for manufacturers + roughly €850m for importers)	High estimate of current compliance based on estimate of volume of EU pharmaceuticals produced by SMEs in generic and OTC sectors. (3700*.5*.7) = 1295 non-compliant EU manufacturers+ (12,300*.18*.5*.7)=712 non-compliant non-EU manufacturers (1295+712)/15,000 = overall proportion of manufacturers that are non-compliant (13.44%) 13.4%*€17,905m (from row L)= row M estimate
N. 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 if there were full current compliance (as claimed by some in industry)
O. Direct Business Cost (Median between low and high estimate)	€ 1,197,799,450	
P. NPV - based on a median direct business cost between the low and high estimates	€ 10,098,774,365	

Policy option 4.3.2(b)

3.31 The second of the policy options to be considered under 4.3.2 (which we call 4.3.2 (b)) 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.

3.32 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.[64] This policy guards against impurities entering the API via an unexpected change in its location of manufacture and as such it would be directly relevant to detecting possible counterfeit supplies. It would be

[64] 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.

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.

3.33 The fixed cost below is equal to the number of finished pharmaceutical product production sites multiplied by the cost of the NIR technology, i.e. one set of kit per plant. We understand that 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.

3.34 If the policy were introduced on a risk-based basis then captive supplies may expect to be exempt.[65] The costs are calculated below on the assumption that all plants in the EU have at least some merchant API supplies coming into them.[66] This assumption means that only running cost would be reduced by this risk-based implementation and not the fixed cost. (Please compare row F with row H in Table 3 below).

3.35 If policy-makers wish to reduce the cost of this policy still further they may consider whether a risk-based implementation can be taken further than captive supplies. Recalling that the point of the policy is to guard against impurities entering the API via an unexpected change in its location of manufacture, a risk-based implementation would give further consideration to which pharmaceutical manufacturers are most likely to suffer such problems with their API supplies.

3.36 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.

3.37 Policy makers may also consider a counterfactual scenario in which in the absence of the introduction of this policy, NIR technology nonetheless becomes more widely used (particularly in those market sectors most at risk of the kind of problems that NIR is well designed to correct). To the extent that this scenario seems realistic, the NPV stated below may overstate the extent of the full business cost. (Please see row J). This is because, over the next 10 years, the use of NIR technology would be expected to increase irrespective of whether this policy is introduced or not.

3.38 However, potential costs of this policy 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.

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[65] API supplies are considered captive when they are produced in a facility owned and controlled by the finished pharmaceutical product manufacturer who will use this API.

[66] Merchant API supplies being non-captive API supplies.

3.39 The number of batches of API in the EU is not known. It has been estimated here on the basis of:

- The value of the market for APIs in the EU given in a Chemical Pharmaceutical Generic Association report entitled "The World APIs Market" (2005). Here it is stated that in western Europe the captive market for APIs in the EU has a value of $US8.29bn and in eastern Europe of $US0.98bn, while the merchant market in western Europe has a value of $US6.21bn and in eastern Europe of $0.84bn.
- An exchange rate between the euro and the dollar of €0.64 to $1.
- The fact that it is reported that the "EU's generic market today is worth around 7 billion euros, compared to around 70 billion euros for the total European pharmaceutical market value".[67]
- The assumption that each batch of API weighs 250kg.
- The assumption that on average each batch of API for the innovative pharmaceutical sector costs $1000 and each batch of API for the generic sector costs $15.

3.40 Using the assumptions above, it is possible to convert the value of the European API market into a volume measure in terms of number of API batches. This figure has been rounded to 800,000 .

[67] http://www.euractiv.com/en/health/generic-medicines/article-117497

Table 3.3: Direct Business Cost of NIR Policy Option – 4.3.2.(b)

	In the EU	Information source and/or equation
A. Cost of NIR technology	Price quotations of €25,000 - €200,000 have been given. We use a figure of €100,000 here	Consultation with industry
B. Number of finished pharmaceutical product production sites	7,000	EMEA
C. Number of batches of API (per year)	800,000	Europe Economics analysis of past report by Chemical Pharmaceutical Generic Association
D. Number of batches of API (per year) - Net of captive supplies	345,000	Europe Economics analysis of past report by Chemical Pharmaceutical Generic Association
E. Cost per NIR inspection (i.e. one hour of average hourly wage)	€ 23.45	Eurostat
F. Gross Direct Business Cost - Fixed	€ 700,000,000	€100,000*7,000
G. Gross Direct Business Cost - Running	€ 18,760,000	800,000*€23.45
H. Direct Business Cost - Net of captive supplies - Fixed	€ 700,000,000	Each site assumed to have at least some non-captive suppliers
I. Direct Business Cost - Net of captive supplies - Running	€ 8,090,250	345,000*€23.45
J. NPV - Based on Direct Business Cost - Net of captive supplies	€ 768,243,942	

Downstream Effects

3.41 One downstream effect may be an increase in employment in firms that produce NIR technologies but we may also see pharmaceutical manufacturers switching 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 option 4.3.2(c)

3.42 The third policy to be considered under 4.3.2 (which we shall call 4.3.2(c)) 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.

3.43 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. The calculations below are based on information that has come into Europe Economics on the proportion of an API manufacturer's 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**.**

3.44 The calculations below are based upon the following:

- That it is estimated that 25 per cent of the costs of API manufacturers are made up of costs associated with becoming GMP compliant.[68]
- That roughly one sixth of EDQM inspections of API manufacturers outside of the EU result in site failures.[69]
- That no evidence has been found of widespread non-GMP compliance amongst EU API manufacturers, which is taken to reflect the fact that many EU API manufacturers supply to the USA where standards of GMP are said to be held up to higher standards than those currently in force in the EU.
- The assumption that profit margins amongst EU API manufacturers are tighter than non-EU API manufacturers. We have assumed 10 per cent for those outside the EU and 2 per cent for those inside the EU.
- The value of the market for APIs in the EU, as reported above, with 80 per cent of this value being captured by non-EU API manufacturers and 20 per cent being captured by EU API manufacturers. These percentages are based on consultations with industry.

3.45 If all EU API manufacturers were already operating to GMP standards, the net cost of this policy option for EU API manufacturers would be zero. In the calculations below, we use a non-compliance indicator in the EU of 1 per cent to reflect the fact that, while there is no evidence of widespread non-compliance, some non-compliance will nonetheless be present. (Please see row B in table 4 below).

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[68] IBM, "Managing the cost of compliance in pharmaceutical operations", (April 2004)

[69] http://www.users.globalnet.co.uk/~sarahx/articles/asiaapis.htm

3.46 However, on the basis of the evidence above, we consider that one sixth of non-EU API manufacturers will face a 25 per cent increase in their costs. To some extent other non-EU API manufacturers will face some increase in their costs also. The size of these additional costs is derived from the size of the market value stated above, given the assumed profit margins and the share of this market attributable to non-EU API manufacturers.

3.47 The calculations below are based on the following equations:

Gross Cost for Non-EU API Manufacturers = A * B * C * D * E

Where:

A = Cost in GMP compliant company attributable to meeting GMP compliance requirements = 25 per cent.

B = Value of one dollar to one Euro = 64 per cent.

C = Proportion of non-EU API manufacturers revenues that are required to cover their costs, i.e. profit measure = 90 per cent.

D = Proportion of EU API merchant market share held by non-EU API manufacturers = 80 per cent.

E = Size of EU API merchant market = $6.21 + 0.84.

And:

Net Cost for Non-EU API Manufacturers = (F * G) + (0.5 * (1-F) * G)

Where:

F = Proportion of non-EU API Manufacturers who will need to meet full cost involved with becoming GMP compliant = One sixth.

G = Gross Cost for Non-EU API Manufacturers.

And:

Gross Cost for EU API Manufacturers = A * B * H * J * E

Where:

A = As above.

B = As above.

E = As above.

H = Proportion of EU API manufacturers revenues that are required to cover their costs, i.e. profit measure = 98 per cent.

J = Proportion of EU API merchant market share held by EU API manufacturers = 20 per cent.

And:

Net Cost for EU API Manufacturers = K * L

Where:

K = Assumed indicator of current non-compliance amongst EU API manufacturers = 1 per cent

L = Gross Cost for Non-EU API Manufacturers.

Table 3.4: Direct Business Cost of giving EU GMP standards on API the legal force of an EC Directive under Policy Option 4.3.3.

API manufacturers	In the EU	Information source and/or equation	Supplying to the EU from outside	Information source and/or equation
Number	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
Gross direct business cost	€0.22bn		€0.81bn	
Net direct business cost (gross direct business cost minus proportion of these costs suspected as already being met) - Rolling Annual Cost	€2.2m		€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	€30.37m		€4.01bn	

Downstream Effects

3.48 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, 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.

3.49 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 (Policy option 4.3.3).

3.50 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 non-compliance 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.

3.51 As we understand these policy options, all 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. In terms of the rows in table 5 below, the annual cost of an audit is equal to:

$$((A*(B+C)*2)+(A*D))/E$$

Table 3.5: 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 - We have taken a figure of €1000 for purposes of this quantification	Based on consultation with EU regulators	800 –1200 € /day/inspector - We have taken a figure of €1000 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) - AC[70]	€ 704	Eurostat	Assume $38		Assume $38
Frequency of inspection	At least once every three years		At least once every three years		At least once every three years

[70] 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.

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