Title:
Consolidation of UK medicines legislation
IA No: 4018

Lead department or agency:
Medicines and Healthcare Products Regulatory Agency

Other departments or agencies:

Impact Assessment (IA)

Date: 09/03/2012

Stage: Final

Source of intervention: Domestic

Type of measure: Secondary legislation

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Summary: Intervention and Options

RPC Opinion: AMBER

Cost of Preferred (or more likely) Option				
Total Net Present Value	**Business Net Present Value**	**Net cost to business per year** (EANCB on 2009 prices)	**In scope of One-In, One-Out?**	**Measure qualifies as**
£9.0m	£8.1m	-£0.9m	Yes	OUT

What is the problem under consideration? Why is government intervention necessary?

The medicines regulatory framework is complex and confusing. This creates three principal problems. First, it makes it harder for the MHRA to carry out better regulation initiatives. Second, costs to the private and public sectors of understanding and applying the law are much higher than necessary. Third, uncertainty about legal requirements can lead to wasteful legal proceedings.

Government intervention to change legislation is necessary because legal certainty is a public good. The free market lacks the incentives to supply public goods adequately. Only Government and Parliament can legislate. Industry bodies have also asked MHRA to address this problem.

What are the policy objectives and the intended effects?

Objective 1. Facilitating future better regulation initiatives, including reviews of policies embodied in the law.

Objective 2. Reduced private and public sector costs of understanding and applying the law.

Objective 3. Reduced litigation costs to the private and public sectors.

The intended effects are to safeguard public health in the most cost-effective and transparent manner, and to reduce regulatory burdens and thereby contribute to productivity and growth in the private and third sectors.

What policy options have been considered, including any alternatives to regulation? Please justify preferred option (further details in Evidence Base)

0. Do nothing. Continue to add to and amend the existing complicated legal framework.

1. Recast the legal framework and cut out redundant legislation to make the law easier to understand.

The MHRA previously considered the option of improving the legislative guidance to help users navigate more effectively through the complicated law. This option was rejected on the grounds that it does not meet the fundamental objective of facilitating future better regulation initiatives.

Option 1 is preferred on the grounds that it addresses the fundamental cause of the problems outlined above - the opaqueness of the regulatory framework. It is further justified on the basis that it provides a positive net present value, even without the inclusion of several significant unquantified benefits.

Will the policy be reviewed? It will not be reviewed. **If applicable, set review date:** Month/Year

Does implementation go beyond minimum EU requirements?			No		
Are any of these organisations in scope? If Micros not exempted set out reason in Evidence Base.	**Micro** Yes	**< 20** Yes	**Small** Yes	**Medium** Yes	**Large** Yes
What is the CO_2 equivalent change in greenhouse gas emissions? (Million tonnes CO_2 equivalent)			**Traded:** 0	**Non-traded:** 0	

I have read the Impact Assessment and I am satisfied that (a) it represents a fair and reasonable view of the expected costs, benefits and impact of the policy, and (b) that the benefits justify the costs.

Signed by the responsible Minister: ---------- Date: 25 June 2012

Summary: Analysis & Evidence

Policy Option 1

Description:

FULL ECONOMIC ASSESSMENT

Price Base Year 2009	PV Base Year 2011	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: -£1.3	**High:** 19.4	**Best Estimate:** 9.0

COSTS (£m)	Total Transition (Constant Price)	Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	1.7		Optional	**Optional**
High	3.1		Optional	**Optional**
Best Estimate	2.4		0.002	**2.4**

Description and scale of key monetised costs by 'main affected groups'

The private sector faces estimated transition costs of between £1.3 million and £2.6 million, and no recurring annual costs. Public sector estimated transition costs are between £0.4 million and £0.5 million (of which £0.26 million are MHRA policy and legal costs). MHRA's annual recurring costs are expected to be £2,000 (PV £19,000).

Other key non-monetised costs by 'main affected groups'

None

BENEFITS (£m)	Total Transition (Constant Price)	Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low			0.2	**1.8**
High			2.8	**21.1**
Best Estimate	0		1.5	**11.5**

Description and scale of key monetised benefits by 'main affected groups'

The private sector is expected to enjoy annual benefits of between £0.12 million and £2.65 million annually (PV £0.45 to £4.04 million). The public sector is estimated to benefit by £0.12 million annually (PV £0.91 million).

Other key non-monetised benefits by 'main affected groups'

1. Public sector economies and efficiencies in future deregulation projects.
2. Reduction in cases where businesses over-comply to ensure they have met obligations under unclear regulations.
3. Reduced litigation cost for public and private sectors.

Key assumptions/sensitivities/risks **Discount rate (%)** 3.5

There are no key unmitigated risks.

BUSINESS ASSESSMENT (Option 1)

Direct impact on business (Equivalent Annual) £m:			In scope of OIOO?	Measure qualifies as
Costs: 0.222	**Benefits:** 1.160	**Net:** 0.940	Yes	OUT

Evidence Base (for summary sheets)

A. What is the problem under consideration? Why is Government intervention necessary?

Medicines are a central part of healthcare in the UK. Medicines regulation provides the framework that underpins safe medicine use by professionals and the public, yet the law is complex and confusing. UK medicines legislation comprises the Medicines Act 1968, around 60 principal statutory instruments and around 130 amending statutory instruments, which reflect developments in pharmaceuticals, wholesale trade, regulatory practice and European harmonisation. The law has become fragmented and potentially impenetrable for users in the public, private and third sectors.

Furthermore, as law has accumulated, some legislation has become redundant and has fallen into disuse. Although no one is now bound by it, it nevertheless litters the legislative landscape and makes it harder for users to understand the law that currently applies.

Legal complexity has created three principal problems:

- The legislative structure hampers MHRA's efforts to improve the effectiveness, transparency and proportionality of its regulation, and to ensure its regulation reflects best practice. Identifying opportunities for burden reduction and ensuring that regulation is consistent across all the legislative framework are difficult, and errors can easily be made.

- Costs to the private and public sectors of trying to understand and apply the law are significantly higher than necessary. An illustration of this comes from practitioners in pharmaceutical law, who estimate that giving legal advice can take several times longer – and therefore cost several times more - than if there were a single, coherent set of regulations[1].

- Uncertainty about legal requirements can lead to wasteful legal proceedings and can, in the extreme, render the law incapable of enforcement.

These problems are becoming more acute over time, as the stock of medicines legislation grows. It is the Government's responsibility to resolve these problems; no-one else, other than Parliament, can legislate in this field.

The private sector provides up-to-date versions of the Medicines Act 1968 and the principal statutory instruments, incorporating the amendments made to them. It also provides an update service about new legislation. However, the providers of these services can only help industry to navigate through a complicated legal framework; they do not provide a single, simplified text; and subscription represents a cost for businesses. The underlying problem – the complicated framework – remains unaddressed. Industry bodies have asked MHRA to tackle this fundamental problem.

Moreover, legal certainty is a public good (if you can supply it to one person you can supply it to all people at no extra cost, and one person's consumption of it does not mean that there is less for others to consume). The free market will undersupply the good, because the private sector is unable to capture its full share of the social benefits of supplying the good to all who would benefit from consuming it.

B. What are the policy objectives and intended effects?

The goal is to simplify the structure of the law, improving its accessibility to industry, professionals and lay readers. This is a significant better regulation initiative that is consistent with the Government's principles of regulation. It will contribute to transparency, legal certainty and the rule of law, and reduce administrative and compliance burdens. This will make it easier for professionals to do their jobs and

[1] A pharmacy lawyer has given an example where drafting a letter of advice supported by reference to the legislation took 8 hours. If there had been a single set of Regulations the work might have been completed in about 2 hours.

simpler for industry to comply, and ultimately patients will benefit from a licensing system fit for the twenty-first century.

Specifically, MHRA aims to achieve the following objectives:

- Facilitated future better regulation initiatives, including reviews of the policies embodied in the legislation;
- Reduced private and public sector costs of understanding and applying the law;
- Reduced litigation costs to the private and public sectors.

MHRA does not expect the changes to have any adverse impact on public health.

The intended effects are:

- to safeguard public health in the most cost-effective and transparent manner
- to reduce burdens, and to contribute to productivity and growth in the private and third sectors.

Achieving the objectives is expected to contribute to the intended effects in two ways:

- Firstly and most importantly, legislative simplification will contribute to cost-effective public health and to growth by facilitating future better regulation initiatives. Although this could be achieved without simplifying the legal framework, these improvements can be introduced more quickly, will be more easily understood and will be less prone to legal mistakes if they are carried out within the context of a simplified legal framework.
- Secondly, the reduced costs of understanding and applying the law, and avoided costs of fruitless litigation, will allow the private and public sector to apply the cost savings to more productive uses. For the same reasons simplification will also reduce regulatory barriers to entry. MHRA does not, however, expect these direct benefits to be large in the context of the pharmaceuticals sector, and has therefore taken a proportionate approach to this final-stage impact assessment.

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C. What policy options have been considered, including any alternatives to regulation?

The MHRA has informally consulted on a number of previous occasions and has found widespread support for the proposal to consolidate the law.

The MHRA has also narrowed down the options along the way. It previously considered the option of rationalising and improving its legislative guidance, rather than the legislation itself. However, better guidance would not provide a platform for further better regulation initiatives. It would therefore not meet a key policy objective. In addition, it would not address the fundamental cause of the costs – the complicated legislative framework. By definition, improved guidance would also present less certainty than improved law itself. It would therefore be a second-best solution and inherently less beneficial than Option 1. For these reasons, the guidance option was considered inferior to Option 1, and was rejected.

Two options therefore remain.

Option 0. Do nothing: MHRA continues to add to and amend the existing legal framework in a piecemeal manner, as necessary.

Option 1. MHRA recasts the legal framework to make it easier to understand and to cut out redundant legislation. Thereafter, MHRA reconsolidates legislation periodically, and meanwhile maintains an up-to-

date informal consolidated text on its website. The Government proposes to bring together the 200[2] or so legislative instruments into one statutory instrument that sets out for the first time almost all of the regulatory requirements for medicines in a single text.[3] An explanation of how this consolidates existing law is at annex A, and a list of the redundant legislation that is being repealed is at annex B.

Option 1 can be seen as phase one in MHRA's regulatory excellence programme. Further initiatives will be introduced on the back of Option 1. Option 1 is a simplifying measure which is intended to reduce net burdens on business. Legislative simplification is an established form of better regulation initiative.[4]

Note that this is not (with certain minor exceptions, which are outlined in the consultation document) intended to be a change to policy. It is a simplification measure that will allow policy to be reconsidered in the future. Alternatives to regulation are therefore irrelevant in this context, although they will be considered during future reviews of the stock of regulation for which MHRA is responsible

D. Analytical assumptions

The appraisal period has been capped at 10 years. This is a conservative approach because we expect substantial benefits to continue well beyond this period.

The social discount rate is the Treasury recommended 3.5%.

A GDP deflator of 0.972 (sourced from the HM Treasury website) has been applied to all 2010 costs and benefits to base prices in 2009 values, in accordance with One-in, One-out procedures.

The public consultation returned 202 responses, of which 62 addressed issues directly relevant to this impact assessment. MHRA followed this up by contacting a further 10 organisations to fill in gaps in the evidence base.

The consultation and follow up revealed the following:

- We had under-estimated the time that firms spend understanding the legislation as it is currently drafted. This was particularly the case for medicines wholesalers. We had previously estimated that the costs to the private sector of understanding the regulations were between £0.64 million and £2.07 million. Our new estimate is between £0.63 million and £5.14 million.
- Our assumption that small pharmacy firms, homeopaths and herbalists rely on their representative bodies for regulatory advice proved correct.
- We had excluded Primary Care Trusts and Strategic Health Authorities from our estimates. This has now been corrected.
- We had under-estimated the cost of the staff time spent on regulatory matters. This was particularly the case with manufacturers, for whom we increased the rate from £25 to £65 per hour.
- We had under-estimated the costs of familiarisation and changing guidance by factor of between 2 and 3.
- We had substantially under-estimated the time savings to Manufacturers as a result of clearer regulations. Whereas we had previously assumed a 5% to 15% saving, consultation responses from several manufacturers and their representative bodies suggested the savings could be as much as 50%.

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[2] Approx 60 principle SIs and 130 amending SIs

[3] We do not at present propose to consolidate (a) fees, a discrete and complex area of legislation which the MHRA intends to simplify and rationalise separately; (b) clinical trials, where there are ongoing negotiations at a European level about the introduction of a Directive that will require substantial changes to the regulation of clinical trials shortly; or (c) prohibition of substances, as there are insufficient legal powers to include these provisions in the consolidated regulations. When the legislation in relation to fees and clinical trials is more settled, the MHRA will explore consolidating it into the consolidated regulations. The consolidation does not cover pharmacies legislation, which is administered by the Department of Health. Part 4 of the Medicines Act 1968 (Pharmacies) will not be repealed and will still need to be read in conjunction with other pharmacies legislation.

[4] The European Commission, for example, frequently uses recasts/consolidations as part of its rolling simplification programme: http://ec.europa.eu/governance/better_regulation/codif_recast_en.htm

E. Baseline: The do nothing option (Option 0)

Although the "do nothing" option implies no change and therefore no incremental costs and benefits, MHRA has estimated the current costs to the economy of understanding the current complicated regulations, and of seeking legal advice. This approach provides the basis for estimating the benefits (in the form of cost savings) to the private and public sectors reported in Section F.

Current private sector costs of understanding regulations

Manufacturers of pharmaceuticals, medicinal chemicals and botanical products (SIC 244)

BIS statistics suggest that there are 385 businesses in this sector (of which 230 are micro and 65 medium sized). MHRA has assumed that between 15 and 180 hours[5] a year are spent by each firm understanding the current regulations. The salary cost is assumed to be £50 per hour[6], to which we have added 30% to account for non-salary staff costs. The total staff cost is therefore £65 per hour. These assumptions yield annual costs ranging from £0.39 million to £4.50 million.

Pharmaceutical industry representative bodies

On the basis of feedback from industry representative bodies, MHRA has gathered that pharmaceutical industry firms do not consult their representative bodies for significant amounts of legal advice and hence these bodies' annual costs of consulting the legislation are negligible.

Pharmacies

Figures from the National Pharmacy Association suggest that there are approximately 4,000 pharmacy companies in the UK. MHRA has assumed that medium and large scale companies (54 and 11 respectively) spend between 20 and 60 hours a year looking at the regulations[7]. From consultation responses and data from ASHE 2010, MHRA believes that salary costs range from £21 to £40 per hour. To this, MHRA has added 30% to account for non-salary costs. MHRA has also assumed that small and micro firms (826 and 3,083) do not refer to the legislation directly but instead rely on their industry bodies or on informal advice networks (this assumption was validated during consultation). Their costs of understanding regulations are therefore negligible. These assumptions yield annual costs ranging from £0.04 million to £0.22 million.

Pharmacy bodies

There are 5 main pharmacy trade bodies: the National Pharmacy Association; the Association of Independent Multiple Pharmacies; the Independent Pharmacy Federation, the Ulster Chemists' Association and Company Chemists' Association (CCA). Consultation responses suggest that each of the 5 main trade associations currently spends between 100 and 200 hours a year scrutinising the regulations. MHRA has assumed that the salary cost per hour is £20.77 (the average salary for pharmacists in 2010 according to ASHE statistics) and has added 30% to account for non-salary costs.

These assumptions yield annual costs of between £0.01 million and £0.03 million.

There are a number of other bodies in the UK and in devolved administrations that represent the interests of sectors of pharmacy and pharmacy technicians. MHRA approached 11 of these during informal consultation and those who replied told us that there would be negligible or unquantifiable impact on an annual basis of the new regulations.

There are also 4 negotiating bodies in each of the parts of the UK who told us that they seldom refer to medicines legislation. The costs of understanding the legislation are therefore assumed to be negligible.

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[5] Estimates come from three sources within the pharmaceutical industry

[6] Taken from consultation responses. PAGB say average of £60 per hour, others are more conservative at approx £40, so £50 taken as an assumed average.

[7] Consultation responses from pharmacy companies suggest that this range is reasonable

Wholesalers

There are currently 1,744 pharmaceuticals wholesale dealer licences in the UK. MHRA assumes that this is an accurate estimate of the number of wholesale businesses. Of these 3 are national (and are assumed to be large sized), 11 are regional (assumed to be medium sized) and 1,730 are assumed to be micro and small sized businesses. Industry body membership is uncommon amongst small and micro wholesale businesses. The consequent lack of industry data makes it impossible to distinguish between medium, small and micro wholesale businesses. MHRA has received consultation responses from three wholesalers (one large and the others small or medium sized) that suggest that large and medium sized businesses each spend between 20 and 150 hours a year scrutinising the regulations, while small and micro businesses spend between 10 and 20 hours a year. Consultation responses also suggest that hourly staff costs (including non-salary costs) are £50.

These assumptions yield total annual costs of between £0.88 million and £1.84 million.

Private sector regulatory bodies

There are 19 professional groups (including doctors, pharmacists, nurses, herbalists and homeopaths) who can sell, supply or administer medicines.[8] The majority of these are regulated by 5 regulatory bodies: the General Pharmaceutical Council; General Medical Council; the Health Professional Council and the Nurses and Midwives Council, and the General Optical Council. MHRA has assumed that each of these 5 bodies spends between 1000 and 2000 hours a year scrutinising the current regulations.[9] The average hourly salary cost is assumed to be £19.47 (2010 ASHE average salary for accounting and legal services). 30% has been added to account for non-salary costs[10]. These assumptions yield total annual costs of between £0.13 million and £0.25 million.

Private Sector Professional Bodies

MHRA has assumed that each of the seven main bodies spends between 520 and 1040 hours a year scrutinising the current regulations. [11] The staff cost is assumed to be £25.31 (including 30% non-salary costs)[12]. These assumptions yield total annual costs of between £0.09 million and £0.18 million. The MHRA has found no evidence during consultation that any of the 12 other professional bodies representing professions routinely scrutinise legislation and so has treated their annual costs as negligible.

Current public sector costs of understanding the regulations

Pharmacy schools

There are 26 pharmacy schools in the UK. The Council of University Heads of Pharmacy Schools (CUHOPs) estimates that each school spends on average 10 days a year scrutinising the current regulations. The cost per day is £250.

These assumptions give annual costs of £0.07 million.

Primary Care Trusts and Strategic Health Authorities

Although the PCT and SHA structure of organising healthcare is in process of being dismantled in England, MHRA believes that the same regulatory functions will still need to be carried out in the NHS. Current PCT and SHA costs are therefore assumed to be representative of future costs.

[8] The full list of professionals includes physicians, nurses and midwives, dentists, opthalmologists, optometrists, herbalists, homeopathists, anthroposophic practitioners, chiropodists / podiatrists, occupational therapists, Orthoptists, Paramedics, Physiotherapists, prosthetists / orthotists, Radiographers, speech and language therapists, Osteopaths, Acupuncturists and naturopathists.

[9] Figures verified by the General Pharmaceutical Council and General Medical Council.

[10] Figures verified by the General Pharmaceutical Council and General Medical Council.

[11] Royal Pharmaceutical Society estimates.

[12] Verified by RPS and PSNI

There are ten SHAs in England. A consultation response from the NHS SHA Leads Group suggests that each SHA will on average spend 12.5 hours a year on understanding medicines regulations as they are currently drafted. MHRA assumes that the relevant hourly salary cost for SHAs is £20.77 (ASHE average hourly rate for pharmacists). With 30% added for non-salary costs the hourly rate is £27. These assumptions yield an annual cost of £3,375.

There are 151 PCTs in England. The NHS SHA Leads Group suggests that on average, each PCT will spend 27 hours a year understanding medicines regulations as they are currently drafted. In line with SHA costs, MHRA assumes an hourly staff cost of £27. These assumptions yield an annual estimated cost of £0.11 million

Current costs of legal advice

MHRA believes that routine legal advice is only sought by large pharmaceutical and other companies that bring new or highly modified regulated products to the market. Legal advice is assumed to be sought between 50[13] and 200[14] times per year. The cost of each consultation is between £300 and £500[15].

This yields annual costs of between £0.02 million and £0.1 million. None of this falls on micro or small businesses.

Total quantifiable current costs under the "do nothing" option

The total annual cost is estimated at between **£0.82 million** and **£5.42 million**.

Of this, MHRA estimates that

- micro businesses (excluding wholesale businesses) bear between £0.23 and £2.69 million
- small businesses (excluding wholesale businesses) bear between £0.07 million and £0.76 million
- small and micro wholesale businesses bear between £0.87 million and £1.73 million.

Unquantifiable current costs under the "do nothing" option

The MHRA regulated public and private sectors face considerable costs of litigation. Occasionally legal cases are argued because of different interpretations of the law. However these specific cases are too infrequent and variable to allow MHRA to estimate a credible annual average cost.

F. Costs and benefits of Option 1

The costs and benefits of Option 1 are described in detail in this section. A summary of the costs, and of the benefits that have been quantified, is set out in a table at the end of the section.

i) Costs:

MHRA and Department of Health (DH) costs

MHRA staff time has already been spent on developing and consulting on Option 1. However, these costs are sunk and therefore not counted in this analysis.

Future MHRA and DH[16] costs of finishing the consolidation exercise are expected to be £0.25 million[17].

[13] Assuming 30 new active substances and 20 major changes to existing substances per year.

[14] Assuming that 100 large companies each seek advice twice a year.

[15] Estimate from Charles Russell LLP.

[16] DH lawyers will be required to work on areas of DH competence

[17] Based on the following assumptions: 1.5 FTE lawyers and 1 FTE policy official for 1.25 years. Lawyer costs £88,000 and policy official costs £65,000 per year (salary and non-salary costs)

Further annual costs of maintaining an informal consolidation of regulation on the website will be borne by MHRA. This will be necessary to ensure that the benefits of the initial formal consolidation exercise do not quickly dissipate as new legislation is introduced. The estimated cost is £2,000 a year[18].

Private sector transition costs

The costs estimated in this section relate to the costs of familiarisation with the new consolidated regulations and costs of changing guidance literature. NB: these are one-off costs.

Firms excluding wholesalers

From consultation responses from two pharmaceutical companies and one trade body, MHRA has assumed that all firms except micro and small pharmacy businesses spend between 15 and 45 hours familiarising themselves with the new consolidated regulations. As in section E, MHRA has assumed a total staff cost of £65 per hour. Micro and small pharmacy businesses are assumed to rely on their industry bodies and therefore do not need to familiarise themselves. This assumption was checked during consultation and found to be valid. The familiarisation costs are estimated at between £0.45 million and £1.36 million.

Wholesaler firms

From consultation responses from three wholesale firms, MHRA has assumed that micro and small wholesale firms will spend between 10 and 15 hours familiarising themselves with the new consolidated legislation. Medium and large firms are assumed to spend between 20 and 70 hours. These assumptions, combined with assumptions about staff costs in section E, yield estimated costs of between £0.88 million and £1.35 million.

Pharmacy representative bodies

From consultation responses from the RPS and PSNI, MHRA has assumed that each of the 5 main trade bodies spends between 100 and 200 hours on familiarisation, reflecting the need to be able to respond to members' questions efficiently. The remaining 11 bodies are expected to spend between 10 and 20 hours on familiarisation. These assumptions, combined with staff costs assumed in section E, yield estimated costs of between £0.02 million and £0.03 million.

Private sector regulatory bodies

From consultation responses received from the GPC and GMC, MHRA has assumed that each of the five bodies spends between 100 and 200 hours on familiarisation, reflecting the importance of a thorough knowledge of the layout of the new regulatory framework. This yields costs of between £0.01 million and £0.03 million.

Private sector professional bodies

From a consultation response received from the RPS, MHRA has assumed that the seven major professional bodies spend between 100 and 200 hours on familiarisation, reflecting the importance of a thorough knowledge of the layout of the new regulatory framework. The other twelve professional bodies are expected to spend a minimal 10 to 20 hours on familiarisation. These assumptions, combined with staff cost assumptions in Section E, yield costs of between £0.02 million and £0.04 million.

Total private sector familiarisation costs

Total costs to the private sector of familiarisation with the new regulations are estimated to lie between **£1.38 million** and **£2.79 million**.

[18] Based on 36 hours per year of a lawyer's time.

Of this total, between £1.15 million and £2.16 million is estimated to be borne by micro and small firms in the manufacturing and wholesale sectors.

Public sector familiarisation costs

Pharmacy schools

MHRA has assumed[19] that each of the 26 pharmacy schools spends between 20 and 30 days on familiarisation, in order to ensure students are properly informed about the law. The cost per day is assumed to be £250[20]. These assumptions yield costs of between £0.13 million and £0.20 million.

SHAs and PCTs

From consultation responses from several PCTs and SHAs, MHRA has assumed that both types of organisation will spend between 10 and 20 hours becoming familiar with the consolidated regulations. This assumption, combined with staff cost assumptions in Section E, yield total familiarisation costs of between £0.04 million and £0.08 million.

Total costs

The total one-off transition costs of Option 1 are estimated to lie between £1.75 million and £3.23 million. The annual costs, which fall entirely to MHRA, are £2,000.

ii) Benefits:

The quantified annual cost savings have been calculated by taking percentage decreases in the current baseline costs set out in Section E.

Quantified private sector cost savings in understanding the regulations

Manufacturers of pharmaceuticals, medicinal chemicals and botanical products (SIC 244)

From consultation responses from several manufacturers, MHRA has assumed that all businesses save between 10% and 50% of their current costs[21]. This yields annual cost savings of between £0.04 million and £2.25 million. Of this total, micro businesses benefit by between £0.23 million and £2.69 million, and small businesses by between £0.07 million and £0.76 million.

Pharmacies

From consultation responses from several companies, MHRA has assumed that medium and large pharmacy businesses will save between 5% and 15% of their current costs[22]. As noted in Section E, small and micro businesses are assumed to bear negligible costs of understanding regulations, and hence these businesses do not benefit from reduced costs. These assumptions yield annual cost savings of between £0.002 million and £0.033 million.

Pharmacy industry bodies

From consultation responses from the Company Chemists Association and Association of Multiple Pharmacies, MHRA has assumed that pharmacy bodies save between 5% and 15% of their current costs. This yields annual cost saving of between £0.001 million and £0.004 million.

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[19] Estimates provided by CUHOPS

[20] Estimate provided by CUHOPS

[21] Consultation responses varied widely with at the low extreme, one manufacturer estimating a 10% saving, while at the other extreme, one major and one minor manufacturer each estimated a 50% saving. PAGB, representing the interests of "over the counter" medicine manufacturers, estimated a 20% to 50% saving.

[22] This is possibly a conservative estimate. One consultee suggested that the time might be halved.

Professional bodies

From a consultation response from the RPS, MHRA assumes that the professional bodies save between 10 and 20% of their current costs. This yields annual cost savings of between £0.01 million and £0.04 million.

Wholesalers

From consultation responses from three wholesalers, MHRA assumes that wholesalers save between 5% and 15% of their current costs. This yields cost annual savings of between £0.04 million and £0.28 million. Of this total, micro and small businesses are expected to benefit by between £0.04 and £0.28 million.

Private sector regulatory bodies

From a consultation response from the Royal Pharmaceutical Council, MHRA has assumed a saving of between 20% and 30% of its current costs. This yields annual cost savings of between £0.03 million and £0.08 million.

Total annual private sector cost savings in understanding regulations

Total annual private sector cost savings in understanding regulations are estimated to be between **£0.12 million** and **£2.67 million**.

Of this total, micro and small businesses are estimated to benefit by between £0.07 million and £1.99 million.

Quantified public sector costs savings in understanding the regulations

Pharmacy schools

MHRA has assumed that pharmacy schools save 50% of their current costs[23]. This yields annual cost savings of £0.03 million.

The NHS SHA Leads group has suggested that PCTs will save 80% of their current costs, while SHAs will save 67%. These assumptions yield total cost savings of £0.09 million.

Quantified private sector cost savings on legal advice

Bringing new active substances to market and major changes to existing substances

MHRA assumes that firms will save 50%[24] of their current legal advice costs. This yields annual cost savings of between £0.01 million and £0.05 million.

Unquantified value of reduction in legal risk

When regulatory obligations are unclear, the most common response among regulated businesses is to adopt a course of conduct that is certain to amount to compliance but goes beyond the minimum necessary. This is particularly common where businesses feel that their reputation would suffer significantly as a result of publicised enforcement action.

A clearer rulebook would allow regulated businesses to identify those areas where their current practice goes well beyond the minimum obligation, and to decide whether it is in their interests to continue.

MHRA has no information it can use to assess these cost savings, although they could be substantial.

[23] This is CUHOPS estimate

[24] Estimated by a private sector legal firm

Unquantified litigation cost savings

Clearer legislation should reduce the number of occasions on which readers of legislation disagree about its meaning. This should reduce the number of occasions on which disagreements result in litigation that produces costs for firms and for the public sector.

These cases are too infrequent and variable to estimate cost savings from clearer legislation.

Unquantified benefit: further opportunities

A unified and more easily comprehensible set of rules will act as a base for further initiatives designed to make the regulation of medicine more effective, transparent and proportionate. It will reduce the cost of carrying out such initiatives; in some cases the MHRA expects that it will allow initiatives to be identified that could not be identified under the current regime.

- For example, it should be much easier to produce improved guidance.
- It may be the case that inconsistencies of treatment or logical errors in the rules are easier to identify and remove.
- It should be easier to review whether a particular regulatory policy has worked as intended, without excessive unintended consequences, when the rules themselves are clearer.
- It would be much easier to carry out an Agency-wide review of criminal sanctions and civil penalties when those penalties can be located in a single document.

Thus, legislative consolidation is expected to improve the economy and efficiency of future projects. In practice, these future projects have yet to be defined sufficiently to allow quantification of the benefits. However, MHRA expects these benefits to be significant.

iii) Option 1 summary of quantified costs and benefits

To summarise:

- MHRA has monetised all the costs of Option 1
- MHRA has monetised only certain of the benefits of Option 1. It has not attempted to monetise the impact of reduce legal uncertainty or the further opportunities created by consolidation.

The NPV estimates provided below are therefore highly conservative. The MHRA believes that they are likely to understate significantly the economic benefits of Option 1.

Incremental costs, benefits and net benefits are summarised in the table below:

		Costs (£'000s)			Benefits (£'000s)			Net (£'000s)		
		Transition	Annual	10 year PV	Transition	Annual	10 year PV	Transition	Annual	10 year PV
Private sector	Low	1342	0	1297	0	123	938	-1342	123	-1694
	High	2724	0	2632	0	2650	20163	-2724	2650	18866
Of which businesses	*Low*	*1294*	*0*	*1250*		*89*	*678*	*-1294*	89	-1860
	High	*2627*	*0*	*2538*		*2537*	*19299*	*-2627*	2537	18049
Of which micro/small	*Low*	*1120*	*0*	*1082*	*0*	*71*	*538*	*-1120*	*71*	-1490
	High	*2099*	*0*	*2028*	*0*	*1985*	*15103*	*-2099*	*1985*	14021
Public sector	Low	408	2	414	0	119	908	-408	117	392
	High	513	2	516	0	119	908	-513	117	494
Total	Low	1750	2	1710	0	243	1846	-1750	241	-1301
	High	3238	2	3147	0	2770	21071	-3238	2768	19360

The net present value of the costs and the quantified benefits over the ten year appraisal period is estimated to lie between -**£1.3 million** and **£19.4 million**.

iv) Risks and uncertainty

The MHRA is not aware of any significant, unmitigated risks associated with this intervention.

v) One in, one out

Equivalent annual costs have been calculated using mid-point estimates of the ranges given in the table above. The equivalent annual costs to businesses are £0.220 million, and the equivalent annual benefits are £1.160 million, giving **a net equivalent annual impact of £0.940 million**. MHRA believes that the consolidation exercise qualifies as an "out".

G. Specific impact tests

Economic

Competition assessment

UK markets for originator medicines that contain innovative active substances are nation-wide, and experience strong dynamic but little static competition. Development of these medicines is always associated with high research and development costs.

UK markets for generic, off-patent medicines are nation-wide and experiences some static competition based on price.

Markets for medicines wholesaling services vary by scope, scale and geography. MHRA believes that there are three national wholesalers who supply a very broad range of medicines (they are full-line wholesalers). These three compete with a further 11 wholesalers who operate regionally and are also full-line. There is also a large number of much smaller wholesalers who generally stock a smaller range of medicines (short-line wholesalers). Competition is strong among all wholesalers. (Information comes from "A Critique of Direct to Pharmacy Distribution, Donald MacArthur, 2010)

Markets for pharmacy services experience competition that is geographically local and mostly static, based on the quality of service. There is some evidence of innovative services such as patient reminders for repeat prescriptions.

It is plausible to argue that the consolidated regulations would remove a barrier to entry – the sunk costs of attaining knowledge of the complicated legal landscape. However, MHRA believes that these barriers are either too small to be of significance (wholesale markets) or are not the most binding constraint to entry. More important barriers include the sunk costs of R&D in originator medicines markets and the maintenance of professional standards among pharmacists.

The consolidation exercise will make no changes to the substance of medicines legislation and hence MHRA believes that there will be no material impact on competition.

Small firms impact test

In assessing the impact on small firms, MHRA contacted relevant industry bodies. With the exception of wholesalers, all micro and small businesses in the regulated sectors are well represented by industry bodies.

The only costs that small firms will bear as a result of the consolidation project are the one-off costs of familiarisation with the simplified regulations. MHRA believes that micro and small pharmacies (3909 firms) will not bear any familiarisation costs because they will continue to rely on their trade associations for legal advice. This assumption has been verified by responses from small businesses and their representative bodies during the consultation.

Of the remaining small and micro firms, wholesalers (1730 firms) are expected to bear familiarisation costs of between £500 and £750 each, while pharmaceutical and botanical medicines manufacturers (295 firms) are expected to bear costs of between £975 and £2925 each.

The total, one-off transition cost for small and micro firms is estimated to be between £1.15 million and £2.16 million.

These costs will be set against benefits with a net present of between £0.54 million and £15.1 million (over a ten year period and using a 3.5% discount rate).

The estimated impacts on small firms and on micro-businesses are presented in more detail in Sections E and F of this Impact Assessment.

MHRA therefore believes that the burdens on micro and small businesses will be small and that **the net benefit for micro and small business will be substantial. Taking the mid-point estimates of cost and benefits, MHRA estimates that the NPV for small and micro businesses will be £6.3 million.**

The consolidation exercise is out of scope of the **microbusiness moratorium** because it qualifies as an "out". Micro firms will receive a net benefit from legislative consolidation.

Equality

We do not consider that the problem of fragmented legislation falls more heavily on the groups with protected characteristics under the Equality Act 2010 of race, disability and gender, age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex and sexual orientation. The problem in comprehension of medicines legislation is universal and applies to anyone who uses the legislation, both specialists and lay readers.

Wider Environmental Impact and Greenhouse Gases Tests

There are no potentially significant impacts on air quality, water quality and quantity, flood risk, biodiversity, landscape or noise arising from these proposals. This policy will have no impact on greenhouse gas emissions.

Social impacts

Health and well being

We have considered the health impact screening questions and do not consider that consolidated medicines legislation will have a significant impact on any of the three questions. Medicines clearly have a fundamental role in the delivery of health and social care services but these regulations do not alter the current arrangements.

Human Rights

The preferred option will have no material impact on any of the 16 Convention rights referred to in s. 1 Human Rights Act 1998.

Justice system

Medicines legislation contains criminal offences and these have been rewritten and grouped together in the consolidated text to reduce the number of offence provisions. This will not change how the offences are used and have no impact on the justice system, so a full Justice Impact test is not needed. We have liaised with Ministry of Justice in reaching this conclusion.

Rural Proofing

Our options have no significant impact on rural communities. The consolidation is not about the delivery of services.

Sustainable development

The policies will have no impact upon sustainability and will not adversely affect future generations

Annex A – description of the consolidated regulations

Part	Description
Part 1 – General	Contains important provisions that apply to much of the rest of the consolidation. These include a description of the role of Ministers and general definitions, including “medicinal product” and “advertisement”. There are further definitions in other parts of the consolidated regulations, for terms that are only used in those particular parts.
Part 2 – Administration	Allows for the continuing functioning of a number of advisory bodies, including the Commission on Human Medicines and the British Pharmacopoeia Commission. It also provides rules for the appointment and role of expert advisory groups.
Part 3 – Manufacturing and wholesale dealing	With several associated schedules, this Part sets out the rules for manufacturing, importing and wholesale dealing. It requires that these activities be the subject of a licence and establishes what the licensing authority must consider when assessing an application for a licence. It also provides rules around the suspension, revocation, and varying of licences and sets out requirements for Responsible Persons and Qualified Persons. This Part implements Titles 4 and 7 of Directive 2001/83/EC and includes provisions that were previously in Part 2 of the Medicines Act 1968 and the Medicines for Human Use (Manufacturing, Wholesale Dealing and Miscellaneous Amendments) Regulations 2005 (SI 2005/2789).
Part 4 – Requirement for authorisation	The requirement that medicinal products be the subject of whichever is appropriate of a marketing authorisation, homeopathic certificate of registration, traditional herbal registration or Article 126a authorisation is a central feature of the legal framework and set out in its own Part, along with provision for its enforcement.
Part 5 – UK marketing authorisations	Contains detailed requirements regarding marketing authorisations. It sets out the material that needs to accompany applications for authorisations, and makes specific provision for generic medicinal products, biological medicinal products, products with well-established medicinal use, and new combinations of active substances. It also establishes the criteria that are considered in determining whether a product needs to be subject to prescription requirements. The Part imposes certain obligations on authorisation-holders, such as a requirement to take into account scientific and technical progress, and contains rules relating to revocation, variation, suspension, withdrawal of authorisations. Finally, it contains enforcement provision for medicinal products that are subject to the Paediatric Regulation. This Part implements Title 3, Chapter 1 of Directive 2001/83/EC and consolidates material found for the most part in the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 (SI 1994/3144)
Part 6 – Certification of homeopathic medicinal products	Implements Chapter 2, Title 3 of Directive 2001/83/EC and consolidates the Medicines (Homoeopathic Medicinal Products for Human Use) Regulations 1994 (S.I. 1994/105). It describes the homeopathic medicinal products to which it applies and sets out information that must be supplied with an application for a certificate of registration. As with marketing authorisations, it imposes certain obligations on registration holders and sets out rules regarding revocation, variation, withdrawals, and suspensions.
Part 7 – Traditional herbal registrations	Describes the traditional herbal medicinal products that are subject to the Part and sets out the information that must accompany an application for a traditional herbal registration. It imposes certain obligations on registration-holders and sets out rules regarding revocation, variation, withdrawals, and suspensions. This Part implements Chapter 2a, Title 3 of Directive 2001/83/EC and consolidates material currently found in the Medicines (Traditional Herbal Medicinal Products for Human Use) Regulations 2005 (SI 2005/2750).
Part 8 – 126a authorisations	A short part that implements Article 126a of Directive 2001/83/EC. This article permits Member States, for justified public health reasons, to authorise the placing on the market of medicinal products authorised in another EEA state in

	the absence of a UK marketing authorisation.
Part 9 – Borderline products	Establishes a process that may be followed when the licensing authority determines provisionally that an unlicensed product is a medicinal product and therefore subject to regulation as such. It permits persons supplying the product to make written and oral representations to the contrary, and for final determination. These provisions are currently found in the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 (SI 1994/3144).
Part 10 – Exception to requirement for marketing authorisation	Brings together exceptions from certain licensing requirements that are found in several different statutory instruments. These include the provision for "specials" in Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 (SI 1994/3144) in accordance with the derogation found in Article 5(1) of Directive 2001/83/EC, These are unlicensed medicinal products that can be supplied providing that certain conditions are met. The part also makes provision for parallel import licences, exempt advance therapy medicinal products and the supply of unlicensed medicines in response to the spread of toxic substances or nuclear radiation.
Part 11 – Pharmacovigilance	Part 11 implements Directive 2010/84/EU, which amends Directive 2001/83/EC in order to introduce a strengthened, clarified and more proportionate regime for pharmacovigilance in the EU market. [NB: implementation of Directive 2010/84/EU is subject to a separate impact assessment.]
Part 12 – Dealings with medicinal products	Brings together many provisions currently found in Part III of the Medicines Act 1968, The Medicines (Pharmacy and General Sale – Exemption) Order 1980 (SI 1980/1924), and the Prescription Only Medicines (Human Use) Order 1997 (SI 1997/1830), among others. Together, these provisions establish rules relating to the sale supply and administration of medicinal products related to their classification as general sale list, pharmacy, and prescription only. It also creates a number of exemptions from the basic rules for hospitals, certain professionals and supply under patient group directions (PGDs).
Part 13 – Packaging and leaflets	Implements obligations found in Title 5 of Directive 2001/83/EC by consolidating provisions currently found in Part 5 of the Medicines Act 1968, the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 (SI 1994/3144), and The Medicines (Child Safety) Regulations 2003 (SI 2003/2317). It sets out the information that must appear on packaging and in leaflets, and contains specific rules for Braille, radionuclides, and homeopathic and herbal medicinal products. In the consolidated regulations we have reflected the current legal provisions in relation to labelling requirements.
Part 14 – Advertising	Implements Title 8 of Directive 2001/83/EC and consolidates the Medicines (Advertising) Regulations 1994 (SI 1994/1932) and the Medicines (Monitoring of Advertising) Regulations 1994 (SI 1994/1933). It contains a variety of prohibitions on advertising including those relating to unlicensed medicines, prescription medicines, recommendations by scientists, and advertisements aimed at children. In addition, it sets out the information that needs to be included in advertisements and establishes rules for sampling, the promotion of medicinal products by medical sale representatives, and hospitality at meetings. This Part also contains a chapter called 'Monitoring of Advertising', which creates a process by which Ministers can determine whether an advertisement breaches these requirements, and in certain circumstances require that corrective action is taken. Finally, it requires Ministers to consider complaints about advertisements and permits Ministers to apply to a court for an injunction prohibiting a particular advertisement.
Part 15 – British Pharmacopoeia	A short part that provides for the publication of the British Pharmacopoeia and related documents. It consolidates several provisions currently found in Part 7 of the Medicines Act 1968.
Part 16 – Enforcement	Sets out how the consolidated regulations are to be enforced in England, Wales, Scotland, and Northern Ireland. It also provides inspectors with powers to enter, inspect, and search premises and seize medicinal products. Where the premises in question are private dwellings, it requires that 24 hours' notice be given to the occupier.

Part 17 – Miscellaneous and general	Contains a variety of technical provisions, including those relating to prosecutions, defences, decisions made under the regulations, and liability. It also introduces Schedules that contain transitional provisions, consequential amendments, and repeals and revocations.

Annex B – principal statutory instruments being revoked through consolidation and not consolidated in effect

The following statutory instruments are redundant and so are, at least in part, being revoked and not consolidated in effect. Much of them have been subject to policy (as opposed to merely consequential) amendments by subsequent statutory instruments, and these will also be revoked.

Legislation title	Year	No.	Why redundant
Medicines (Standard Provisions for Licences and Certificates) Regulations 1971	1971	972	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Applications for Product Licences and Clinical Trial and Animal Test Certificates) Regulations 1971	1971	973	Redundant because superseded by subsequent medicines legislation.
Medicines (Control of Substances for Manufacture) Order 1971	1971	1200	Relates to products now regulated by veterinary medicines legislation.
Medicines (Surgical Materials) Order 1971	1971	1267	Relates to products now regulated as medical devices under the Medical Devices Regulations 2002 (SI 2002 618), as amended.
Medicines (Importation of Medicinal Products for Re-exportation) Order 1971	1971	1326	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Exemption from Licences) (Foods and Cosmetics) Order 1971	1971	1410	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Exemption from Licences) (Special and Transitional Cases) Order 1971	1971	1450	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Exemption from Licences) (Special Cases and Miscellaneous Provisions) Order 1972	1972	1200	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration

			under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Data Sheet) Regulations 1972	1972	2076	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Extension to Antimicrobial Substances) Order 1973	1973	367	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Renewal Applications for Licences and Certificates) Regulations 1974	1974	832	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Exemption from Licences) (Ingredients) Order 1974	1974	1150	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Dental Filling Substances) Order 1975	1975	533	Relates to products now regulated as medical devices under the Medical Devices Regulations 2002 (SI 2002 618), as amended.
Medicines (Exemption from Licences) (Wholesale Dealing in Confectionery) Order 1975	1975	762	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Specified Articles and Substances) Order 1976	1976	968	Relates to products now regulated as medical devices under the Medical Devices Regulations 2002 (SI 2002 618), as amended.
Medicines (Breathing Gases) Order 1977	1977	1488	Provides that gases sold for non-medicinal reasons are not medicinal products for the purposes of regulation. This is not necessary, as the products can be classified as non-medicinal under the definition of medicinal product in the consolidated regulations.

Medicines (Fluted Bottles) Regulations 1978	1978	40	Fluted bottles are no longer manufactured and pharmacists and manufacturers (where this was a provision of the marketing authorisation) can therefore no longer comply.
Medicines (Exemption from Licences) (Assembly) Order 1979	1979	1114	Provides an exemption from requirements under section 8(2) of the Medicines Act 1968 from requirements for a manufacturer's licence. We do not see that this instrument creates any necessary or useful safeguards on top of those in other medicines legislation.
Medicines (Contact Lens Fluids and Other Substances) (Exemption from Licences) Order 1979	1979	1585	Relates to products now regulated as medical devices under the Medical Devices Regulations 2002 (SI 2002 618), as amended.
Medicines (Contact Lens Fluids and Other Substances) (Labelling) Regulations 1979	1979	1759	Relates to products now regulated as medical devices under the Medical Devices Regulations 2002 (SI 2002 618), as amended.
Medicines (Cyanogenetic Substances) Order 1984	1984	187	Extends the scope of the Medicines Act 1968 to include cyanogenetic substance. This is not necessary, as cyanogenetic substance meet the definition of medicinal product in the consolidated regulations.
Medicines (Exemption from Licences) (Importation) Order 1984	1984	673	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC (see paragraphs 6.3 to 6.5 in the consultation document).
Medicines (Control of Substances for Manufacture) Order 1985	1985	1403	Relates to products now regulated by veterinary medicines legislation.
Medicines Act 1968 (Hearings by Persons Appointed)(Scotland) Rules 1986	1986	1700	Redundant because superseded by subsequent medicines legislation.
Medicines Act 1968 (Hearings by Persons Appointed) Rules 1986	1986	1761	Redundant because superseded by subsequent medicines legislation.
Medicines Act 1968 (Application to Radiopharmaceutical-associated Products) 1992	1992	605	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration under Directive 2001/83/EC.
Medicines (Exemption from Licensing) (Radiopharmaceuticals) Order 1992	1992	2844	Redundant because superseded by subsequent medicines legislation.
Medicines (Applications for Grant of Product Licences—Products for Human Use) Regulations 1993	1993	2538	Redundant because it relates to the product licensing regime under the Medicines Act 1968 that is being incorporated by the consolidated regulations into the unified scheme for authorisation and registration

			under Directive 2001/83/EC
Medicines (Advisory Board on the Registration of Homoeopathic Products) Order 1995	1995	309	The intention is that, once the consolidated regulations come into force, the Advisory Board on the Registration of Homeopathic Products will not be provided for in law.
Herbal Medicines Advisory Committee Order 2005	2005	2791	The intention is that, once the consolidated medicines regulations come into force, the Herbal Medicines Advisory Committee will no longer be provided for in law.

Title:
Transposition of Pharmacovigilance Directive 2010/84/EU
IA No: 4011

Lead department or agency:
Medicines and Healthcare Products Regulatory Agency

Other departments or agencies:
Department of Health

Impact Assessment (IA)

Date: 20/04/2012

Stage: Final

Source of intervention: EU

Type of measure: Secondary legislation

Contact for enquiries: MHRA Central enquiry point
info@mhra.gsi.gov.uk

Summary: Intervention and Options

RPC Opinion: AMBER

Cost of Preferred (or more likely) Option				
Total Net Present Value	**Business Net Present Value**	**Net cost to business per year** (EANCB on 2009 prices)	**In scope of One-In, One-Out?**	**Measure qualifies as**
-£17.0m	-£39.7m	£4.6m	No	NA

What is the problem under consideration? Why is government intervention necessary?

Pharmacovigilance exists to monitor medcines' effects on the general population after marketing authorisation. Without this information patients can not fully assess how safe medicines are. This information assymety provides justification for government intervention. However, the current EU derived pharmacovigilance system does not solve the info asymmetry as efficiently as it could. In parts it imposes unjustified burdens on industry and in other parts it does not focus the greatest effort at the greatest risk.

What are the policy objectives and the intended effects?

The policy aims to remove unjustified costs placed upon industry by regulators under the current European legal framework, through the use of worksharing and harmonised processes. The policy also aims to ensure that pharmacovigilance resource is expended (in both the pharmaceutical industry and the MHRA) in a targeted way at areas of greatest risk to patients. The intended effect is to alleviate burdens upon industry whilst at the same time maintaining public health, and reducing the numbers of adverse drug reactions in the general population.

What policy options have been considered, including any alternatives to regulation? Please justify preferred option (further details in Evidence Base)

Option 0: Do nothing

This option is used as a comparator to act as a baseline for current costs of Option 2. It considers the current UK legal framework for pharmacovigilance.

Option 1: Implement the Directive

The Directive contains several discrete interventions, affecting different parts of the industry's pharmacovigilance activities. These proposals have been incorporated into one option, but in effect contain several sub-options where the UK has the chance to maximise the benefit of implementing the Directive. This option also contains a number of derogations, which have been used to benefit the pharmaceutical industry wherever possible. This is our preferred option.

Will the policy be reviewed? It will be reviewed. **If applicable, set review date:** 07/2017

Does implementation go beyond minimum EU requirements?			No		
Are any of these organisations in scope? If Micros not exempted set out reason in Evidence Base.	**Micro** Yes	**< 20** Yes	**Small** Yes	**Medium** Yes	**Large** Yes
What is the CO_2 equivalent change in greenhouse gas emissions? (Million tonnes CO_2 equivalent)			**Traded:** 0	**Non-traded:** 0	

I have read the Impact Assessment and I am satisfied that (a) it represents a fair and reasonable view of the expected costs, benefits and impact of the policy, and (b) that the benefits justify the costs.

Signed by the responsible Minister: ..... Date: 25 June 2012

Summary: Analysis & Evidence

Policy Option 1

Description: Implement the Directive

FULL ECONOMIC ASSESSMENT

Price Base Year 2011	PV Base Year 2012	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: -53.6	**High:** 19.8	**Best Estimate:** -17.0

COSTS (£m)	Total Transition (Constant Price)	Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	Optional		Optional	**Optional**
High	Optional		Optional	**Optional**
Best Estimate	10.2		6.5	**65.9**

Description and scale of key monetised costs by 'main affected groups'

Costs to pharmaceutical industry of increased reporting requirements for ADRs, completion of post authorisation safety and efficacy studies and introduction of new processes. Costs to the MHRA in terms of extra burden for admininstering new systems, publishing further pharmacovigilance data to the public, and audits of its national pharmacovigilance system.

Other key non-monetised costs by 'main affected groups'

Possible minor impact upon health for reduced additional monitoring requirements, but there is no evidential link between pharmacovigilance changes and cost to public health, and for this reason the exact costs cannot be quantified.

BENEFITS (£m)	Total Transition (Constant Price)	Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low	Optional		Optional	**Optional**
High	Optional		Optional	**Optional**
Best Estimate	0		5.7	**48.9**

Description and scale of key monetised benefits by 'main affected groups'

Reduction in literature monitoring requirements for industry, removal of DDPS, and harmonisation of several processes allowing reduced reporting requirements.

Other key non-monetised benefits by 'main affected groups'

Possible impact upon health for several areas, including infringement notices and introduction of RMS

Key assumptions/sensitivities/risks **Discount rate (%)** 3.5

The Directive contains multiple elements, the details of which will be decided by working parties at the European Medicines Agency. These are unlikely to be finalised by the time this Directive is implemented, and will have an impact on the estimated costs and/or benefits of the proposed measures.

BUSINESS ASSESSMENT (Option 1)

Direct impact on business (Equivalent Annual) £m:			In scope of OIOO?	Measure qualifies as
Costs: 7.6	**Benefits:** 3.0	**Net:** 4.6	No	NA

Glossary

ADR **Adverse Drug Reaction(s)**

An unintended consequence of a medicine that is reported to the regulator or marketing authorisation holder by a health professional or patient.

CAP **Centrally authorised product**

A medicinal product authorised through the EU centralised authorisation procedure and results in one marketing authorisation the terms of which apply across all EU member States.

DDPS **Detailed Description of Pharmacovigilance System**

A document that describes the system that the marketing authorisation holder has in place in order to fulfil legal requirements in relation to pharmacovigilance.

EMA **European Medicines Agency**

An Agency of the European Union, responsible for the scientific evaluation of medicines developed by pharmaceutical companies for use in the European Union.

IN **Infringement Notice**

A compliance tool proposed by the MHRA to assist them in ensuring marketing authorisation holders comply with legal requirements in relation to pharmacovigilance.

MAH **Marketing Authorisation Holder**

A company with the right to market their medicine within the UK, the EU, or globally.

Member State

A member state of the European Union that is party to the treaties of the European Union and the obligations that EU membership entails.

MHRA **Medicines and Healthcare products Regulatory Agency**

The UK medicines regulator, responsible for making sure that medicines and medical devices work, and are acceptably safe.

NCA **National Competent Authority**

The authority within the UK that has the responsibility for all aspects of medicines regulation for UK marketing authorisations – this is the MHRA.

PAES **Post Authorisation Efficacy Study**

A study undertaken after a medicine has been authorised for use to provide more information on how effective the medicine is on the condition it is treating.

PASS **Post Authorisation Safety Study**

A study undertaken after a medicine has been authorised for use to provide more information on how safe the medicine is on the population.

PRAC **Pharmacovigilance Risk Assessment Committee**

The Committee at an EU level responsible for pharmacovigilance matters, particularly relating to harmonised and centralised procedures.

PSMF **Pharmacovigilance System Master File**

A file that contains details of the pharmacovigilance system operated by the marketing authorisation holder.

PSUR **Periodic Safety Update Report**

Reports on available safety data that must be made by marketing authorisation holders to the respective national regulators on the safety of their products – at fixed periods and covering defined time points from the point of authorisation.

QPPV **Qualified Person in charge of Pharmacovigilance**

A person employed by an MAH with overall responsibility for establishing and maintaining the MAH's Pharmacovigilance System, and named as such on the authorisation.

RMP **Risk Management Plan**

A plan drawn up by the marketing authorisation holder describing the risk management system introduced for managing the risks inherent in a medicine.

RMS **Risk Management System**

The system introduced for a medicinal product that includes a set of risk minimisation measures and pharmacovigilance activities to optimise the safe use of the product and gather further information on its safety profile.

Signal

Information from any data source that suggests that a medicinal or herbal product may be associated with a new risk or that the magnitude or nature of a known risk may have changed.

One In One Out

1. The proposals are to transpose European legislation, which will be implemented largely through copy-out, and contain no gold plating. Whilst the proposals will be implemented 19 days early, on 2 July 2012, this is to ensure consistency between the Directive and the accompanying EU Regulation, which comes into force on 2 July 2012. These proposals do not fall within the remit of OIOO, as they implement a Directive.

Sunset Clause

2. As these proposals are European, they will not carry a sunset clause. A duty to review will be placed within the UK regulation, which will take place by 2 July 2017.

What is the problem under consideration?

3. Government intervention in pharmacovigilance is justified because, in the complicated world of drug safety, patients can not be expected to work out for themselves how safe a medicine is. This is a problem known as information asymmetry (for a more complete analysis of why government intervenes in pharmacovigilance see the next section). Pharmacovigilance exists to correct information asymmetry as efficiently as possible. The problem addressed by this IA is that the current pharmacovigilance framework is not as efficient as it could be in addressing the information asymmetry.

4. The European Commission implied in its impact assessment accompanying the Directive that current EU pharmacovigilance policy imposes burdens upon industry that are not justified on public health grounds. They evaluated the current system and surmised that burdens are primarily imposed on industry through convoluted working procedures, lack of proper communication and harmonisation between member states, and an outdated system for recording and reporting of safety signals. We do not believe that the link drawn between pharmacovigilance changes and public health in their calculations can be adequately drawn; however, although we would agree that removal of these burdens is likely to have minimal, if any detrimental effect upon health.

5. The previous medicines Directive that implemented some pharmacovigilance processes, 2001/83/EC[1] went some way towards harmonising the approach across member states, thereby reducing regulatory burden on the pharmaceutical industry. However, improvements, such as cutting out duplicative reporting procedures across EU member states can still be made, without compromising public health.

6. The European Commission also believes that insufficient focus is currently placed on structured evaluations of the risk:benefit profile of marketed products. The Commission believes that there is currently insufficient information available to medical practitioners and patients on the risks of medicines and how to minimise the risks. The evidence that the Commission used to support its case comes from the incidence of preventable adverse drug reactions (ADRs). In the UK, the most convincing evidence comes from a 2004 study on patients in two Merseyside hospitals[2]. During the study period (which spanned late 2000 and early 2001), 6.5% of admissions related to an ADR, with the ADR directly leading to the admission in 80% of cases. Over 70% of ADR admissions were deemed to be "possibly" or "definitely" avoidable. Over 2% of patients admitted with an ADR died.

7. Extrapolating these admissions and average length of stay data to the whole of the whole of the UK (the NHS in England, NHS Scotland and NHS Wales and Health and Social Care in Northern Ireland), we have estimated that the annual cost of hospital admissions directly attributable to avoidable ADRs in 2009/2010 was £508 million[3]. This figure excludes the lost productivity and the pain and suffering of those admitted. We have conservatively estimated that this cost in 2009/10 was £3,188 million[4].

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[1] Directive 2001/83/EC - http://tiny.cc/ow70l

[2] Pirmohamed et al "Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients" BMJ Volume 329, 3 July 2004

[3] The total number of emergency admissions in the UK in 2009/10 (the most recent year for which data is available) was approximately 6,000,000. We took this number, multiplied it by the Pirmohamed 6.5% ADR admissions rate, the 80% directly caused by ADR and the 72%

8. We have been unable to estimate the cost to the UK healthcare systems and individual patients with ADRs that are dealt with at primary care level.

9. Our quantified estimate of total harm from ADRs to the UK in 2009/10 is £3,695 million. This is a lower limit estimate of the harm from ADRs.

10. The Commission's impact assessment for the new Directive does not examine the causality between insufficient information generated by pharmacovigilance systems and costs to healthcare systems and patients. The causality is difficult to prove. While some ADRs are the result of patients ignoring information, other ADRs have their roots in inadequate information used by physicians when prescribing medicines. However, some ADRs are caused by physicians not taking into account known contra-indications and interactions between medicines. There are also cases where the contra-indications and interactions are either not currently known or are under-researched. This last category of ADR cases is the pharmacovigilance problem identified by the Commission. However, there is no evidence on its extent or its susceptibility to improvement.

11. A more detailed discussion of the background to pharmacovigilance can be found at Annex 3.

Why is Government intervention necessary?

12. The EU pharmacovigilance regulatory system has been judged by the Commission to place unnecessary and unjustified burdens upon industry that can be replaced with more streamlined processes designed to avoid negatively affecting public health outcomes. Only the EU can remove these burdens through legislative change.

13. As noted above, government intervention in pharmacovigilance is justified on the basis of information asymmetry – in the esoteric world of drug safety, without the right sort of information, patients can not be expected to determine for themselves how safe drugs are. This asymmetry is addressed by pharmacovigilance, but the current EU framework does not do its job as efficiently as it could. This provides the fundamental reason for corrective action by the EU.

14. Industry is unlikely to provide sufficient drug safety information. The information generated by pharmacovigilance systems is a public good (if you provide it to one person, you can provide to everyone at no extra cost, and consumption of the good by one person does not mean that there is less available for other people to consume). Because patients and practitioners can access pharmacovigilance information without paying for it, the private sector providers of pharmacovigilance information can not capture their full share of the profits, and will, from a societal perspective, undersupply the market. Corrective government intervention is theoretically justified.

What are the policy objectives and their intended effects?

- Unjustified costs on industry removed
- Pharmacovigilance effort targeted at the greatest risk

15. The policy aims to alleviate the burdens that currently exist in pharmacovigilance processes whilst at the same time ensuring that public health safety is not compromised.

16. In line with Commission assumptions, enhanced pharmacovigilance requirements will result in greater targeting of effort by marketing authorisations holders so that the greatest effort is directed at the greatest risk, with the intended effect of reducing ADRs.

avoidable rate to get the total number of hospital admissions that were directly attributable to avoidable ADRs. We assumed that the cost of each ADR admission was the same as the average long stay non-elective NHS cost in England in 2010 (£2,197) (NHS reference costs).

[4] We conservatively estimated that the average number of QALYs lost to individuals who die prematurely from ADRs is 10. We used the standard Dept of Health QALY value of £60,000.

What policy options have been considered?

Status quo (or 'do nothing')

17. This option is the law as it stands at present, with no incremental costs or benefits incurred (as if the Directive had never existed). For the sake of demonstrating the effects of the adoption of the Directive, we have chosen the current regulatory framework as the baseline against which we measure the costs and benefits of intervention.

18. The do-nothing option is not a realistic option because of the UK's obligation to adopt EU Directives into national law[5].

Implement the Directive

19. The Directive contains several discrete interventions, affecting different parts of the industry's current pharmacovigilance activities, as well as those activities currently undertaken by the MHRA. For the sake of convenience, we have incorporated all these proposals into one option, partly because in some cases there is no member state discretion on how to implement the Directive.

20. Nevertheless, in a number of minor areas, there are some instances where there is discretion in the form of member state derogations. In line with Government guidance on transposition of European legislation, in each area of discretion we propose to choose the option that maximises benefit and minimises costs for UK businesses and shareholders.

21. So, in effect, our single option contains several sub-options where the UK has the chance to maximise the net benefits of implementing the Directive. We have included cost and benefit information for each discrete intervention, so that each can be judged and justified on its own merits.

Overview of policy measures

22. The Commission produced proposals in 2008 to improve the EU's current regulatory framework for pharmacovigilance. The UK actively engaged in negotiating on these until December 2010, when they were published as a Directive to be transposed into UK law by July 2012. The main features of the Directive are set out briefly below and explored further in the analysis.

Reductions in the numbers of Periodic Safety Update Reports required

23. Legislative changes to produce a risk-based approach to what is currently mandatory reporting on safety issues, as well as increase coordination and worksharing between member states in order to reduce burdens upon industry.

Risk Management Plans and Risk Management Systems

24. A move towards a more holistic approach for risk management, encouraging industry to embed pharmacovigilance principles as a foundation of their business, and to take a proactive approach to safety monitoring. Imposition of a new layer of pharmacovigilance monitoring and responsibility upon industry.

Movement from the use of a Detailed Description of the Pharmacovigilance System to the Pharmacovigilance Master File

25. Removal of mandatory and repeated updates to marketing authorisations through a shift in how the information is kept and reported by industry.

[5] Because of an EU fine for each day that the UK would be non-compliant, the UK would be liable for an infinite fine if it continuously failed to implement the Directive. Even the most expensive way of implementing the Directive would look attractive by comparison, and so the "do nothing" option is automatically ruled out.

Additional pharmacovigilance responsibilities

26. Mandatory audits of the pharmacovigilance systems of both industry and regulators at regular intervals. The possibility of delegation of pharmacovigilance responsibilities between member states.

Revised requirements for Post Authorisation Safety and Efficacy Studies

27. The strengthening of current requirements to conduct and complete safety studies – now included as specific licence conditions. The introduction of efficacy studies in rare situations in order to collect data on the usefulness of the product where this is still unclear.

Additional monitoring arrangements

28. Minor changes to the UK's current systems to fit with a now harmonised EU system for monitoring new substances more closely, and encouraging reporting of adverse reactions from patients and healthcare professionals.

Centralisation of literature monitoring for certain substances

29. European plans to decrease the number of journals that the industry currently monitors in order to look for safety signals relating to their products. The European Medicines Agency will perform this function centrally from now on. However, industry reporting requirements for literature will remain for literature not monitored by the EMA.

Harmonisation of reporting processes through the use of the EudraVigilance Database

30. Centralisation of reporting by industry of individual case safety reports to a single EU database, as opposed to many member state databases at present. Coordination of requests for further information from member states. Not due to be functional until early 2015.

31. Introduction of the use of the EudraVigilance Medicinal Product Dictionary (EVMPD); a database aimed to support the collection, reporting, coding and evaluation of authorised and investigational medicinal product data in a standardised way.

Greater accessibility to the public of key safety documents

32. Duties of industry to provide key safety documents that will now be published on the MHRA's website. Simplification of certain documents to make them more digestible by the general public.

Penalties for failure to meet the conditions of an authorisation

33. New effective, proportionate and dissuasive penalties to be introduced to ensure compliance with the particulars of the Pharmacovigilance Directive.

Introduction of infringement notices

34. MHRA proposals to introduce a new regulatory compliance tool to ensure that companies meet their pharmacovigilance responsibilities.

Incremental costs and benefits of implementing the Directive

Formal consultation responses

35. MHRA received 22 responses to its formal consultation on the new Directive. The majority made no comments on the IA. However, the few IA comments that we received have prompted us to make changes to the IA:

- One consultee pointed out that an EU reduction in the amount of safety reporting from companies (Product Safety Update Reports) would not lead to a cost saving to firms who sell their products in non-EU markets where the reporting will still be required. For this reason, and the continued uncertainty about what exactly the EU will require in terms of PSUR reporting (the EU is still consulting on the changes), we have removed all PSUR cost saving estimates from the IA.

- Three consultees suggested that we had under-estimated the incremental costs to firms from having to report non-serious adverse drug reactions. We subsequently sought new estimates from industry and increased our estimate by a factor of over 2.5.
- Two consultees pointed out that we had failed to include an estimate of the costs to firms of complying with the new Eudravigilance Medicinal Products Dictionary. We subsequently gained an estimate of this cost from industry and included it in the IA.

Assumptions used in the analysis

36. The standard appraisal period of ten years has been used.

37. We have assumed that 950 firms will be affected by the Directive. This is based on the number of companies that supply the UK market and we assume that this is representative of the EU as a whole.

38. Assessing the UK economic welfare effects of costs and benefits to multinational firms (such as large pharmaceutical firms) is not straightforward. Whichever approach is taken, significant assumptions have to be made. While scrutinising an earlier draft of this final stage IA, the RPC informally challenged the methodology that we had used, unchallenged, in the consultation IA. In response, we have added additional explanation and justification of our methodology. However, we recognise that further evidence-gathering and debate may be necessary before a robust methodology can be mutually agreed.

39. On the assumption that firms are effective at minimising costs at each level of output, in the short to medium term, the interventions contained in this Directive will affect firms' profits. The effects of intervention will therefore be felt through changes to the returns to the capital of firms' investors. This analysis is interested in how the interventions will affect UK citizens, and hence we need to know the proportion of UK shareholding in the firms that supply the EU market. Unfortunately, we know little about this proportion. The World Health Organisation estimated that in 1999 the UK had a 6% share by value in world pharmaceutical production[6]. Taking this figure as our baseline, we have assumed a range of plus and minus 3% to reflect the substantial uncertainty we feel about the exact proportion.

40. In the longer term, we would expect profits in pharmaceutical firms to normalise around the risk adjusted capital market average rate of return, as markets shift capital around in response to differentials in rates of return across investments. When this happens, it is not clear what the welfare effects of the intervention will be. Pricing of patented pharmaceuticals in the UK is based on the health value that the medicines provide and is not related to firms' costs. Consequently, originator firms can not pass regulatory cost changes on to buyers[7]. The only option for firms is to adjust their levels of output in some way. At the margin, this might mean spending more or less on R&D and/or rent-seeking. The welfare effects of these adjustments are extremely difficult to predict. For instance, by itself, spending less on rent-seeking would have no welfare impact whatsoever because the activity is economically wasteful. By contrast, spending less on R&D might have welfare impacts that are felt in the future, albeit that firms would cut marginal R&D that has low social net benefits.

41. One simplification is to assume that shareholders bear the cost of the changes throughout the whole of the ten year appraisal period. There is a reasonable rationale for this position. Pharmaceutical firms that engage in substantial R&D look at the expected costs and benefits of a project, and if they decide to undertake it, they fund the R&D. If all goes well, after ten years or more a marketable product emerges. If we impose some additional cost on these firms, it means they get less profit once the drugs are launched. It's too late for them to do anything about it in respect of the pipeline of drugs that are already in development - and which will emerge over the next ten years or more. So their profits on these will be reduced. But they will factor the increased costs into their future decisions to invest. So in ten or more years' time everything will be back to normal, as the increased costs are factored in to investment decisions[8].

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[6] http://apps.who.int/medicinedocs/en/d/Js6160e/3.html#Js6160e.3 The basis for this calculation is not clear and it might not be based on UK shareholding.

[7] Unless perhaps there is some adjustment in the quality of service that the pharmaceutical firms provide.

[8] This approach ignores (at least) two important factors. First, decisions on R&D actually happen on a continual basis - and there will be some ongoing projects at the margin that would be stopped as a result of the increased costs, thereby reducing the profit impact. Second, there will

42. We have also made two further adjustments. Firstly we have assumed that some of the profits made by branded manufacturers are spent on rent seeking, such as competitive advertising that increases a firm's share of a market without increasing overall societal welfare. Evidence provided by Gagnon and Lexchin[9] suggests that branded manufacturers spend 15% of profits in this way. Manufacturers of unbranded medicines do not engage in this sort of rent seeking. In 2010 in the UK, approximately 70% of the value of all pharmaceutical expenditure was spent on branded medicines. Using this proportion as a weight, we estimate that overall, 10.5% of pharmaceutical profits earned from medicines sales in the UK are spent on rent seeking.

43. The second adjustment is made to account for the marginal utility of income to UK shareholders. On the assumption that shareholding is a linear function of wealth, the following calculation for the distributional weight applies to UK share ownership.

Quintile	% of wealth*	Green Book weight**	weighted contribution to overall multiplier for shareholders
5	59%	0.5	0.295
4	20%	0.8	0.16
3	13%	1	0.13
2	6%	1.3	0.078
1	1%	1.9	0.019
		overall multiplier	**0.682**

* from http://www.hmrc.gov.uk/stats/personal_wealth/menu.htm

** from page 94, http://www.hm-treasury.gov.uk/d/green_book_complete.pdf

Note this is an over-estimate because a) there will be an additional concentration of wealth, probably highly significant, within the top quintile (top decile has 45%); b) the weightings used are the most conservative cited in the Green Book

44. Pricing of generic drugs is very closely related to firms' costs and so we would expect a fairly rapid transfer of regulatory cost changes to buyers. We assume that costs will be passed on to the UK in proportion to its share of the value of the global generics market[10]. Chapter 4 of the 2004 WHO World Medicines Situation reports that the estimated value of global generics sales in 2000 was over $80 billion. The UK's share of this was $4.5 billion, less than 5.6% of the global total. In 2010 in the UK, generics accounted for approximately 30% of total pharmaceutical expenditure[11].

45. Our assumptions yield a range of between 1.8% and 5.5% for the UK welfare effects from regulatory cost changes experienced by global branded pharmaceuticals manufacturers (branded expenditure accounts for 70% of total the UK pharmaceutical expenditure). Combined with our estimated cost pass-through to UK buyers of generic pharmaceuticals (30% of total UK expenditure), the overall range that we have applied to global cost changes is from 3% to 5.5%.

46. We have applied a zero weighting to impacts on overseas interests. In our summary section, however, for the sake of transparency, we have presented our estimates of the cost to the global pharmaceutical industry from the changes that will be effected by the Directive.

47. In estimating incremental costs and benefits, we have made various assumptions about staff costs.

- A pharmaceutical industry average annual salary of £70,000 and a senior annual salary of £105,000[12] have been used (supplied by a pharmaceutical firm and assumed to be representative of the industry). These yearly salaries have been converted to hourly rates assuming a 215 day working year, and a 7.5 hour working day. Non-salary costs are assumed to

probably be some reduction in spending on post-launch rent seeking, which will also have the effect of reducing the profit impact. These two factors should be explored properly when time permits. At the moment we believe that the figure of 6% is an over-estimate of the impact.

[9] Gagnon and Lexchin (2008). "The cost of pushing pills: a new estimate for pharmaceutical promotion expenditures in the US" PLoS Med 5 (1)

[10] This assumes that demand is price inelastic and hence all cost changes are passed on to buyers. The effect of relaxing this assumption would be to lower the cost pass-through to buyers.

[11] Prescriptions Dispensed in the Community, 27 July 2011, NHS Information Centre

[12] Figures sourced from industry contacts

add 30%. These assumptions yield average staff costs of £56 per hour and senior staff costs of £85 per hour.

- MHRA annual staff time is assumed to cost £55,300 or £33,600 depending on the seniority of staff required. We have assumed a 220 day working year, a 7.2 hour working day, and 30% non-salary costs. These assumptions yield hourly rates of £45 and £28.

Reductions in the numbers of Periodic Safety Update Reports (PSURs) required

What is currently in place and how does it work?

48. The current system under 2001/83/EC requires that Marketing Authorisation Holders (MAHs) collect information on adverse reactions on each and every medicine that they are currently marketing. This information is collected and assessed, and then submitted to the MHRA (and other member states where the products are centrally authorised across the EU) at regular intervals. A single report may cover all products containing the same active substances produced by a MAH (for instance, all paracetamol products produces by a single MAH would be covered by the same PSUR), and are intended to provide a continuously updated picture of the worldwide safety of a medicinal product.

What's wrong with the current system?

49. The submission of PSURs is seen to be one of the areas where burdens upon industry could be significantly reduced – currently the ongoing cycle of collation and submission, assessment by the MHRA and subsequent changes to the safety profile is seen as onerous when applied across the spectrum of different categories of medicines. The repetitive nature of the work and stringent requirements relating to how and when these reports are submitted has been highlighted by the Commission as unnecessary in their analysis of the current system. When PSURs are submitted to individual member states, each of these states can query and ask for further information, which can lead to significant duplication of effort across the 27 European Member States.

What has the Commission done to intervene?

50. The Commission aims to reduce the numbers of PSURs submitted by industry to various regulators. They will look at how much risk each medicine carries and decide the frequency of reporting upon this basis. For generic medicines (those medicines where the 'exclusivity' of the developer has expired, allowing others to copy the drug, e.g. ibuprofen), medicines for which the risks are well known, homeopathics and traditional use registered products (e.g. Echinacea or Ginkgo Biloba), although PSURs may need to be produced, the interval between their submission is likely to be greatly increased, reducing the overall burden on industry. National Competent Authorities will be able to review whether or not a PSUR is required and if not increase the interval between PSUR submission for drugs where there are no new safety indications and because the effect of drugs which have been on the market for a long period of time, are well known.

51. National regulators, such as the MHRA will still have the power to require the production of PSURs in future where specific safety concerns have been identified.

52. For those still required to submit information on PSURs, the work will be coordinated among the national regulators of the member states in future. Worksharing between member states will mean that there is a single centralised request for further information. MAHs will only need to respond to one set of queries on each PSUR for all of Europe.

53. PSUR reports will also be submitted electronically to the EU's central repository (the European Pharmacovigilance Issues Tracking Tool, or EPITT) by MAHs to further reduce burdens.

What costs and benefits arise from the new approach?

54. This area of the legislation should see a reduction in the number of mandatory PSURs required by regulators from industry, and thus will most heavily affect UK businesses in terms of a reduction in costs. It will be especially helpful to those elements of the pharmaceutical industry whose main trade is in generics, registered traditional use products, and homeopathics, although the innovative sector (those producing new medicines) will also receive a fair proportion of the benefits.

55. The list of products that will require PSURs in future is currently being determined by a working group in the European Medicines Agency, and thus there is some uncertainty surrounding how extensive this list might be. The UK will encourage as short a list as possible through participation in EMA working groups.

56. There was an expectation that the EPITT database would be ready by the time of transposition in July 2012 however due to a lack of funding at a European level it is unlikely that this will be ready before 2015 and therefore the associated benefits will not be accruing until it is operational.

57. We have assumed that there will be no negative health impact to these changes, as further ADRs will not arise as a direct result of a reduction in reporting requirements by industry. Any possible negative health impact will be negated by the alternative and parallel systems that the Commission intends to put in place as part of the Directive, including the more holistic approach to pharmacovigilance under risk management systems. However, this is merely an assumption – we have not been able to obtain evidence to prove a direct evidential link between any pharmacovigilance change and the numbers of deaths due to ADRs. We have estimated that ADR harm would have to increase by approximately 0.04% in order for the estimated benefits to industry to be offset by health losses. We are not claiming that this would happen in practice.

Private Sector benefits (cost savings)

58. On average, the MHRA reviews 4,500 PSURs per year at present. We have taken this figure as representative of all PSURs produced by the pharmaceutical industry for the EU market. The costs provided by industry of preparing, reviewing and submitting a PSUR (assuming a single request for further information from member states) is £5,756[13]. We cannot definitively answer how many PSURs will no longer be required under the new system, but the MHRA does not expect to request a large number of PSURs per year under the new Directive.

59. PSURs will continue to be required for new products. However where a product has been on the market for some time the frequency of PSUR submission will be reduced. This frequency will be reviewed and the interval at which this is required can be extended if the product has been on the market for a significant period of time and there are no safety indications. There is therefore expected to be a reduction in the actual number of PSURs produced however quantifying this into a percentage of the number currently submitted is difficult.

60. The EMA has yet to publish a final list of timeframes and requirements for the submission of PSUR's and therefore the actual impact is currently difficult to assess. Futhermore, PSURs will still be required by non-EU regulators and hence companies that sell their products in non-EU markets are unlikely to see a substantial reduction in their PSUR burden. Given the continued uncertainties, we feel unable to give an estimate of the cost saving from reduced demand for PSURs in Europe[14].

61. Member states can also ask for further information for each PSUR, and industry estimates that between 0-3 of these requests are received per application, costing between £0 and £10,560[15] per application. This situation is mirrored across Europe, as the majority of PSURs are submitted to multiple member states. Benefits should therefore accrue from an increase in worksharing between member states, leading to a single set of queries arising from any PSUR submission and a single response required from MAHs in response to these queries. The benefit likely to accrue from this is a reduction in the number of requests for further information – the range of worksharing costs will now be between £0 and £3,520 per application. These assumptions and our UK welfare effect assumptions yield estimated annual UK benefits of between £0 and £1.749 million. The NPV is between £0 and £12.463 million (annualised at between £0 million and £1.637 million).

62. Total UK benefits for the PSUR changes are given below

Total UK benefits from PSUR changes	Annual (£million)	NPV (£million)	Annualised (£million)
Lower	0.000	0.000	0.000
Upper	1.749	12.463	1.448
Midpoint	0.875	6.231	0.724

[13] Industry supplied figures: 90 hours @ £56 for preparation of a PSUR, followed by 8hrs @ £85 for review and clearance of the PSUR.

[14] As a scenario to illustrate the possible scale of cost savings, let's assume that 75% of marketing authorisations will continue to require PSURs. These assumptions, and our 2.1% - 6.2% UK impact assumption, yield annual UK benefits of between £0.134 million and £0.404 million starting from July 2012. The NPV is between £0.960 million and £1.920 million (annualised at between £0.112 million and £0.335 million).

[15] Figure supplied by industry – responding to a single request for information - £3,520.

Risk Management Plans and Risk Management Systems

What is currently in place and how does it work?

63. Risk Management Plans were introduced as part of Directive 2001/83/EC as a way of providing a more planned, focussed and proactive approach to the monitoring of pharmaceuticals within the general population (as opposed to the previous, reactive approach, which relied heavily upon ADR reports). They are important, as they are currently the primary tool by which MAHs and the MHRA agree plans for individual monitoring of each pharmaceutical product placed upon the market.

64. RMPs are currently required for all new active substances, as well as in a variety of other situations where the safety profile of the medicine needs to be more carefully monitored, and are assessed by the MHRA. RMPs also contain the details of extra requirements that may have been imposed upon MAHs, such as the requirement to carry out post-authorisation safety studies.

What's wrong with the current system?

65. The Commission's view was that risk management plans as currently formulated focus on individual products and the minutiae of their operation. They detract from a more coordinated and holistic approach that regulators would like to encourage MAHs to move towards. Risk management plans have also been very technical documents in the past, and are unlikely to be understood by the general public, who are increasingly interested in medicines information available.

What have the Commission and the MHRA done to intervene?

66. The new requirements surrounding the Risk Management System are a detailed description of activities above existing Risk Management Plans for individual products, to be set up and adhered to by the MAH. They are a new requirement placed upon MAHs to ensure that a more proactive approach is taken towards the collection and use of pharmacovigilance data, and are designed to focus industry to embed risk management systems into their culture. Elements of the Risk Management System are now conditions of the marketing authorisation (allowing action to be taken against the MAH if they fail to conduct these key elements).

67. Risk Management Plans are to be made more accessible to the public and healthcare professionals, and lay summaries (in plain English) of these are to be prepared by MAHs and will be published as publicly accessible documents.

68. It is expected that RMP's will need to be submitted on the same cycle as the PSUR's, (which is the same as the existing system, and therefore no additional burden is accrued). This will mirror the situation for PSUR's in that it will be a less frequent submission for drugs which have been on the market for a long period of time and who have well established safety profiles. However RMP's would need to be submitted if there are any significant changes in the RMP for example if there was a new safety signal which meant the drug required additional safety monitoring.

69. In certain circumstances (currently unknown but expected to be very infrequent), where it is judged by the marketing authorisation holder that they do not have to submit an RMP as part of their application, they will instead need to provide a justification of this decision to the MHRA. Clarification from the EU will also be sought as to the procedure for maintaining RMPs where they already exist upon introduction of the Directive. We have assumed that the proposals will have an unquantifiable positive effect upon public health, as an approach towards embedding pharmacovigilance as a main part of each company's business should lead them to spot safety signals arising from ADRs more promptly and/or frequently. We assume that this would translate into faster action to revise safety data and disseminate it to the public and healthcare professionals, resulting in a reduced level of ADRs. However, we have been unable to ascertain direct links between pharmacovigilance system changes and health benefits, and are aware that there is no monitoring available to the MHRA that will allow us to test this assumption to the degree of accuracy required.

Private Sector Costs

70. The EMA's interpretation of the Directive is likely to require more RMP production than current levels. All new substances will require a RMP including generic drugs. This is a new requirement, however the costs will be minimised for the manufacture of generic drugs as they will only be required to complete an abbreviated form of the RMP. It is currently not known what the cost of the abbreviated RMP production will be; the EMA is currently consulting with Industry on this issue.

71. Lay summaries (descriptions of the risk management plan in plain English) will need to be prepared for all new RMPs. From data provided by industry, we have estimated that this will cost an extra £340[16] in administrative burden. Around 200 applications are received by the MHRA each year that require risk management plans, and we have assumed that this is representative of RMP requirements in the EU as a whole. These assumptions yield annual costs to the UK of between £0.002 million and £0.004 million.

72. Each firm supplying the EU market will now require a Risk Management System (RMS) to sit over its RMP's. The one-off cost per firm is estimated to be £10,158[17]. The total one-off discounted cost to the UK is estimated to between £0.286 million and £0.533 million.

73. Each of the 950 firms will also be required to update RMS annually on their progress in meeting authorisation conditions, estimated to cost £621[18] per review. These assumptions yield annual UK costs estimates of between £0.017 million and £0.033 million.

74. There is a presumption in favour of producing RMP's. However there may be occasions where an MAH feels that this is not necessary and they will want to request an exemption for this activity. In this event they would need to submit a justification to the MHRA. This situation is expected to occur infrequently and therefore the likely burden is minimal. Where these justifications are required industry estimate that they may cost in the region of £1,020 in administrative burdens[19]. However this would potentially have the impact of reducing the burden on the company by removing the requirement to submit a full RMP. For this reason, we have assumed that the impact is cost neutral.

75. The key elements of risk management plans will now also be a condition of the MAH's authorisation – leading to the chance that the MHRA will take action against the MAH if they fail to meet the conditions of their RMP. This is explored in more detail under the 'penalties for failure to meet the conditions of a marketing authorisation' section below.

Total UK costs from RMP and RMS changes	One-off (£million)	Annual (£million)	NPV (£million)	Annualised (£million)
Lower	0.286	0.019	0.415	0.048
Upper	0.533	0.036	0.773	0.090
Midpoint	0.410	0.028	0.594	0.069

Benefits to public health

76. The Commission has produced an impact assessment on the Pharmacovigilance Directive that considers the impact of avoidable adverse drug reactions upon the healthcare systems in Europe, particularly on hospital admissions.[20] However, the IA provides no evidential link between the numbers of avoidable ADRs and the efficacy of the RMP and RMS changes in preventing the ADRs. We have trawled the literature for further evidence but have found nothing. We therefore feel unable to provide estimates of the benefits of these changes[21].

77. However, to put the scale of the costs into context, the RMP and RMS changes would have to reduce the UK's ADR costs by less than 0.002% in order for the benefits to justify the costs. Note that we are not claiming that this reduction would be achieved in practice.

Derogation for Risk Management Plans

78. If the MHRA does not avail itself of a derogation within the Directive, and instead requires all UK Marketing Authorisation Holders to produce risk management plans for products that were authorised before 2 July 2012, we would expect there to be added costs. The MHRA has records of around 28,400

[16] Industry estimate – 4hrs @ £85

[17] Industry estimate – 150 hrs @ £56 and 20 hrs @ £85

[18] Industry estimate – 5hrs @ £56 and 4hrs @ £85

[19] Industry estimate - 5hrs @ £56 followed by 8hrs @ £85

[20] Commission impact assessment on Pharmacovigilance: http://tiny.cc/byjw9

[21] If we had a monetised estimate of the ADR costs that better pharmacovigilance could prevent, we could have provided an estimate of the amount of harm that the RMP and RMS changes would have to prevent in order to justify their costs. However, even then we would have been unable to make a reasonable judgement on how likely this amount of harm reduction would be realised, not least because other factors that are beyond the scope of the changes, such as information dissemination and patient and practitioner behaviour, would also determine the desired outcome.

authorisations for medicinal products on the UK market at present, and industry has supplied us with the costs of preparing and submitting a risk management plan as part of our calculations above, and we would estimate, based on knowledge of the discussions ongoing at the EMA at present, that around a third of these would need to comply with the RMP requirements and continue to comply with the annual requirements. The remaining two thirds would need to prepare and submit a justification for not producing an RMP

79. However, it should be noted that it is difficult to tell whether other member states will exercise this derogation – therefore meaning that those who trade in Europe (this is a significant proportion, estimated to be 85%) may still need to prepare risk management plans for some other member states. We therefore assume that no significant cost savings will arise from the utilisation of this derogation.

MHRA and Department of Health (DH) Costs

80. The MHRA will need to enforce the new authorisation conditions, as well as assess RMPs for each new product as well as updates to RMP requirements. It is expected that this will require adjustment to fees, but any changes to fees will be costed and consulted upon separately, and is not expected to take place until the 2013/14 financial year, in order to allow data to be collected by the MHRA on what levels of fee adjustment may be necessary. We expect there to be associated administrative and resource costs to industry in preparing the paperwork for such fees changes. The scale of these costs is currently uncertain, but we would judge them unlikely to materially affect the proposals put forward by this impact assessment. A separate consultation exercise will take place in 2012, which will be accompanied by its own impact assessment, and the MHRA will have gathered enough information to accurately identify costs at this point.

Movement from the use of Detailed Description of the Pharmacovigilance System (DDPS) to the Pharmacovigilance Master File

What is currently in place and how does it work?

81. The Detailed Description of the Pharmacovigilance System (DDPS), which is submitted at the time of an application for a marketing authorisation, broadly summarises key pharmacovigilance activities undertaken by the MAH in order to meet legislative requirements. These activities range from a record of the contact details of the Qualified Person responsible for Pharmacovigilance (QPPV) through to an effective pharmacovigilance system for monitoring the safety of every authorised medicine. The current Directive introduced this record and required its submission with every licence application.

What's wrong with the current system?

82. Due to the size of global pharmacovigilance systems, the DDPS is often very complicated and can take a significant time to compile and review. Currently, MAHs need to supply full details of the DDPS with each marketing authorisation application and certain variations; this is considered to be unnecessary duplication of information as often the pharmacovigilance system operated by the MAH will be identical across different products. Furthermore, as the DDPS is a document supporting the authorisation, any slight modification to the document requires submission of a variation to the NCA as variations are required where any change to the marketing authorisation is proposed. Submission of a variation application to make minor changes to a DDPS, which may not have a significant impact on the operation of a pharmacovigilance system, currently have considerable resource implications for MAHs and NCAs.

What have the Commission and the MHRA done to intervene?

83. The new Directive removes the need for applicants to submit a DDPS and instead requires them to submit summary information about the pharmacovigilance system (QPPV details and the location of the master file). The detailed description of the pharmacovigilance system is contained in the Pharmacovigilance System Master File, which is submitted *at the request* of competent authorities. This allows MHRA to choose under which circumstances it may be appropriate to request and review the master file. A move from a requirement to submit the DDPS to the use of the Pharmacovigilance System Master File should bring about a great deal of cost savings. Under the new system, the master file is prepared and maintained in a current state by companies and covers the pharmacovigilance system irrespective of the number of authorised products. The only sections of the Pharmacovigilance System Master File that MAHs need to notify as part of the marketing authorisation application will be the location of the file itself and the details of the QPPV, although European Medicines Agency Working groups are looking at ways to further reduce this burden at present.

84. The new Directive demands that the move from DDPS to Master File be made, at a maximum, three years after the introduction of the Directive in 2015. The MHRA proposes to make this move more quickly and allow marketing authorisation holders the opportunity to make the switch from the implementation of the Directive in July 2012. This should provide cost savings for those marketing authorisation holders that currently have DDPS requirements, reducing the variations burden on both industry and competent authorities.

Private Sector costs and benefits

85. The pharmaceutical industry has provided us with an outline of the costs of the DDPS system at present – it is estimated that preparing a new DDPS for each product costs £4,402[22], and there are 2,900 new applications received by the MHRA per year (which we take as representative of the EU as a whole). The DDPS also needs to be regularly updated, and although many of these variations are fee free, we have estimated from data provided by industry that the administrative burden associated with each update is £168. We believe that there is a stock of 15,060 DDPSs. Industry reports that on average there are 6 updates per DDPS every year. These assumptions yield annual UK cost saving estimates (starting in 2015) of between £0.832 million and £1.550 million, with an NPV of between £4.000 million and £7.447 million.

86. Instead of individual DDPS for each product, a single master file will be required for a company's portfolio of products (and their risk profile). Industry has provided us with figures to estimate how much this new system will cost to set up and prepare – it is estimated that this will be a one-off cost of £2,144[23] for each pharmaceutical company (total cost based on 950 eligible companies. Maintenance of the master file will be ongoing, with an additional estimated cost of £1,129 per annum[24] for each company starting in 2015. These assumptions yield estimated UK costs that have an NPV of between £0.205 million and £0.383 million (which can be annualised at between £0.024 million and £0.044 million)

87. The master file must be submitted to the MHRA upon request (estimated in 10% of all cases – see below) – and notifications of major changes must be made available to us, however the need for MAHs to submit Summaries of Pharmacovigilance Systems for inspection purposes will be removed for those MAHs operating a Pharmacovigilance Master File, which should deliver a net reduction in regulatory burden.

88. Under the new Directive, the QPPV must *operate* and reside in the EU from now on, and inform the MHRA of their name and address - this is not anticipated to impose any greater cost than under the present system, particularly as EMA working groups are working to simplify this process.

89. All of the respondents to the MHRA's questionnaire said that they would be very unlikely to ever submit a variation to change the location of the master file, as it is now electronic. Thus no extra cost is anticipated from this change.

UK private sector net benefits from DDPS and Master File changes	One-off (£million)	Annual (£million)	NPV (£million)	Annualised (£million)
Lower	-0.060	0.800	3.794	0.441
Upper	-0.112	1.490	7.065	0.821
Midpoint	-0.086	1.145	5.430	0.631

90. The MHRA will experience costs savings from not having to deal with DDPSs. We have assumed that each new DDPS requires 5 hours of Grade 7 time to review and that each updated DDPS requires 1 hour of Grade 7 time. This yields annual cost savings of £4.870 million, which start in 2015. The present value is £22.872 million (annualised at £2.719 million).

91. The MHRA will experience new costs of dealing with master files, but only in cases where this is the first marketing authorisation in Europe, there are significant issues with the drug in question, or safety concerns. The MHRA representative from the EMA working group estimates that this will happen in no more than 10% of all marketing authorisations. We have assumed that each new Master file requires 5

[22] Industry figures - £440 unjustified, £3,480 is 40hrs @ £56 for preparing the DDPS and 12hrs @ £85 for reviewing the DDPS

[23] Industry figures – 20hrs @£56 (assuming that DDPS can be used as a base) for preparation of master file, and 12 hrs @ £85 for clearance at a senior level

[24] Industry figures - £440 unjustified, £1,200 is 20hrs @ £56

hours of Grade 7 scrutiny, and that annual updates require 3 hours of Grade 7 time. These costs start in 2015. The present value of these costs is £0.185 million (annualised £0.021 million).

Health impacts

92. We have assumed that there will be no impact upon health, either negative or positive, arising from these proposals. Updates to the DDPS are almost universally an administrative burden imposed upon industry, and have limited impact upon public health. The Pharmacovigilance System Master File will continue to be reviewed at regular inspection intervals by MHRA inspectors, which will continue to identify any areas for action at the same rate as previously. Links between pharmacovigilance and improvements to public health are tenuous, however, so we cannot test this assumption. We have estimated that ADR harm would have to increase by approximately 0.02% in order for the estimated benefits to industry to be offset by health losses. We are not claiming that this would happen in practice.

Additional transitional proposals

93. To ensure that benefits are realised as soon as possible, the UK aims to remove the need for MHRA to receive DDPS from MAHs from the implementation date of 2 July 2012 rather than wait until the final implementation in 2015.

94. In order for companies to start using Master Files rather than DDPS, there is a requirement for the EU to produce a set of guidelines related to variation categorisation. However these will not be available by July. In order to ensure that companies in the UK can benefit from these burden reducing provisions, the MHRA are working with European colleagues to use part of the legislation to agree across Europe the categorisations that should be applied until the Guideline is in place. This would ensure that there is a system in place from July which would enable MAHs to voluntarily introduce the Master File and remove their responsibility to maintain a DDPS via submission of a Type 1A variation. And therefore allowing companies to realise the benefits of this provision.

95. The present value of the savings to the UK of this transition would likely be between £1.492 million and £2.985 million (annualised at between £0.173 million and £0.347 million). However, given the uncertainties involved in our estimate we do not feel confident in claiming this as a robustly estimated regulatory “Out”.

Additional Pharmacovigilance responsibilities

What’s wrong with the current system?

96. There is a perception from the Commission that not enough time is taken by both industry and regulators to regularly evaluate and update their pharmacovigilance systems to ensure that they are fit for purpose. This was implied by their 2008 impact assessment on how the pharmacovigilance system could be improved. Issues with pharmacovigilance systems operated by marketing authorisation holders are reported regularly as a result of MHRA Good Pharmacovigilance Practice inspections.

97. It is also accepted that in some cases one member state may have a particular expertise that can be brought to bear on pharmacovigilance monitoring, but at the moment there are no provisions that allow one member state to undertake the pharmacovigilance monitoring responsibilities for a product in another country.

What have the Commission and the MHRA done to intervene?

98. Under Directive 2010/83, MAHs will now be required to audit their pharmacovigilance system at regular intervals. The appropriate frequency of this audit should be determined by the MAH (although the Commission may establish a minimum frequency) and it is expected that this would be determined by a number of factors, including the number/extent of changes to the pharmacovigilance system and company changes (e.g.. mergers). A risk-based model may be utilised to determine the frequency and scope of audits, and inspectors will review the rationale for the frequency of such audits at regular intervals.

99. As well as a responsibility of the marketing authorisation holder, there is now also a duty upon the MHRA to regularly review its own pharmacovigilance monitoring system from 21 September 2013. This is not an independent audit, but instead one to be carried out by the MHRA themselves (led by personnel who are independent of the operational activities to be audited).

100. The Directive also allows the MHRA to delegate responsibility for pharmacovigilance tasks for certain products or substances to another member state. The MHRA would be extremely unlikely to ever

do this, although it does give the MHRA the opportunity to take responsibility for another member state's pharmacovigilance tasks, although this is likely to be limited in the guidelines produced by the European Medicines Agency.

Private Sector costs

101. In reality, the vast majority of companies already operate a quality assurance programme which includes performing audits that focus on one or more aspects that make up the pharmacovigilance system. For global Pharma, the number of audits relating to the pharmacovigilance system conducted per year could be 10 or more, whereas a UK-only company, an audit once every two to three years may be sufficient. The industry has provided us with data from which we have estimated the cost for a single audit at £677[25]. These assumptions yield a present value of UK costs at between £0.045 million and £0.084 million (annualised at between £0.005 million and £0.010 million)

MHRA and Department of Health (DH) Costs & Benefits

102. The MHRA will need to conduct a review of its own pharmacovigilance system once every two years beginning in 2013. We have assumed, based upon previous audits of other systems that each audit takes 40 hours of Grade 7 time. These assumptions yield a present value cost of £0.006 (annualised at £0.001 million)

103. We cannot, at present, quantify what taking on another member state's responsibilities for pharmacovigilance monitoring might cost – this would be very much based on the circumstances, the member state and the type of medicine involved. However, this it is unlikely to present much opportunity cost – in most cases we would be already monitoring the product in question.

Public Health benefits

104. The Commission's impact assessment on the Pharmacovigilance Directive considers the impact of avoidable adverse drug reactions upon the healthcare systems in Europe, particularly on hospital admissions. However, the IA provides no evidential link between the numbers of avoidable ADRs and the efficacy of the auditing changes in preventing the ADRs. We have trawled the literature for further evidence but have found nothing. We therefore feel unable to provide estimates of the benefits of these changes.

105. However, to put the scale of the costs into context, the new audit requirements would have to reduce the UK's ADR costs by less than 0.0002% in order for the benefits to justify the costs. Note that we are not claiming that this reduction would be achieved in practice.

Revised requirements for Post Authorisation Safety and Efficacy Studies

What is currently in place and how does it work?

106. The requirement for certain MAHs to conduct Post Authorisation Safety Studies (PASS) is not new, and was introduced under Directive 2001/83/EC. These studies are often required where clinical trials have not adequately identified the risks inherent in the medicine, and may be useful in identifying previously unsuspected adverse reactions or to confirm the safety profile of the medicine under normal conditions of use. PASS may not be conducted in such a way that promotes the medicine involved.

What's wrong with the current system?

107. There is widespread acceptance within the pharmaceutical community that PASS studies are rarely completed, and if so are not of a quality which allows conclusions on the safety profile of the medicine to be adequately drawn.

108. The system is also costly for industry, who need to respond individually to requests from member states when further information is required. This can mean a number of duplicative submissions to up to 27 member states to answer their queries on the PASS studies.

What has the Commission done to intervene?

109. The new Directive introduces a harmonised guiding process for and regulatory submission of non-interventional (those likely to have the lowest risk) PASS studies. All PASS studies will now be considered at an EU level, which will mean that MAHs will only need to respond to a single set of queries on their studies from all of the EU. There should not be a rise in the numbers of PASS studies required.

[25] Industry estimate – auditing of 12hrs @ £56

There will be greater amounts of guidance available and more emphasis on the completion of PASS in order to benefit public health.

110. Post Authorisation Efficacy Studies (PAES) are a new addition to the regulatory suite, and allow Member States to request that MAHs perform further trials to prove that their medicine treats the condition for which it is prescribed under normal conditions (e.g. when the understanding of the disease or the clinical methodology indicate that previous efficacy evaluations might have to be revised significantly).

111. These are anticipated to be a very rare occurrence, for which guidance is being drawn up by the European Medicines Agency.

112. PASS and PAES will now be conditions of a marketing authorisation, enabling the MHRA to take stepped regulatory action against those who fail to meet these requirements.

Private Sector costs

113. From our involvement in the EMA working group developing these proposals, and from the publication of the draft guidance on GVP (Good Pharmacovigilance Practice) related to PASS we do not expect the number of PASS studies to increase as a result of this new legislation. However, we are expecting the rigour of PASS studies to increase, leading to higher costs per PASS. The Commission's IA assumed a 25% cost increase although provided no evidence to support this assumption In order to provide an estimate, we have adopted the Commission's assumptions, however these may be subject to change as industry will have a more accurate view on the costs associated with the changes as a result of the ongoing consultation on the guidance (due to close on the 18 April 2012). The Commission's IA reports survey results from which it has estimated that £310 million is spent annually by the industry on PASSs. Applying the Commission's 25% increase and our estimate of the UK share of costs yields a present value of between £16.393 million and £30.522 million (annualised at between £1.904 million and £3.545 million)

114. Industry will now be required to submit an abstract of the final PASS study report alongside a final submission as part of the conditions of their marketing authorisation.

115. The MHRA does not expect to impose post-authorisation efficacy studies as part of a condition of authorisation very often. We estimate that PAESs will be required between once and twice a year for the whole industry. Industry estimates that the costs of PAES studies range from £2.64m to £12.32m.[26] These assumptions yield present value costs of between £0.558 million and £9.693 million (annualised at between £0.064 million and £1.126 million).

Both PASS and PAES will be included as part of the risk management plan, will be monitored through the master file, and will become conditions of the marketing authorisation. For this reason, it is expected that these will be completed in better time and to a greater level of data quality than currently takes place. This will benefit patients and the public, as well as industry, who will benefit from better information about the performance of substances within the population and be able to better target existing medicines

Annual (£million)	NPV (£million)	Annualised (£million)
0.078	-8.475	-0.985
0.680	-20.108	-2.336
0.379	-14.292	-1.660

Public Health benefits

116. The Commission's impact assessment on the Pharmacovigilance Directive considers the impact of avoidable adverse drug reactions upon the healthcare systems in Europe, particularly on hospital admissions. However, the IA provides no evidential link between the numbers of avoidable ADRs and the efficacy of more robust PASSs. We have trawled the literature for further evidence but have found nothing. We therefore feel unable to provide estimates of the benefits of these changes to public health.

[26] Based upon estimates for a typical interventional clinical trial in more than one European country

117. However, to put the scale of the costs into context, the PASS and PAES changes would have to reduce the UK's ADR costs by less than 0.04% in order for the benefits to justify the costs. Note that we are not claiming that this reduction would be achieved in practice.

Additional monitoring arrangements

What is currently in place and how does it work?

118. In the UK, we currently have a scheme called the 'Black Triangle' (▼), a symbol that is placed upon literature related to a medicine (namely in the British National Formulary (BNF), monthly index of medical specialties, ABPI Medicines Compendium, on advertising material and in drug safety updates). This symbol denotes that the medicine is under a period of intensive monitoring. Typically, the black triangle is applied to new medicines where the side effects are not fully known, and it is intended to both inform prescribers and patients that less is known about the medicine than in some other cases, and to encourage them to be vigilant and report any adverse reactions to the medicine.

What's wrong with the current system?

119. The UK's black triangle system is a national system, and quite unique within Europe at present. The Commission has decided, from evidence supplied by the MHRA, that additional monitoring would be a useful regulatory tool for all of Europe.

What has the Commission done to intervene?

120. The new Directive 2010/84/EU creates an 'additional monitoring scheme' that closely mirrors the UK's current systems. The major change is that it will now be applied across Europe evenly to a set list of substances - which may be slightly different from the UK's current list, requiring adaption or phased transition. Medicines information will need to be updated to take account of the specifics of the additional monitoring scheme.

Private sector costs

121. We expect that in future, fewer products will be covered by additional monitoring than are currently by the Black Triangle Scheme in the UK, although this is still being decided by an EU working group. Industry has calculated that on average it costs an extra £4,700[27] per annum for products that are on the black triangle scheme at present. Industry have also supplied us with a figure of 5% cost saving likely to take place due to the changing requirements brought about by the new Directive.

122. Medicines information will need to be updated to take account of the specifics of the additional monitoring scheme. This involves updating the Product information Leaflet and the Summary of Product Characteristics with specific text and the symbol for additional monitoring from the new Directive, which the EU has estimated will take 24 hours of work per product - calculated to be £1,354 per product (24 x hourly staff cost of £56). However in order to assist industry standardised text on the Additional Monitoring Scheme will be produced which they will be able to use in literature. The MHRA are also looking at ways in which industry can be supported and to introduce this scheme to minimise the impact on industry in the UK such as implementing a phased transition to the new scheme.

123. Currently there are 215 drugs on the black triangle scheme. The total cost for the production of the material required for the additional monitoring scheme would therefore be approximately be £291,000 for the whole industry, of which we estimate UK interests will bear between £8,000 and £16,000. However this list is subject to change and can increase or decrease as new drugs come to the market and other drugs are able to be removed.

124. The MHRA may from time to time request that additional products be added to the list (subject to EU agreement) once the list has been developed by the European Medicines Agency – we would expect this to happen only very infrequently.

Public health impact

125. The systems surrounding the black triangle scheme in the UK are very similar to those put forward by the Commission under additional monitoring arrangements. However, any reduction in the numbers of those medicines covered by the scheme could conceivably lead to a higher level of ADRs –

[27] Unjustified figure supplied by industry

as safety signals for new products not being intensively monitored could lead to a slight lag in the action taken upon them. We assume that this would only happen exceedingly rarely, but note that as the link between pharmacovigilance and increases in public health cannot be proven by our analysis, nor any that we can locate, there remains a possibility that the impacts could be greater (or lesser).

MHRA and Department of Health (DH) Costs & Benefits

126. The MHRA will be required to publish a list of those products covered by the additional monitoring scheme, although we do not expect this to cost us anything further in terms of resource compared to the current system, as a list of Black Triangle Scheme products is already produced and made publicly available by the MHRA.

Centralisation of literature monitoring for certain substances

What is currently in place and how does it work?

127. As part of their marketing authorisation, MAHs must at present perform literature monitoring to ensure that any extra studies or individual case reports printed among certain journals are taken into account as part of their continuous evaluation of the safety profile of the drug. They must also report to the competent authorities a subset of individual case safety reports identified and also incorporate information on published studies in PSURs that may have a bearing upon the safety profile of the medicine.

What's wrong with the current system?

128. The monitoring of hundreds of journals and many other forms of media for specific entries on certain medicines is an onerous task for the industry. This is particularly a problem for the generics industry – many of whom are duplicating effort (sourcing and reporting the same reports), and are small businesses who expend resource in outsourcing the literature monitoring role to companies who perform it for them.

What has the Commission done to intervene?

129. The new Directive removes the obligation to monitor for a set list of medicines (extent yet to be determined), and obliges the European Medicines Agency to perform this task in future. The reports will be entered onto a centralised system known as the EudraVigilance database. However, whilst the monitoring elements have been reduced, MAHs will still be required to report to the EMA on reports contained within any other literature where these concern their products.

Private Sector costs and benefits

130. The burden of literature reporting will be reduced, as MAHs will not be required to report ADRs published in the literature for certain substances from publications reviewed by EMA, throughout the EU. The costs for this task will move from businesses to the European Medicines Agency. Whilst the new legislation may reduce burden in terms of reporting of suspected ADRs from the literature, MAHs will still be required to review the scientific and medical literature to detect any new safety data that concerns their products and factor these data into their ongoing safety monitoring. If MAHs have reporting responsibilities outside of the EU, the same literature may nevertheless have to be monitored for reportable ADRs, depending on how quickly EMA make available each reportable case through EudraVigilance. Finally, following budget constraints within Europe, the EMA is considering ways in which this role could be reduced or removed.

131. Some benefits would unambiguously arise if the European Medicines Agency makes the reports on EudraVigilance available to all via their web-portal. This is not likely to aid larger companies, who already contract agencies to conduct literature monitoring for them, but may have a positive impact on smaller companies, who may not need to purchase these articles from web archives in future. The purchasing of articles online typically costs £10-12 per article, and industry contacts that are smaller companies have estimated that on average they would have to purchase 75 of these per year. The EU estimate (according to the Pharmacovigilance Directive's impact assessment) on the size of the pharmaceutical market would put 20% of companies as having fewer than 100 employees. These assumptions yield annual benefits to the UK of between £0.005 million and £0.009 million starting in 2015.

Health impact

132. We have assumed that there will be no negative impact upon public health arising from these proposals. Literature monitoring forms a very small part of the total monitoring of safety signals that companies perform, added to which is the fact that reporting of these signals will still have to take place. Essentially, the industry will receive and process the same number of reports as they had in the past, and no safety signals will be missed, leading to no change in public health.

Harmonisation of reporting processes through the use of the EudraVigilance Database

What's wrong with the current system?

133. At present, there is no reliable database in the EU that can store essential information, such as adverse drug reactions and is accessible to all. The EudraVigilance database already exists, but is not fully functional, or fit for purpose. The Commission views this central information repository as an essential step towards ensuring that harmonisation of member states' systems and decisions takes place.

134. There is also no centralised product dictionary which allows EudraVigilance to accurately interpret the data sent to the database. Therefore there may be duplication of information included on EudraVigilance.

What has the Commission done to intervene?

135. As mentioned by a number of other areas above, the Commission proposes to further develop its existing EudraVigilance database, so that it can be used a single portal for receipt of reports (such as Adverse Drug Reaction reports (ADRs)) from MAHs, as well as simultaneously transmit these safety update reports to the competent authorities in which the marketing authorisation is held. This single reporting portal should significantly reduce the amount of duplicate reporting that MAHs currently undertake. However, the portal is unlikely to go live until 1 January 2015, to ensure that it is fully functional (and to give it time to be independently audited as such).

136. Added to this, and an area of real benefit, is that because of worksharing arrangements, there will be a single request for further information on these ADRs (rather than at present, where up to 27 member states can request further information), and MAHs will only need to reply to this single request.

137. The MHRA will continue to run the UK's existing national Yellow Card Scheme in order to encourage healthcare professionals and patients to report ADRs directly to the MHRA. This ensures that a link is kept between prescribers, patients and the MHRA, as well as the already well established link between industry and the MHRA. It also aims to preserve wider access to reports that might not have been captured or notified to the MAH and gives the MHRA a broader view of the safety profile of any given substance within the general population.

138. Under the new legislation a product dictionary will be created which will allow EudraVigilance to be more effective, preventing duplication of adverse drug reaction reports and allowing EudraVigilance to be effectively searched. Overall the aim of this dictionary is to make the use of EudraVigilance more efficient and effective.

139. MAH's have to provide information about all their products for the EVMPD (Eudravigilance Medicinal Product Database). The commission set out their initial plans as to what information would be submitted to the database however following consultation with industry the number of mandatory fields which must be filled in have been reduced with the aim of reducing the burden on industry. Additionally the population of the QPPV (Qualified Person in charge of Pharmacovigilance) details and the master file location, will remove the requirement for Marketing Authorisation Holders to submit variations associated with the DDPS (Detailed Description of Pharmacovigilance System) or master files updates.

Private Sector benefits from harmonised reporting

140. The impact of these proposals varies widely – the Commission IA expects that some companies will see little benefit, others as much as 80% from improved worksharing and reduction in duplicate reporting. During MHRA's informal consultation Industry has estimated a likely benefit of £72,800[28] per year per company for these proposals. These assumptions yield annual benefits of between £2.051 million and £3.819 million starting in 2015 (present value of between £9.857 million and £18.353 million).

Private sector costs of implementing the EVMPD

[28] Industry estimate 1FTE reduced to 0.2FTE because of the proposals

141. The formal consultation revealed that we had not included the impacts of the new EVMPD requirements. We subsequently consulted industry and received an estimate of the cost per firm. From this we have assumed that each of the 950 firms will need to employ an extra 4 FTE staff for 6 to 9 months. These assumptions yield annualised costs of between £0.596 million and £1.663 million (present value of between £5.127 million and £14.320 million)

Private sector costs from having to report non-serious ADRs

142. Non-serious ADRs in Europe will now also need to be reported to EudraVigilance, whereas in the past this had not been the case. This will increase the numbers of reports that will need to be sent by companies to EudraVigilance. Our formal consultation revealed that the previous version of this IA may have under-estimated the cost of non-serious reporting. We subsequently asked industry sources for a new estimate. The most plausible estimate was based on employing an additional 1.5 FTE staff per company (we have previously assumed that there are 950 companies). Given our estimate of the cost of a FTE staff member of £91,000, our assumptions yield annualised costs to the UK of between £2.147 million and £3.998 million starting in 2015 (present value of between £18.482 million and £334.412 million).

143. The costs associated with additional ADR reporting will depend on the profile of the products which a company produces, for example there is likely to be a greater increased in reporting requirements for companies who's drugs are mainly over the counter products compared to prescription only medicine. Overall the EudraVigilance system will reduce the need for MAH;s to have to send individual reports to all member states affected therefore this change in process should yield efficiencies as it will mean companies will not have to send reports to each member state separately.

144. Currently, ADRs reported by industry to the regulator are required to be confirmed by a health care professional; however MAHs will be required to report all ADRs irrespective of health care professional confirmation from July 2012. Therefore, it is likely that the impact on companies who predominantly market over-the-counter products (e.g. mouth ulcer products, indigestion tablets, cough syrups etc.) will be greater. These companies receive a greater proportion of non-serious ADRs that are unlikely to be confirmed by a healthcare professional, as a proportion of their total ADR dataset and would have to expend more resource on the reporting of ADRs, as a proportion of their current workload relating to reporting.

Total UK costs EVMPD and ADR reporting changes	One-off (£million)	Annual (£million)	PV (£million)	EANC (£million)
Lower	5.127	3.846	23.610	2.743
Upper	14.320	7.160	48.733	5.662
Midpoint	9.724	5.503	36.171	4.202

Public Health benefits from reporting of non-serious ADRs

145. Greater attention being given to non-serious ADRs by industry could conceivably lead to safety signals being addressed earlier, thereby avoiding further ADRs relating to the same issue. The Commission's impact assessment on the Pharmacovigilance Directive considers the impact of avoidable adverse drug reactions upon the healthcare systems in Europe, particularly on hospital admissions. However, the IA provides no evidential link between the numbers of avoidable ADRs and the efficacy of reporting of non-serious ADRs. We have trawled the literature for further evidence but have found nothing. We therefore feel unable to provide estimates of the benefits of these changes.

146. However, to put the scale of the costs into context, the new EVMPD and non-serious ADR requirements would have to reduce the UK's ADR costs by 0.11% in order for the benefits to justify the costs. Note that we are not claiming that this reduction would be achieved in practice.

Greater accessibility to the public of key safety documents

What's wrong with the current system?

147. The Commission would like to encourage greater transparency of the safety profiles of medicines in circulation. The general public is increasingly able to access and use information to make informed

decisions on the medication that they are prescribed, and greater accessibility to these documents, as well as drafting them in a way that can be understood by the layman will encourage them to do so.

What has the Commission done to intervene?

148. Various documents are now to be posted upon the national web portals of the MHRA and the European Medicines Agency – for the former, this will be;

- Public Assessment Reports;
- Summaries of Product Characteristics;
- Patient Information Leaflets;
- Lay summaries of Risk Management Plans;
- The list of those products subject to additional monitoring; and
- Information to healthcare professionals and the public on ways to report suspected ADRs via the web.

MHRA, Department of Health (DH) and wider Government Costs & Benefits

149. It is likely that greater access to certain key safety documents will have a beneficial effect – both in terms of their confidence in medicines and knowledge that safety is continually being assessed by the pharmaceutical industry and the Government. This may also have the beneficial effect of encouraging further reporting from those who have suffered ADRs. These reputational costs are difficult to quantify and are therefore listed only qualitatively. However, the MHRA already has a good reputation in the EU, as we already accept patient reports and follow up with enquiries, as well as proactively work to encourage such reporting.

150. There will be a minor incremental cost to the MHRA of publishing these documents, expected to be the equivalent of 24hrs per annum of an HEO's time. These assumptions yield an annual cost of £662 (present value £4,715)

Penalties for failure to meet the conditions of an authorisation

What is the situation at present?

151. The UK already has a series of penalties that apply to failure to meet the conditions of a marketing authorisation granted by the MHRA. The most severe penalties that we can impose for these failures is: on summary conviction (in a Magistrate's Court), to a fine (not exceeding the prescribed sum); on conviction on indictment (in Crown Court), to a fine or to imprisonment for a term not exceeding two years or to both.

What has the Commission done to intervene?

152. The Pharmacovigilance Directive requires that:

'Where appropriate, the Member State concerned shall take the necessary measures to ensure that a marketing authorisation holder is subject to effective, proportionate and dissuasive penalties'

153. Further penalties are proposed as part of these transposition measures, although many are based upon previous or similar penalties. The costs of these will be determined at a later date with the aid of the Ministry for Justice (see the Justice Impact Test section below). The MHRA operates a step-wise process to tackling non-compliance, therefore it is very unlikely that these penalties would be used as a first option by the MHRA and only in rare circumstances would this be considered; if a breach of an obligation results in significant harm to patients or is considered to be in the public interest. The MHRA has so far never brought a case based upon pharmacovigilance offences only.

Introduction of infringement notices

What's wrong with the current system?

154. Criminal prosecution is a challenging, time-consuming and resource-intensive option. Investigations with a view to criminal prosecution for pharmacovigilance offences have been conducted (most notably the Seroxat investigation[29]), but, to date, no case has been brought to court. The pursuit of a criminal penalty for the majority of offences committed within the area of pharmacovigilance is unlikely to be in the public interest. They cost too much to the justice system, are based upon an extremely

[29] MHRA press release on Seroxat investigation: http://www.mhra.gov.uk/home/groups/comms-po/documents/news/con014162.pdf

technical piece of law, and cost the MHRA a great deal of resource in terms of bringing evidence to a prosecutable criminal standard of proof. Instead, the MHRA is more likely to take action against the Marketing Authorisation (e.g. variation, suspension or revocation) and/or require detailed commitments from the MAH in the form of a Corrective and Preventative Action plan.

How does the MHRA propose to intervene?

155. The MHRA considered a number of civil sanctions that would complement the existing and new criminal sanctions proposed by the Directive. These were rejected as disproportionate options.

156. The MHRA instead intends to use the 'infringement notice' – a notice sent to an organisation where MHRA has objective grounds to consider a breach of an obligation has occurred. This would specify the steps that the organisation must take and in what timeframe, in order to rectify the non-compliance and also take steps to prevent a further case of non-compliance. This notice would be made publicly available and it would also be sent to the EMA and the European Commission.

Private Sector costs and benefits

157. It should be noted that no additional regulatory requirements would be created by introducing the infringement notice, so there will be no impact on the vast majority of MAHs that are compliant. It is not envisaged that this would place additional burden on industry; the only cost to non-compliant MAHs would be the cost to comply with existing requirements.

MHRA and Department of Health (DH) Costs

158. The introduction of the infringement notice process would place some additional administrative burden on the MHRA, but it is anticipated that these notices would only be used in a small number of cases (approximately 4 per year). It is proposed that the existing Inspection Action Group (IAG) would determine whether an infringement notice was appropriate in the first instance. Since IAG already discuss and administer warning letters and the Inspectorate holds company meetings, this burden is likely to be negligible.

Public health impacts

159. The only foreseeable change to public health might be a minor benefit as those companies that are persistent in their non-compliance become compliant more quickly. This would result in their pharmacovigilance systems becoming more effective, and the chance that specific ADRs are turned into safety signals that affect the way the medicine is prescribed. This in turn might lead to a reduction in ADRs. However, this assumption is tenuous at best, and given the lack of evidence that we have been able to source between these proposals and public health, the impact is unquantifiable.

Summary and net benefits

160. The table below sets out the private sector costs and benefits of the directive. It includes our estimated of the Expected Annual Costs, the Expected Annual Benefits and the Expected Annual Net Costs.

Private sector UK (£ million)	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	PV	Annualised (EAC/EAB/ EANC)
Transition costs	9.74	0.41	0.00	0.00	0.10	0.00	0.00	0.00	0.00	0.00	10.22	1.19
Annual costs	0.00	2.02	4.05	4.05	9.58	9.60	9.60	9.60	9.60	9.60	55.50	6.45
Total costs	9.74	2.43	4.05	4.05	9.68	9.60	9.60	9.60	9.60	9.60	65.72	7.64
Transition benefits	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Annual benefits	0.00	0.44	0.87	0.87	5.00	5.00	5.00	5.00	5.00	5.00	26.06	3.03
Total benefits	0.00	0.44	0.87	0.87	5.00	5.00	5.00	5.00	5.00	5.00	26.06	3.03
Net benefits	-9.74	-2.00	-3.17	-3.17	-4.68	-4.60	-4.60	-4.60	-4.60	-4.60	-39.66	-4.61

161. The table below sets out the overall societal costs and benefits of the Directive.

	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	PV	Annualised
Transition costs	9.7	0.4	0.0	0.0	0.1	0.0	0.0	0.0	0.0	0.0	10.2	1.2
Annual costs	0.0	2.0	4.1	4.1	9.6	9.6	9.6	9.6	9.6	9.6	55.7	6.5
Total costs	9.7	2.4	4.1	4.1	9.7	9.6	9.6	9.6	9.6	9.6	65.9	7.7
Transition benefits	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Annual benefits	0.0	0.4	0.9	0.9	9.8	9.8	9.8	9.8	9.8	9.8	48.9	5.7
Total benefits	0.0	0.4	0.9	0.9	9.8	9.8	9.8	9.8	9.8	9.8	48.9	5.7
Net benefits	-9.7	-2.0	-3.2	-3.2	0.0	0.1	0.1	0.1	0.1	0.1	-17.0	-2.0

162. This summary table should be read with some caution. In several sections of this IA[30], we have acknowledged that we have been unable to estimate the public health benefits of measures that introduce new burdens on the private and public sectors. The table below summarises the costs of the burdens for which we have been unable to estimate benefits.

	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	PV	Annualised
Transition costs	9.7	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	10.0	1.2
Annual recurring costs	0.0	2.0	4.0	4.0	9.5	9.5	9.5	9.5	9.5	9.5	55.2	6.4
Total annual costs	9.7	2.3	4.0	4.0	9.5	9.5	9.5	9.5	9.5	9.5	65.2	7.6

163. To put the scale of the costs into context, the new cost imposing measures would have to reduce the UK's ADR costs by 0.21% in order for the benefits to justify the costs. Note that we are not claiming that this reduction would be achieved in practice.

164. Having put these costs into context, we should do the same for the cost savings (benefits) that accrue to industry (annualised estimate £3.03 million). Throughout this IA we have assumed, plausibly we believe, that these cost saving measures have no impact on public health. However, we should allow for the possibility that the assumption is wrong. We have estimated that ADR harm would have to increase by 0.1% in order for the cost savings to be offset entirely by ill health effects. Again, note that we are not claiming that this increase would occur in practice.

165. We estimate that the NPV to the global pharmaceutical industry is -£903 million (annualised at -£105 million)

166. In conclusion, we have estimated costs and cost-savings attached to a wide variety of discrete pharmacovigilance activities, each of which has the potential to change the harm caused by ADRs. The evidence that links relatively small changes in pharmacovigilance activities to ADR harm is too weak to

[30] "Risk Management Plans and Risk Management Systems", "Additional Pharmacovigilance responsibilities", "Revised requirements for PASS and PAES" and "Harmonisation of reporting processes through the use of the EudraVigilance database".

complement our cost change estimates with the estimated value of changes in public health. Our estimated NPV of -£1.9 million is therefore unlikely to represent the true balance between costs and benefits of this package of pharmacovigilance measures. We have pointed out what scale of health changes would be required for the costs and cost-savings to yield a £0 NPV but have been unable to comment on the likelihood of these changes occurring in practice.

167. Summary of impacts by cost category

	UK		Industry Total	
	NPV	Annualised	NPV	Annualised
	£ million	£ million	£ million	£ million
Cost savings from fewer PSURs required				
Midpoint	0.00	0.00	0.00	0.00
Cost savings from fewer PSUR follow-up questions				
Midpoint	6.23	0.72	146.84	17.06
Cost of plain English requirement for RMP				
Midpoint	-0.02	0.00	-0.48	-0.06
Cost of setting up RMS				
Midpoint	-0.40	-0.05	-9.32	-1.08
Cost of annual update of RMS				
Midpoint	-0.18	-0.02	-4.20	-0.49
Industry cost savings from not having to produce and update DDPSs				
Midpoint	5.72	0.66	134.87	15.67
Industry cost from creating and updating master files				
Midpoint	-0.29	-0.03	-6.93	-0.80
MHRA cost savings of not having to deal with DDPSs				
Point estimate	22.87	2.66		
MHRA costs of dealing with Master Files				
Point estimate	-0.18	-0.02		
Industry audits and updates				
Midpoint	-0.06	-0.01	-1.53	-0.18
MHRA audits and updates				
Point estimate	-0.01	0.00		
UK costs from conducting more robust PASS				
Midpoint	-23.46	-2.73	-552.78	-64.22
UK costs from conducting PAES				
Midpoint	-5.13	-0.60	-120.78	-14.03
UK costs of changing patient information for new black triangle scheme				
Midpoint	-0.01	0.00	-0.29	-0.03
Cost savings to SMEs from having free access to EudraVigilance				
Midpoint	0.03	0.00	0.75	0.09
Cost savings from fewer PSURs required				
Midpoint	14.11	1.64	332.39	38.62
Cost of EVMPD requirements				
Midpoint	-9.72	-1.13	-229.14	-26.62
Cost of new, non-serious ADR reporting				
Midpoint	-26.45	-3.07	-623.22	-72.40
MHRA admin costs				
Point estimate	0.00	0.00		
Total Costs				
Midpoint	-65.92	-7.66	-1,548.68	-179.92
Total Benefits				
Midpoint	48.96	5.69	614.86	71.43
Net Benefits				
Midpoint	-16.95	-1.97	-933.82	-108.49

Equalities

168. Pharmacovigilance and adverse drug reactions are areas that are not confined to any single area of the general public, and affect all equally. The MHRA currently makes sure that the information on its website and the reporting systems that it encourages the public to use are as accessible to the public as possible, and will continue to do so in future. We will also continue to look for ways to strengthen the reporting and receipt of timely information from all sections of the public on the safety of medicines.

Risks and Uncertainties

169. There is a great deal of work ongoing at the European Medicines Agency to determine the detail on how many of the procedures introduced under the Pharmacovigilance Directive will operate in future and there is still a significant amount of uncertainty as to how these provisions will work in practice. The complexity or simplicity of those procedures and the roles of the industry and regulators will determine the costs and benefits of these proposals. some of these proposals will not be decided until after the UK's transposition arrangements come into force. Currently the first wave of Good Pharmacovigilance Practice guidance has been published in draft form for consultation purposes. This consultation ends at the end of April and includes the major areas of change for industry, there may therefore be a clearer picture of the additional burdens which this legislation may impose once this consultation has closed. Overall there continues to be a real and unavoidable lack of knowledge that arises from continued development of these proposals in Europe.

170. A greater focus on the benefit:risk balance, as provided for by 2010/84/EC, may lead to more pharmaceutical companies employing physicians instead of scientists. In general, physicians verify the conclusions drawn on active substances by scientists, and an increased focus on benefit:risk will raise their profile. The MHRA does not mandate how these decisions should be made within pharmaceutical companies, or by whom, but it is worth noting that a shift in emphasis could affect the types of people employed by these businesses in future.

Specific impact tests

Justice Impact Test

171. The transposition of the Pharmacovigilance Directive could introduce some new and updated offences relating to pharmacovigilance activities. The Ministry of Justice has been approached about the introduction of offences, and has agreed that the MHRA should engage with them to justify their introduction following the close of the public consultation on the proposed text.

Competition impact assessment

172. EU markets for originator medicines that contain innovative active substances are to some extent national. Originator companies attempt to segment markets using their control over the distribution of their products. Nevertheless parallel exports and imports have some impact on making the markets EU-wide. These markets experience strong dynamic but little static competition. Development of these medicines is always associated with high research and development costs.

173. EU markets for generic, off-patent medicines are largely EU-wide and experience some static competition based on price.

174. The costs of pharmacovigilance are without doubt a barrier to entry into both originator and generic markets. The scale of the changes brought in by the Directive is significant compared with the overall cost to industry of its pharmacovigilance activities. The EU estimates that pharmaceutical firms spend annually Euros 832.7 million on meeting the current EU pharmacovigilance requirements. We have estimated that the changes brought in by the new Directive are expected to increase this amount by approximately Euros 70 million (this is the total amount to the 950 firms that supply the EU market, and not the adjusted amount that measures UK impact) .

175. We therefore conclude that there will be some impact on increasing barriers to entry. We expect this only to affect competition in the generics sector. The originator sector has several much more substantial barriers to entry connected with scientific knowhow and the huge R&D costs of bringing drugs to market. We therefore do not expect that the changes brought about by the Directive will alter competition in originator markets.

176. Answering the competition assessment questions, we believe that the measures:

1. Are unlikely directly to limit the number or range of suppliers

2. May indirectly limit the number or range of suppliers in generics markets. However, the bulk of the impact will not be felt generics suppliers because their products' safety profiles are well understood (their medicines have been prescribed for many years)

3 Are unlikely to limit the ability of suppliers to compete

4 Are unlikely to reduce suppliers' incentives to compete vigorously

Small Firms impact test

177. Originator firms (those that bring new patented medicines to market) spend billions of pounds on R&D and require very substantial sales to justify their investments. It is therefore inconceivable that any originator firms would have turnovers of less than £6.5 million. Information on the size of generics firms (those that produce out-of-patent medicines) has proven very difficult to acquire. During the consultation and subsequently we approached BIS and the British Generics Manufacturers Association but neither could provide information on the existence small firms (identified by employee numbers and turnover) who have marketing authorisations. In the absence of information, we have assumed that there are some small generics firms that will be affected by the changes.

178. The EU impact assessment does not provide an in-depth analysis of the impacts on small firms. However, it does conclude that "SMEs" will disproportionately benefit from the cost-saving measures. This seems plausible because such firms tend to produce established products for which the safety profile is well known. The new Directive specifically reduces the regulatory burden for producers of such products.

179. Costs will be borne in proportion to the number of products that a firm markets. We have no reason to believe that small firms market proportionately more products than their larger counterparts and hence we would not expect the cost burden to fall disproportionately on small firms.

Health impact test

180. The impact upon health has been considered in a specific impact test, although as outlined in previous discussions, we cannot define an adequate link between these specific pharmacovigilance system changes and increases to public health through a reduction in ADRs. For this reason, the public health benefits of the proposals have been considered 'not important' using the criteria of the Department for Health's health impact assessment.

Title:	Impact Assessment (IA)
Pharmacy proposals - Repeal of Section 10(7) of the Medicines Act	**IA No:** 4023
Lead department or agency: Medicines and Healthcare products Regulatory Agency	**Date:** 27/07/2010
Other departments or agencies: Department of Health	**Stage:** Final
	Source of intervention: EU
	Type of measure: Secondary legislation
	Contact for enquiries: MHRA central enquiry point: info@mhra.gsi.gov.uk

Summary: Intervention and Options

What is the problem under consideration? Why is government intervention necessary?

The Medicines Act 1968 contains an exemption which allows pharmacies in the UK to trade pharmaceutical products without the requirement to hold a wholesale dealers' licence. This law is incompatible with more recent EU legislation (see page 5), and trading in future will need to be only where it meets the needs of public health, is in small quantities, is infrequent, and is not for profit. There is a great deal of trading between pharmacies at present, particularly within the NHS, and we would not wish to impose the full licensing arrangements upon a public service, as this would be disproportionate. Government intervention is necessary for the repeal of Section 10(7), but also to provide a regime under which essential supplies of medicines continue to reach patients in need.

What are the policy objectives and the intended effects?

The policy objectives are to create a regime which brings the UK into compliance with EU legislation, whilst taking account of the UK's National Health Service (which is relatively unique among Member States as a health service open to all without the need for private insurance). A repeal of the 10(7) exemption without any mitigating solutions would cause serious problems in terms of supplies of medicines for patient care, extra regulatory cost and administrative burden, particularly for the NHS, and the policy seeks to preserve continued medical supplies above all other concerns.

What policy options have been considered, including any alternatives to regulation? Please justify preferred option (further details in Evidence Base)

1. Repeal section 10(7) and allow trade in medicines where this performed to the direct benefit of patients (the 'healthcare suppliers' model). This is the preferred option. Non-regulatory action has been considered, but a repeal of legislation cannot take place without legislative instruction.

2. Do nothing - no change to the law but running the risk of possible EU infraction proceedings

3(a) Repeal the 10(7) exemption without any further mitigating factors - essentially requiring all trading in medicines beyond limited perameters to be undertaken under a wholesale dealers' licence

3(b) Implement a 'hub and spoke' model by which smaller pharmacies become satellites of a larger pharmacy

3(c) Implement an 'agency' model by which smaller companies can be considered as part of a larger central pharmacy for pharmaceutical trading purposes

Will the policy be reviewed? It will be reviewed. **If applicable, set review date:** 5/2017	
What is the basis for this review? Duty to review. **If applicable, set sunset clause date:** Month/Year	
Are there arrangements in place that will allow a systematic collection of monitoring information for future policy review?	Yes

SELECT SIGNATORY Sign-off For final proposal stage Impact Assessments:

I have read the Impact Assessment and I am satisfied that (a) it represents a fair and reasonable view of the expected costs, benefits and impact of the policy, and (b) the benefits justify the costs.

Signed by the responsible Minister: ..... Date: 25 June 2012

Summary: Analysis and Evidence

Policy Option 1

Description:

The 'healthcare suppliers' model

Price Base Year 2011	PV Base Year 2011	Time Period Years 10	Net Benefit (Present Value (PV)) (£m)		
			Low: -£47.215	**High:** -£9.443	**Best Estimate: -£28.328**

COSTS (£m)	Total Transition (Constant Price)	Years	Average Annual (excl. Transition) (Constant Price)	Total Cost (Present Value)
Low	£0.303		£1.061	**£9.443**
High	£1.516		£5.309	**£47.215**
Best Estimate	£0.910		£3.185	**£28.328**

Description and scale of key monetised costs by 'main affected groups'

Costs to any pharmacist (or other entity) that wishes to trade in medicines for profit - a wholesale dealers' licence will be required (present value £19.0 million, annualised £2.2 million).

Costs to a small proportion of 'end users' who will need to trade with wholesale dealers' licence holders in future (present value £9.4 million, annualised £1.1 million).

Other key non-monetised costs by 'main affected groups'

BENEFITS (£m)	Total Transition (Constant Price)	Years	Average Annual (excl. Transition) (Constant Price)	Total Benefit (Present Value)
Low				
High				
Best Estimate	unquantifiable		unquantifiable	**unquantifiable**

Description and scale of key monetised benefits by 'main affected groups'

Massive reduction in administrative cost and regulatory burden associated with other opions. Avoidance of infraction proceedings from the Commission.

Other key non-monetised benefits by 'main affected groups'

Effectively excludes much of the current practice in medicines trading between pharmacies whereby compliance with EU legislation is achieved through minimum impact on the UK. NHS almost entirely excluded.

Key assumptions/sensitivities/risks

Maximum of 8 lines

Discount rate (%) 3.5

Direct impact on business (Equivalent Annual) £m):			In scope of OIOO?	Measure qualifies as
Costs: £3.291	**Benefits:** £0	**Net:** -£3.291	No	NA

Enforcement, Implementation and Wider Impacts

What is the geographic coverage of the policy/option?			United Kingdom		
From what date will the policy be implemented?			02/06/2012		
Which organisation(s) will enforce the policy?			MHRA		
What is the annual change in enforcement cost (£m)?			None		
Does enforcement comply with Hampton principles?			Yes		
Does implementation go beyond minimum EU requirements?			No		
What is the CO_2 equivalent change in greenhouse gas emissions? (Million tonnes CO_2 equivalent)			**Traded:** n/a	**Non-traded:** n/a	
Does the proposal have an impact on competition?			No		
What proportion (%) of Total PV costs/benefits is directly attributable to primary legislation, if applicable?			**Costs:** n/a	**Benefits:** n/a	
Distribution of annual cost (%) by organisation size (excl. Transition) (Constant Price)	**Micro**	**< 20**	**Small**	**Medium**	**Large**
Are any of these organisations exempt?	No	No	No	No	No

Specific Impact Tests: Checklist

Set out in the table below where information on any SITs undertaken as part of the analysis of the policy options can be found in the evidence base. For guidance on how to complete each test, double-click on the link for the guidance provided by the relevant department.

Please note this checklist is not intended to list each and every statutory consideration that departments should take into account when deciding which policy option to follow. It is the responsibility of departments to make sure that their duties are complied with.

Does your policy option/proposal have an impact on…?	**Impact**	**Page ref within IA**
Statutory equality duties[1] Statutory Equality Duties Impact Test guidance	No	17
Economic impacts		
Competition Competition Assessment Impact Test guidance	No	14
Small firms Small Firms Impact Test guidance	No	14
Environmental impacts		
Greenhouse gas assessment Greenhouse Gas Assessment Impact Test guidance	No	15
Wider environmental issues Wider Environmental Issues Impact Test guidance	No	15
Social impacts		
Health and well-being Health and Well-being Impact Test guidance	No	14
Human rights Human Rights Impact Test guidance	No	15
Justice system Justice Impact Test guidance	No	14
Rural proofing Rural Proofing Impact Test guidance	No	15
Sustainable development Sustainable Development Impact Test guidance	No	15

[1] Public bodies including Whitehall departments are required to consider the impact of their policies and measures on race, disability and gender. It is intended to extend this consideration requirement under the Equality Act 2010 to cover age, sexual orientation, religion or belief and gender reassignment from April 2011 (to Great Britain only). The Toolkit provides advice on statutory equality duties for public authorities with a remit in Northern Ireland.

Evidence Base (for summary sheets) – Notes

Use this space to set out the relevant references, evidence, analysis and detailed narrative from which you have generated your policy options or proposal. Please fill in **References** section.

References

Include the links to relevant legislation and publications, such as public impact assessments of earlier stages (e.g. Consultation, Final, Enactment) and those of the matching IN or OUTs measures.

No.	Legislation or publication
1	MLX 357: Consultation on measures to strengthen the supply chain and reduce the risk from counterfeit medicines: http://tiny.cc/eofui
2	MLX 365: Measures to strengthen the medicines' supply chain and reduce the risk from counterfeit medicines: http://tiny.cc/j716a
3	EC consultation and impact assessment on falsified medicines proposals: http://tiny.cc/ad2cn
4	Directive 2001/83/EC - http://tiny.cc/1aq8p

+ Add another row

Evidence Base

Ensure that the information in this section provides clear evidence of the information provided in the summary pages of this form (recommended maximum of 30 pages). Complete the **Annual profile of monetised costs and benefits** (transition and recurring) below over the life of the preferred policy (use the spreadsheet attached if the period is longer than 10 years).

The spreadsheet also contains an emission changes table that you will need to fill in if your measure has an impact on greenhouse gas emissions.

Annual profile of monetised costs and benefits* - (£m) constant prices

	Y_0	Y_1	Y_2	Y_3	Y_4	Y_5	Y_6	Y_7	Y_8	Y_9
Total Transition costs	0.910	0	0	0	0	0	0	0	0	0
Total Annual recurring cost	3.547	2.944	2.944	3.547	2.944	2.944	3.547	2.994	2.994	3.547
Total annual costs	3.547	2.944	2.944	3.547	2.944	2.944	3.547	2.944	2.944	3.547
Total Transition benefits										
Total Annual recurring benefits										
Total annual benefits										
Business transition costs	0.910	0	0	0	0	0	0	0	0	0
Business annual recurring costs	3.547	2.944	2.944	3.547	2.944	2.944	3.547	2.944	2.944	3.547
Business annual costs	3.547	2.944	2.944	3.547	2.944	2.944	3.547	2.944	2.944	3.547
Business transition benefits	0	0	0	0	0	0	0	0	0	0
Business annual recurring benefits	0	0	0	0	0	0	0	0	0	0
Business total annual benefits	0	0	0	0	0	0	0	0	0	0

* For non-monetised benefits please see summary pages and main evidence base section

Microsoft Office Excel Worksheet

Evidence Base (for summary sheets)

What is the problem under consideration?

The vast majority of trading of pharmaceuticals within the EU is undertaken by companies that hold a Wholesale Dealer's Licence. These licences require the holder to meet a specific standard of expertise for storing and trading medicines, as well as employ others (particularly a 'Responsible Person') who have responsibilities to ensure that these standards are upheld on the trading sites.

Arrangements under Section 10(7) of the Medicines Act 1968 allow trading between pharmacies without the need for a Wholesale Dealer's Licence. It has been informally accepted by companies and the MHRA that this applies for up to 5% of the pharmacy company's turnover, although this has never been codified in law. The MHRA considered that the 5% limit could be open to exploitation, as the amounts traded could vary hugely dependent on the pharmacy's turnover, and were subject to no regulatory oversight or guidelines to pharmacists on how they should behave.

Whilst exploring the options for codifying the duties of those trading under the Section 10(7) exemption, the MHRA became aware of a conflict between the UK's stance on trading and that of the European Union. It became clear that EU law required any trading between pharmacies undertaken without a Wholesale Dealer's Licence to be limited to a set of defined circumstances, namely that it be in the interests of public health, in limited circumstances, in small quantities, and not for profit. The current informal arrangement of allowing 5% trading without the need for a Wholesale Dealer's Licence is clearly incompatible with the intentions of the European Union, and will need to change if we are to avoid infraction proceedings.

Many pharmacies and other businesses (such as optometrists, midwives, nursing homes, dentists and oil rigs) rely on the Section 10(7) exemption to get limited supplies of pharmaceutical stock from pharmacies, as well as return unused stock to those pharmacies without the need for either party to hold a Wholesale Dealer's Licence. It is clear that the impact upon these businesses, should the Section 10(7) exemption be repealed, could be huge, and so the MHRA has considered a number of different solutions to try to resolve this problem.

Another significant series of entities that currently utilises the Section 10(7) exemption is the National Health Service. Now increasingly decentralised, the NHS is a series of separate legal entities, ranging in size from large hospital trusts to legal entities that exist as small mental health wards in a wider hospital. These legal entities use Section 10(7) to trade pharmaceutical supplies and return unwanted stock within the NHS structure. Any repeal of the exemption could have a massive impact on UK NHS services, both in terms of continued supply of medicines and imposing cost upon the NHS.

The MHRA, in conjunction with the Department for Health and the General Pharmaceutical Council, has considered a number of options available to try to alleviate the impact of this conflict with European legislation. These were developed by a specific group, and the options discussed below have received approval from legal counsel as methods to address the problem. The costs and benefits laid out below have been sourced from the pharmaceutical industry and the Department of Health.

One In One Out

Whilst these proposals will have an effect on the private sector, they are considered in the context of achieving compliance with existing EU legislation under Directive 2001/83/EC (see Ref 4, above). The Government's policy on the implementation of European legislation is that this is not covered by OIOO, and instead effort should be made at negotiation and formulation stage to ensure that European legislation imposes as little burden and as much benefit to UK businesses ads possible. Unfortunately, as 2001/83 EC was negotiated well before the introduction of this policy, and its subsequent transposition missed the areas of incompatibility with the Medicines Act 1968, we now need to implement European legislation that may increase the burden upon industry. We have thus explored five options that could allow us to do this, and we propose to take forward the one that imposes the least regulatory burden upon industry.

Sunset Clause

Section 10(7) of the Medicines Act – that which is in conflict with the European Directive – will be repealed via a domestic legislative instrument. It is not appropriate to set a sunset clause upon a repeal achieving compliance with European law, although a review of the repeal of the exemption and its effects will be undertaken after 5 years, as discussed in Annex 1.

Policy objectives and their intended effects

The policy objectives are to ensure that the UK becomes compliant with EU law whilst at the time limiting the cost to the pharmaceutical and healthcare sector (particularly the NHS), and ensuring a continued supply of medicines to the public. Whilst we expect that as a result of these changes, some entities will need to or choose to become Wholesale Dealers, we would seek to limit the impact and cost of the changes upon others wherever possible.

The existing Section 10(7) exemption has been in place for a long time; transition from it will be difficult and may throw up unforeseen challenges. The MHRA has sought to mitigate this risk by spending 9 months considering the responses to consultation MLX 365 (Ref 1 and 2 above) to try to find the most equitable solutions for as many of the businesses involved as possible, as well as collecting information from the industry to outline the true impact of the proposals on current trading practices.

Policy options considered

Although this is a final stage impact assessment, we have chosen to lay out the costs of all of the policy options considered during the development process. The reasons for this are twofold – firstly that the costs of the options are the reasons that further options have been explored, and secondly to give a true understanding to readers of the impact that these proposals could have on the UK market if not properly formulated to suit the intricacies of NHS and industry relationships.

The options considered below were selected on the basis of best fit and adaptability to the varied circumstances of pharmacies trading in medicines at present. The overriding concern was to make sure that the proposals put forward achieved compliance with European law to reduce the risk of infraction from the EU. The second concern was to make sure that NHS supply to the general public was not compromised through these changes. The third concern was to make sure that the proposals were the most cost effective for all those involved in the trading of medicines whilst still meeting the first two criteria.

Preferred option: Option 1: The ‘healthcare suppliers’ model

Under this model we would repeal Section 10(7) of the Medicines Act, and thus remove UK legislation that is in conflict with EU provisions. This would also have the effect of removing the schedule under which a large range of individual healthcare providers and organisations (such as oilrigs, hospices etc.) that need to hold stocks of medicines from which to supply individual patients’ needs are currently supplied.

We would require community and hospital pharmacies that wanted to engage in commercial trade in medicines to hold a Wholesale Dealer’s licence to comply with all the regulatory obligations associated with this, including the requirement to be or to have available a Responsible Person and for inspection of their commercial trading outlet by the MHRA.

We would exempt pharmacies that sell only to individuals and organisations that hold stocks for onward supply to patients from the requirement to hold a Wholesale Dealer’s licence. We would also not require the recipients of such stocks of medicines to apply for Wholesale Dealers’ licences. We would provide advice on how to ensure stocks of medicines held in this way meet appropriate standards for their storage. We could also, to provide additional reassurance about compliance with appropriate standards and to facilitate returns of unused stock (for example from outstationed wards to hospital pharmacy), require an agreement on appropriate standards for storage to be drawn up between supplier and recipient. This regime would also permit pharmacies to supply small amounts of medicines on an occasional, not for profit basis to meet individual patients’ needs.

The MHRA would take action if evidence came to light that in fact such a pharmacy was “trading on” medicines as opposed to supplying them for stock for later supply to patients.

Rejected options

Option 2: Do Nothing

This is the baseline option. The current situation of the UK has been described in detail above, but in short there is currently an exemption under UK law that allows for pharmacies to trade without a

Wholesale Dealer's Licence. To do nothing would allow the current informal arrangement of 5% trading between pharmacies and other legal entities without any further requirements. This will allow the established practice of pharmacies supplying (relatively) small quantities of stock to other pharmacies and end users (such as optometrists, midwives etc.) without compliance with any Wholesale Dealing Licence requirements. Pharmacies are also able to return and be refunded for unused stock by their supplier without the need for a licence, and also have the ability to supply medicines nearing the end of their shelf life to pharmacies where they can be allocated to patients, thus reducing wastage.

This option would perpetuate our continuing non-compliance with EU legislation, which could be brought to the attention of the Commission at any point, leading to infraction proceedings against the UK and a required change to UK law and/or unlimited fine. Whilst it is unknown whether the Commission has noted our proposals to change the procedures around pharmacy trading, the Commission has shown interest in UK pharmaceutical developments in the past.

Option 3(a): Enforce the requirement that any pharmacy dealing in medicines must hold a Wholesale Dealer's licence

This option considers a simple revocation of the current Section 10(7) exemption under the Medicines Act 1968 with no further action. All pharmacists would immediately be required to comply with EU requirements that all trading without a Wholesale Dealer's Licence be in the interests of public health, occasional, not for profit and in small quantities. Effectively, this would require any supplying (hospital or community) pharmacy to hold a Wholesale Dealer's Licence and, if we require a regime that will allow unused medicines supplied under this regime to be returned to the pharmacy, so would the recipient. The recipient could be the out-stationed ward in a hospital Trust – but it could also be, for example, a dispensing GP, an optometrist or other similar independent healthcare providers or a hospice. This option would significantly increase the numbers of Wholesale Dealer Licence holders, requiring them to comply with full Good Distribution Practice standards, have at their disposal (or be qualified themselves as) a "Responsible Person" to ensure standards are maintained, and pay the necessary fee to the MHRA. Under this regime they would also be subject to routine inspection to ensure standards are maintained.

Some manufacturers have chosen not to supply their high value, low volume products (such as Glivec: http://tiny.cc/f2lva) to wholesalers. Instead, pharmacies must contact the manufacturer directly and have the order dispatched by courier. This has increased procurement costs as pharmacies often do not have the electronic ordering systems required to order directly from the manufacturer. Medicines also take longer to reach patients – dispatch in these cases can take between 24-48 hours. The options proposed will likely not impact on this practice, although it is worth noting that option 3(a) will therefore not solve all wholesaling issues. All pharmacy and end-user supply will be impacted when the 10(7) exemption is removed – pharmacies and end users will no longer have the option of approaching other pharmacies to obtain medicines – they may instead need to contact the manufacturer directly.

Whilst this is, of course, the safest option and would ensure that we are fully compliant with the EU legislation, it is not a solution that is proportionate to the risks from counterfeit medicines entering this part of the supply chain, nor does it meet the "reducing regulation" test. It would significantly increase the costs and administrative burden on a wide range of healthcare providers and private pharmacies as well as on the MHRA.

Option 3(b): A 'hub and spoke' model

This option arose as a consideration of the German model used to deal with a similar issue. It appeared that Germany had solved problems with trading without a Wholesale Dealer's Licence by creating a single legal entity comprising a central pharmacy with "satellite" pharmacies across several hospital entities. In this model, neither the central pharmacy nor the "satellites" would require Wholesale Dealer's licences as they would be deemed to be a part of the same legal entity. Under the German pharmacies' supply contract, an individual hospital pharmacy, named "the central pharmacy", contracts for a period of five years with a group of named hospitals to supply the latter with "a sufficient stock" of medicines and also to take over the supply of medicines to patients. The hospitals agree to obtain medicines exclusively from the central pharmacy. The central pharmacy agrees to handle the medicines in accordance with statutory requirements and to supply appropriate staff. The contract lays down arrangements for the ordering and delivery of medicines, for emergency supplies, for storage, for inventories and for the destruction of expired or otherwise unusable medicines, for the transfer of medicines between different units operated by the receiving hospitals and for the crediting of unused medicines in good condition with at least 6 months validity. The central pharmacy also agrees to maintain drug information documentation and records, provide advice, provide training to carers and other non-professional staff, undertake data

collection and analysis, provide recommendations for the planning, organising and monitoring of drug traffic, changes and additions to the drug list and for the storage of medicines in the wards.

However, whilst this option could be made available for use it is not an option that would solve the majority of the NHS' problems as in general the recipients of medicines in out-stationed wards in the UK are not pharmacies, and thus cannot be considered as part of a single 'pharmacy' entity. Neither would this provide a solution for healthcare providers in the community as the recipients of supplies of medicines do not tend to have pharmacies.

Nevertheless, this option is judged to be legally sound - although in drawing up guidance the UK Government would need to have regard to EU competition law and procurement rules. Some NHS hospital pharmacies may be attracted to this option where supplier and recipients of supplies of medicines are pharmacies and this would avoid the need for either operator to hold a Wholesale Dealer's Licence. The framework underpinning this arrangement could be set out in guidance issued by MHRA and checked on inspection.

Option 3(c): 'Contracting out' pharmacy supplies – the 'agency' model

Under this model we remove Section 10(7) and the supplying pharmacy (hospital or community) would need to hold a Wholesale Dealer's licence in order to supply the recipient with stocks of medicines. The supplier will act as the recipient's agent. However, because the supplies would remain the property of the supplier, but held under a contract arrangement by the recipient (e.g. an out-stationed ward, a healthcare professional in the community, a hospice), the recipient would not need a Wholesale Dealer's licence. The contract between supplier and recipient would cover arrangements for storage etc and include provisions for return of the supplier's unused stock to his pharmacy. Payment to the agent would be retrospective (eg monthly) based on the stock used, and the supplier could charge an administrative fee for the service.

Agency arrangements are already used in the context of pharmaceutical trading, although primarily between manufacturers and wholesalers at present, allowing the manufacturer to effectively continue to own the stock held by the manufacturer and therefore have more control over the terms of supply to other entities, including discounts offered to pharmacies.

Lawyers are confident that such a regime is reasonably safe from legal challenge, although they point out that – as with any contracting arrangement – there is a risk of problems arising from failure to pay for medicines used. We will also need to have regard to EU competition law and procurement rules. The framework for contracts to underpin this arrangement could be set out in guidance issued by MHRA and checked on inspection.

COSTS AND BENEFITS

Summary of Findings

Our estimated compliance costs of scenarios considered in this IA are summarised in the table below

	Present value of costs (£million)	Annualised costs (£million)
Option 1 (preferred)		
Lower bound	9	1
Upper bound	47	5
Option 3a		
Lower bound	851	99
Upper bound	1,358	158
Option 3b		
Lower bound	848	99
Upper bound	1,352	157
Option 3c		
Lower bound	165	19
Upper bound	769	89

We have noted below that public and private sector organisations would be free to innovate in order to minimise their compliance costs, probably using widespread contractual arrangements. Consequently, Options 3a and 3b are extremely pessimistic scenarios. Option 3c is therefore a more realistic comparator to our preferred Option 1.

Under Option 1, we estimate that small and micro businesses would bear present value costs of between £3.651 million and £18.254 million (annualised at between £0.424 million and £2.120 million).

We can not estimate the benefits of this option because we do not know the probability that the EU will notice our non-compliance, and the added probability that the EU will not accept our “least cost” approach to compliance described by Option 1.

Analytical Assumptions

We have adopted the standard 10 year appraisal period and the standard Treasury social discount rate of 3.5%. Non-salary staff costs are assumed to add 30% to salary costs, and we have assumed a 215 day working year, and 7.5 hour working day.

Preferred Option: Option 1: The ‘healthcare suppliers’ model: Impacts, Costs and Benefits

Costs

This option has the advantage of being applied to the current market without the need for those players in the NHS or elsewhere to take steps to integrate themselves into a new regulatory or contractual system. There are no costs imposed upon the NHS or its contractors because these entities do not trade for profit. All healthcare providers can continue to gain their supplies from the usual routes as long as the healthcare provision is direct to patients.

Commercially, there may be larger pharmacies that make the decision that they wish to continue trading medicines for profit. This will be a commercial decision, based on the company’s projected turnover from the trade in medicines, and thus no party will be forced to obtain a wholesale dealers’ licence unless it is financially viable. We assume a range of between 1% and 5% of community pharmacies (There are 10,691 community pharmacies - NHS Business Services Authority, March 2010, http://tiny.cc/f75vt) in the UK that wish to get a wholesale dealers’ licence in future. We estimate that the cost of applying for a wholesale licence is £2,478, the annual cost of maintaining a licence is £5,822, and the three yearly costs of inspection are £1,882 (Table 1 in Annex 3 gives our assumptions).

Other commercial entities (we estimate 15,286 in total – see table 3 in Annex 3) that are also affected by the repeal who need to change to get their supplies from a wholesale dealer in future, and between 1% and 5% may need to switch suppliers. The incremental costs of dealing with wholesalers as opposed to pharmacies are £244 as a one-off cost and an annual cost of £2,347 (Table 2 of Annex 3 sets out our assumptions).

If 1-5% of the current community pharmacies decides to apply for wholesale dealers licences, there will be an impact on the MHRA, as an extra 106 to 535 new licence holders require more work for the wholesale licensing and inspectorate divisions. This will, however, be met by current fees charged for licensing.

We estimate that the total ten year present value costs are between £9.443 million and £47.215 million (annualised at between £1.097 million and £5.485 million).

The private sector would bear all of these costs. We believe that 3,909 of the community pharmacies are either small or micro businesses, and that 2,058 of the remaining private sector entities are small and micro businesses (see Annex 3 for our assumptions). We estimate that small and micro businesses would bear ten year present value costs of between £3.651 million and £18.254 million (annualised at between £0.424 million and £2.120 million)

Benefits

We can not estimate the benefits of this option because we do not know the probability that the EU will notice our non-compliance, and the added probability that the EU will not accept our "least cost" approach to compliance described by Option 1.

Rejected options

Option 2: Impacts, Costs and Benefits of a 'Do Nothing' Option

The impact on the targeted groups – pharmacies and their dependents - will be nothing, and will continue to be so unless we are targeted for infraction proceedings by the European Union. Infraction proceedings have recently been revised under the Lisbon Treaty (now the Treaty on the Functioning of the European Union) to allow for faster infraction proceedings and fines for member states not achieving compliance. In practice, according to Treasury Solicitors, the main cost of infraction proceedings tends to stem from the costs of legal counsel, and in a particularly difficult contest in 2007, amounted to around £45,000. More typical contested infraction trials usually cost the UK £15,000 per trial. Non-contested infraction proceedings (where the UK admits to its mistakes and agrees timescales by which they can be rectified) are drafted in-house by Treasury Solicitors and cost the UK a negligible amount.

It is worth noting that the reputational damage to the UK arising from infraction proceedings could be more costly than the legal costs. The UK is currently considered by the EU (particularly in the field of medicines regulation) to be knowledgeable, cooperative and a leader among the member states for innovative medicinal regulation. The damage from infraction proceedings could see us losing this position and a loss of any weight given to our opinions and suggestions when negotiating new EU medicines legislation.

The Commission, under TFEU Article 260(3), has the option to fine any Member State under infraction an amount that it deems fit for non-compliance. This fine is unlimited and can be applied retrospectively for every day of non-compliance that the member state has avoided proper implementation of the EU proposals. The minimum lump sum of for a fine that can be imposed upon the UK is €9.6m (£8.2m), with a variable daily charge (dependent on seriousness of the infringement) for every further day of non-compliance with the court's judgement (in the two most recent cases, this has been a daily charge of €178,560/£152,271 (case IT 2006/2114) and €36,926/£31,488 (Case IE 2002/5076)). Given that the parliamentary process in the UK takes a minimum of 21 days, this would cost a total of between £8,861,248 and £11,397,691 at a minimum. This is very unlikely to happen to us in this case – the UK has never been fined in infraction proceedings during its membership of the EU – but we would be wise to accept that it is a vague possibility, and could be even more damaging to our stance in Europe.

Option 3(a): Enforce the requirement that any pharmacy dealing in medicines must hold a Wholesale Dealer's licence: Impacts, Costs and Benefits

Costs

The impacts of the repeal of the Section 10(7) exemption would be wide ranging and very costly without any mitigating strategies available. It would require all those pharmacies wishing to trade in medicines

beyond the limited circumstances of in the interest of public health, in small quantities, occasionally and not for profit to apply for a Wholesale Dealer's Licence.

There are 10,691 community pharmacies (NHS Business Services Authority, March 2010, http://tiny.cc/f75vt) in the UK, and an estimated number of 130 acute trusts in the NHS (England only) not already in possession of a wholesale dealers' licence. If these entities wished to continue their current trading patterns, they would need to apply for and maintain wholesale dealer's licences (costs of doing this are summarised in Table 1 of Annex 3).

It is also possible that those pharmacies that do decide to become wholesale dealers will not wish to incur extra cost by licensing multiple premises, all of which would need to be inspected by the MHRA and therefore incur further inspection costs of £1,882 per day of inspection on a three-year rolling timetable. Where a pharmacy business has a number of premises, it is likely that only the largest will be licensed, meaning that community pharmacies and others may have to travel farther to obtain their stock. This outcome would also see a negative impact on community pharmacies in rural areas, which are much less likely to have a local wholesale dealer within easy reach. For illustrative purposes, we have assumed that between 10% and 90% of pharmacies (both commercial and NHS) choose to become wholesalers. We estimate that the cost of applying for a wholesale licence is £2,478, the annual cost of maintaining a licence is £5,822, and the three yearly costs of inspection are £1,882 (Table 1 in Annex 3 gives our assumptions).

NHS, other public sector and commercial organisations (for example dentists, fire services and podiatrists) that hold prescription only medicines for onward supply to patients will no longer be able to get their supplies from pharmacists. Instead they will have to deal with wholesalers. The incremental costs of dealing with wholesalers as opposed to pharmacies are £244 as a one-off cost and an annual cost of £2,347 (Table 2 of Annex 3 sets out our assumptions). We estimate that there would be 13,449 NHS entities and 15,286 non-NHS entities affected (see table 3 in Annex 3 for a breakdown)

Given that the MHRA currently considers all applications for Wholesale Dealer Licences in the UK, and also aims to inspect each licence holder on a 5-year rolling basis, if every pharmacy in the UK were to become a wholesale dealer this would require a significant allocation of resource. Indeed there are currently 1744 wholesale dealers in the UK – a further influx of 1,100 (in the 10% scenario) would create a very serious backlog, although ultimately not more cost for the UK Government – the MHRA is a trading fund, and as such, recoups its costs (for example inspections, assessment and administrative work) from the fees it charges to industry for this work.

We estimate that the total ten year present value costs are between £851 million and £1,358 million (annualised at between £99 million and £158 million).

Of this amount, the private sector would bear between £572 million and £1,076 million (annualised a between £67 million and £125 million).

We should emphasise that in practise, the public and private sectors would innovate (probably through contractual solutions – see options 3b and 3c) to reduce their compliance costs. The headline cost figures given above therefore provide a very high upper-bound to potential costs.

Benefits

The benefits arising from Option 3(a) would be that of the greatest clarity within the UK – only those with a Wholesale Dealer's Licence authorising them to trade in medicines in the UK would be permitted to undertake this activity. It would provide legal clarity on these points and defend the UK from the possibility of reputational damage and the possibility of an unlimited fine – both issues that might arise from infraction proceedings.

Option 3(b): A 'hub and spoke' model: Impacts, Costs and Benefits

Costs

This option considers the possibility of a single central pharmacy becoming the 'hub', with other pharmacies that have agreed to become 'satellites' and thus part of the same legal entity. This option would mean that the satellites would need to relinquish a proportion of their individual decision making responsibilities in order to be considered a single legal entity.

This solution is unlikely to meet the needs of community pharmacies, and is not tailored to be appropriate for use between a pharmacy and any other entity. It is most likely that NHS hospital trusts would act as hubs in this instance, of which there are 388 in the UK at present. We have assumed that one hub serves nine spokes (costs are insensitive to this ratio and so we have not presented a range). Compared

with Option 3a, the NHS cost savings of Option 3b arise because of not having to maintain wholesale licences and to pay the annual incremental costs of dealing with wholesalers.

The main costs arise from the legal costs of setting up a recognised agreement between the entities which allows the hub to absorb the satellites under a single legal umbrella. Many of the initial costs could be avoided by the MHRA setting up a standard template contract and guidance for these agreements, which we would plan to have in place before any repeal of the Section 10(7) exemption, which have been taken into account when costing the proposals (Annex 3).

Our estimated cost of drawing up and signing a contract would be £2,183 (assumptions summarised in Annex 3).

All community pharmacies and end users would also be excluded from this option, leaving them with the costs that arise from Option 3(a) above, namely those of applying for or contracting with a company that holds a wholesale dealer's licence as well as an increased level of inspections and the possibility of greater wastage costs. For illustrative purposes (as with Option 3a) we have assumed that between 10% and 90% of community pharmacies become wholesalers. We estimate that the cost of applying for a wholesale licence is £2,478, the annual cost of maintaining a licence is £5,822, and the three yearly costs of inspection are £1,882 (Table 1 in Annex 3 gives our assumptions) (costs summarised in Table 1 of Annex 3). We also assume that all other entities bear the incremental costs of dealing with wholesalers. The incremental costs of dealing with wholesalers as opposed to pharmacies are £244 as a one-off cost and an annual cost of £2,347 (Table 2 of Annex 3 sets out our assumptions).

We estimate that the total ten year present value costs are between £848 million and £1,352 million (annualised at between £99 million and £157 million).

Of this amount, the private sector would bear between £572 million and £1,076 million (annualised a between £67 million and £125 million).

We should emphasise that this option only benefits the NHS because we have assumed that the private sector would not adopt this approach. However, the private sector would certainly innovate (probably through some other contractual means – see option 3c) to reduce its costs, and hence our headline figure for private sector costs represents a very high upper bound for potential compliance costs.

Benefits

The benefits arising from Option 3(b) would be that many of the key organisations in the NHS could continue to trade simply and without the need (and additional cost) of wholesale dealers' licences. This would avoid imposing extra burden upon the NHS at a time when the Government is looking to utilise its resources in healthcare in the most efficient manner possible.

Option 3(c): An 'agency' model: Impacts, Costs and Benefits

Costs

The agency model considers the possibility that, under contract, any entity can act under agency to procure from and return medicines to the principal. This option should be appropriate for a large number of the players that act within the framework of pharmaceutical supply, and should only incur the costs of a standard contract. We estimate that the cost of drawing up and signing a contract would be as considered by Option 3(b) above to be £2,183 per contract (assumptions summarised in Annex 3). For illustrative purposes, we have assumed that between 10% and 90% of public and private sector entities will enter into contractual relationships

Those who act as principals also have the option under this arrangement of charging a handling fee for their services. This may lead to a modest rise in the amount charged for pharmaceuticals, although we expect that it is currently standard practice for the vast majority of those currently acting under the section 10(7) exemption to charge a handling fee for their services. We therefore assume no incremental cost associated with handling fees.

The agency model necessitates companies to relinquish some of their decision-making powers, and some entities may be unwilling or unable to enter into contracts that allow another legal entity to have a degree of control over their business practices. Whilst the model contract envisaged would aim to keep the transfers of power to a minimum in order to allow for seamless trading between entities.

It should be considered that there may be some wholesalers who would be resistant to entering into an agency contract with those they currently supply, as this could cut their profits. Likewise, the agency model could become so widespread that it is the preferred trading arrangement, meaning that wholesale

dealers are no longer approached for trade by smaller pharmacies and end users. However, we assume that any loss of profit experienced by wholesalers is merely transferred to pharmacies as increased profit.

There will need to be some MHRA consideration of EU competition law and procurement rules to make sure that the Agency model is sound, although we expect that these legal issues should be resolved without greater resource required than the MHRA's current complement. It should be noted, however, that if an area of serious mismatch arises, this option may become non-viable.

To make the assumptions consistent with those adopted for option 1, we have assumed that between 1% and 5% of pharmacies would wish to apply for and maintain wholesale licences because they find it profitable to do so. We estimate that the cost of applying for a wholesale licence is £2,478, the annual cost of maintaining a licence is £5,822, and the three yearly costs of inspection are £1,882 (Table 1 in Annex 3 gives our assumptions).

We estimate that the total ten year present value costs are between £467 million and £769 million (annualised at between £19 million and £89 million). Note that the public and private sectors would be free to choose the most effective method of minimising their compliance costs and hence, we would expect actual compliance costs to be towards the lower end of our estimated range

Benefits

The benefits arising from Option 3(c) are that it is an option that can be used by the majority of healthcare organisations with minimal cost, and will not require the onerous and resource-intensive requirement that all trading be under a wholesale dealer's licence. There should be very little disruption to the 'business as usual' scenario, which is the main objective that the MHRA and the Department for Health are attempting to avoid. It will also reduce the possibility of wastage from unwanted or unused stock, and may improve current levels of wastage, as the principal has a greater margin of control over supply as at present.

Risks and Assumptions

We have come up against some difficulty in obtaining the figures for 'end users', which have in some cases been derived from unverifiable internet sources where estimates have been given. It should also be noted that we have used an assumption based on Northern Irish figures obtained to ascertain how the number of a certain type of professional relates to the number of individuals or companies that offer these services. In Northern Ireland (2008 data from NINIS), 864 dentists operate out of 349 surgeries, giving an approximate matrix of 2.48 dentists per surgery – a matrix that we have also applied to chiropodists/podiatrists and paramedics.

A number of the figures quoted, particularly those on the number of healthcare providers, are sourced from the NHS, which covers only England. Some of the information (such as that on wholesale dealers and responsible persons) comes from all of the UK. The overall costs that arise from this impact assessment will likely be higher when applied to all of the UK.

There are a number of risks that arise out of these options, many of which can be avoided, but some of which could create some tricky problems later on. One of these is the current trading practices of manufacturers (particularly those trading in branded medicines), some of whom who have recently begun limiting the number of wholesalers who can supply their products to two or three national suppliers. In general these are the full-line wholesalers – a limited number of wholesalers in the UK that stock almost all of the medicines required by the NHS in the UK, at least 20,000 product lines. If this trend continues, it would certainly have an impact on options 3(a)-(c) in terms of whom the wholesaler pharmacy, hub or principals able to trade with in future, as well as the number of specific wholesalers that pharmacies would need to have contracts with in order to be supplied with specific pharmaceutical products. Full-line wholesalers are also those who are most likely to be unwilling to trade in low volumes with smaller pharmacy and other businesses. A summary of key manufacturer's supply arrangements can be found on the Pharmaceutical Services Negotiating Committee's website at http://www.psnc.org.uk/distribution.

We have also tended to assume that the market for supplying medicines will adjust to take account of any changes that the MHRA makes, for instance where wastage costs may go up due to an inability to sell stock back to other companies, this will eventually lead to pharmacies and other end users keeping a closer eye on their stock levels in order to reduce this wastage. Also where the market currently charges surcharges to low-use trade, a greater number of wholesalers specializing in pharmacy trade will eventually emerge into the UK market to reduce these costs.

Public Sector burdens – data, reporting and admin

If we were to move forward with Options 3(a), (b) or (c), these would likely have high impact on the NHS, who would need to apply for a large number of wholesale dealers' licences, as well as put in place the necessary arrangements for making sure that the requirements of holding such a licence, such as having a qualified responsible person, continued to be met.

The MHRA's inspectorate team would need to take on more licensing of wholesale dealers and inspections of premises for any of the above options, although it should be noted that option 3(a) would be particularly onerous, requiring many new licences in the UK and raising the MHRA's workload by at least 100%. Our preferred option may see a rise in inspection and licensing workload of up to 33%, although this is likely to be a much lower figure.

Wider impacts

We have conducted a number of other assessments to ascertain the impact of this policy in certain areas:

Justice Impact Assessment and New Offences Clearance

We have considered the justice impact test and expect there to be no impact on the justice system, as we are not creating any new offences – merely aligning the UK with European law. We would also ensure that there is a well-advertised transition period before the repeal of the current 10(7) exemption. Those pharmacies found to be trading without a wholesale dealer's licence after the repeal will be targeted for compliance by the MHRA's enforcement team, and we do not expect there to be any rise in the number of cases brought before the courts.

Equalities Impact Assessment

We have considered the screening questions provided in the Equalities Impact assessment, and have concluded that there will be no significant positive or negative effects of the policy that affect the populations listed.

Health Impact Assessment

The health impact assessment identified three areas that might be affected by the proposals, these being a direct impact on health, which may arise from any temporary pharmaceutical supply shortages to pharmacies, particularly rural communities, a minor effect on the environment due to the possibility of greater numbers of pharmaceutical deliveries, and a possible shift in demand from one service provider to another if certain medicines cannot be sourced by those currently providing healthcare services. None of these impacts were deemed to be important (using the criteria of the assessment), particularly if our preferred option is taken forward. It was noted that any problems affecting rural communities could raise media interest, and that mitigation measures should be taken to avoid shortages wherever possible.

Small firms' impact

The proposals are intended to affect all companies equally, and as such will cost the same amount to small firms as large. The use of option 1 has sought to minimise the impact upon small businesses such as optometrists, podiatrists etc. It is accepted that there may be some minimal impact upon these businesses where they may need to switch suppliers, but we cannot see any way of exempting them from the repeal of section 10(7) without conflict with European law - other than applying option 1 above. We have consulted informally with the trade associations that represent these businesses, and many of the costs included in their responses have been incorporated into the calculations above.

As this is a repeal that brings us into compliance with EU law, it is considered that it is exempt from the microbusiness moratorium.

Competition impact

There is a possibility that the repeal of the Section 10(7) exemption will move those who currently get their supplies from a pharmacy to wholesalers, particularly those full-line wholesalers in the UK who can supply the 20,000 product lines needed by the NHS. The number of full-line wholesalers in the UK is limited to less than five, and the changes could be considered to be decreasing competition within the pharmaceutical trading sector. However, it is likely that these full-line wholesalers will need to adapt their trading practices to accommodate small businesses and pharmacies, and in time other smaller businesses will emerge to meet the needs of pharmacies and end users or act as intermediaries between wholesaler and pharmacist.

Charitable sector costs

There should be no impact on the charitable sector - charities that exist to provide healthcare to the public, such as hospices, will be exempted under the preferred Option 1.

Wider Environmental Impact and Greenhouse Gases Tests

There are no potentially significant impacts on air quality, water quality and quantity, flood risk, biodiversity, landscape or noise arising from these proposals. This policy will have no impact on greenhouse gas emissions.

Human Rights

The preferred option will have no impact on any of the 16 basic rights of the Human Rights Act.

Rural Proofing

The preferred option will have no significant impact on rural communities.

Sustainable impact test

The policies will have no impact upon sustainability and will not adversely affect future generations

Annexes

Annex 1 should be used to set out the Post Implementation Review Plan as detailed below. Further annexes may be added where the Specific Impact Tests yield information relevant to an overall understanding of policy options.

Annex 1: Post Implementation Review (PIR) Plan

A PIR should be undertaken, usually three to five years after implementation of the policy, but exceptionally a longer period may be more appropriate. If the policy is subject to a sunset clause, the review should be carried out sufficiently early that any renewal or amendment to legislation can be enacted before the expiry date. A PIR should examine the extent to which the implemented regulations have achieved their objectives, assess their costs and benefits and identify whether they are having any unintended consequences. Please set out the PIR Plan as detailed below. If there is no plan to do a PIR please provide reasons below.

Basis of the review: [The basis of the review could be statutory (forming part of the legislation), i.e. a sunset clause or a duty to review , or there could be a political commitment to review (PIR)]; Under Government guidance, the repeal of the exemption would need to be reviewed after five years.
Review objective: [Is it intended as a proportionate check that regulation is operating as expected to tackle the problem of concern?; or as a wider exploration of the policy approach taken?; or as a link from policy objective to outcome?] We would be looking to make sure that the removal of the exemption has not interrupted essential medicines supplies, particularly within the NHS.
Review approach and rationale: [e.g. describe here the review approach (in-depth evaluation, scope review of monitoring data, scan of stakeholder views, etc.) and the rationale that made choosing such an approach] The review would consist of an evaluation of wholesale dealer applications over the previous five years, as well as an assessment of supply issues over the five years since implementation. Stakeholder views would be essential to ascertain how the repeal and mitigating options had bedded down.
Baseline: [The current (baseline) position against which the change introduced by the legislation can be measured] Current numbers of wholesale dealers and trends for applications, compliance trends, supply shortages and medicines counterfieting activity (from cases brought by the MHRA, and medicines recalls within the supply chain).
Success criteria: [Criteria showing achievement of the policy objectives as set out in the final impact assessment; criteria for modifying or replacing the policy if it does not achieve its objectives] Success would be a shift away from the use of the current exemption to a UK position compatible with EU law, with little or no disruption in medicines supply, particularly within the NHS.
Monitoring information arrangements: [Provide further details of the planned/existing arrangements in place that will allow a systematic collection systematic collection of monitoring information for future policy review] The MHRA has a number of routes through which it can monitor the wholesale dealer and counterfeiting activity trends, including our own data recording from wholesale dealer applications and court cases that we bring on counterfeiting activities. We also monitor medicines supply shortages (in conjunction with the Department for Health) as a part of our routine work.
Reasons for not planning a review: [If there is no plan to do a PIR please provide reasons here] n/a

Annex 2: Equality Impact Assessment

Screening template

Title of policy: Pharmacy proposals: Repeal of section 10(7) of the Medicines Act
Short description of policy: The policy aims to align the UK with EU law to prevent pharmacists from trading in medicines for profit without holding a valid wholesale dealer's licence. The options are; • Continue to operate as a pharmacists and source all medicines from someone who holds a wholesale dealer's licence; • Apply for and meet the standards of the licence, giving the pharmacy an ability to undertake wholesale dealing activities; • Apply a 'hub and spoke' model where by pharmacies become satellites of a larger pharmacy; or • Employ the 'agency model' and where pharmacies and others become an agent of a principal pharmacy. • Allow trading between pharmacies and other entities where they are providing healthcare to patients. The last model is considered the most cost effective with the least impact on current medicines trading arrangements.

Negative impact
How could the policy have a **significant** negative impact on equality in relation to each area?
Age None
Disability None
Ethnicity None
Gender (including transgendered people) None
Religion or belief None
Sexual orientation None
Socio-economic groups None

Positive impact
How could the policy have a **significant** positive impact on equality in relation to each area?
Age None
Disability None
Ethnicity None
Gender (including transgendered people) None
Religion or belief None

Sexual orientation None
Socio-economic groups None

Positive impact
Could the policy have a **significant** positive impact on equality by reducing inequalities that already exist? Explain how will it meet our duty to:
1. Promote **equal opportunities** None
2. Get rid of **discrimination** None
3. Get rid of **harassment** None
4. Promote **good community relations** None
5. Promote **positive attitudes** towards disabled people None
6. Encourage **participation** by disabled people None
7. Consider **more favourable treatment** of disabled people None
8. Promote and protect **human rights** None

Evidence
What is the evidence for your answers to the above questions? The policy applies to the business practices of pharmacists and other end users in the medicines supply chain. Thus it does not promote or exacerbate inequalities in the community.
What does available research say? The available research considers that any changes will need to take place gradually to make sure that there is no interruption in supply to communities of much-needed medicines. Thus the MHRA has considered carefully the options proposed and believes that the preferred option is the most measured and proportionate available to bring us into compliance with EU law.
What further research or data do you need to fill any gaps in your understanding of the potential or known effects of the policy? None –although the repeal of the exemption will be reviewed in five years to monitor the effect that it has had on the current system.
Have you thought about commissioning new data or research? We do not anticipate that new data or research will be required, as we have spent nine months gathering the contents of the current impact assessment.

Screening assessment
Now that you have looked at the evidence, do you think that the policy needs a **Full EqIA**? No

Next steps
If you do **not** need to do a **Full EqIA**:
What else might you need to do to make sure the policy **promotes equality** and **gets rid of discrimination**? We do not feel that the policy requires amendment to address these issues.
How will you **monitor** the situation as the policy develops and takes effect? Through routine collection of data and a review following five years of the policy being in force.
What **further research** do you need? None

Annex 3: Parameters used in the cost calculations

The costs of applying for and maintaining a wholesale dealer's licence

Table 1: Estimated costs associated with a Wholesale Dealer's Licence

Activity	Transition cost	Annual Cost	Recurrent	Calculation notes
Administrative cost of application preparation	£733	N/A		20 hours at average national salary of £25,500 p/a* (£21 an hour), followed by 8 hour of verification/signoff at £50,000 p/a (£40 an hour)
Licence cost	£1754 application fee	N/A		
Cost of complying with regulatory requirements	N/A	£822		40 hours at average national salary of £25,500*
Cost of responsible person		£5,000		On-going training costs
Inspections	N/A		£1,882	Inspection first year and every three years subsequently
Total	£2,488	£5,822	£1,882	

* Office of National Statistics (http://www.statistics.gov.uk/cci/nugget.asp?id=285)
† Based on estimates from the Chartered Institute of Personnel and Development (2006)
‡ Based on estimates from respondents to previous MHRA consultations

Costs of dealing with wholesalers

Those pharmacies and other end users that did not become wholesale dealers would likely incur a higher level of wastage each year as unused or close to out-of date stock was not returned. Evidence from stakeholders responding to MLX 365 (RXchange reply) suggests that about 4% of stock is wasted in pharmacies at present, resulting in around £320m of costs per year. There is also evidence that wholesalers will only supply full packs of medicines to those with whom they trade – if only a part-pack is required by the pharmacy in question, this could also lead to a greater level of wastage of stock within pharmacies. It should be noted that many of these problems should either be mitigated by better stock control in future or by more flexible trading practices as trading between wholesalers and smaller businesses becomes more commonplace, but there would be an impact in the short to medium term as the market adjusts to these practices, and we have allowed for a possible 1% (or £80m) rise in wastage in our calculations.

It should also be considered that there will be costs imposed on those who choose not to become wholesale dealers, but will continue to need supplies sourced from an existing (or new) wholesale dealer. The MHRA engaged with industry bodies to source these costs. The first cost imposed on these operators is likely to be that of switching suppliers, which is calculated to cost £122.10, based on a calculation of 10 man-hours at the average UK salary of £25,500 (ONS statistic). There is also likely to be increased costs that arise from managing contracts with these suppliers (as these may need to be multiple with a number of suppliers), and the manpower required to chase and manage these supply problems, calculated to be at least another 30 man-hours per annum. Greater stock quantities may also need to be held, as sourcing from a licensed wholesaler is likely to take longer than simply sourcing from another local pharmacy – pharmacies will need the extra space (and possibly refrigerated conditions in some cases) in which to keep this stock.

Many of these operators will require small quantities of medicinal products on an infrequent basis – in many cases wholesale dealers are known to currently charge a 'low use' service charge. Currently it

would seem to be standard practice that premiums of at least 5% (and frequently higher) are charged to those businesses who do not regularly order large amounts of pharmaceuticals on a regular monthly basis. Discounts apply to those who order large quantities of stock – these are not likely to be able to be utilised by pharmacy and other end user trade. Fuel surcharges are also common practice, particularly when trading with full-line wholesalers – these are applied monthly to all accounts (in December 2010, Alliance Healthcare's fuel surcharge was £17.50 per month). Ordered in error surcharges are also applied to an account where the level of error stock is equal or greater than 2% of the number of units that month (in December 2010, Alliance Healthcare's charge was £50) - thus much more likely to apply to the smaller trades undertaken by pharmaceutical and other end users. Although the supply of lower amounts of medicine to such people is likely to become more widespread (and thus a reduction in costs would be expected in the medium to long term as the market adjusts), these charges will impact on end users such as podiatrists, optometrists etc. for at least the first one to two years.

Table 2: Summary of costs provided by industry contacts for those who require the services of a wholesale dealer following a repeal of the section 10(7) exemption

Activity	**Estimated Cost**	**Estimated frequency**	**Estimated total (annual)**
Switching wholesalers	£122	Twice (total)	£244 (first year only)
Managing supplies and deliveries	£366	Annual	£366
Wastage of pharmaceutical products	£1,671†	Annual	£1,671
Low use charge	5% of turnover	Monthly	[Not quantifiable]
Fuel surcharge	£17.50	Monthly	£210
Ordered in error surcharge	£50	Estimated twice yearly	£100
Total			**£2,591**

†This cost applies evenly across the sector, and thus a 1% rise of £80m is split evenly between end users and wholesale dealers.

There are a large number of other businesses, both NHS and private, that will be directly affected by the repeal of section 10(7). This is because, under the current legal framework, they regularly receive supplies of medicines from pharmacies, and would instead incur further costs by switching contracts to wholesalers in future. The numbers and types of these individuals are set out in table 2 below, and they will be referred to as 'end users' for the remainder of this document. In total, they number 15,286 private entities/sites and 13,449 NHS entities/sites that would likely be affected.

Cost of drawing up and signing contract

There are legal costs associated with the preparation of contracts, and we have estimated that even with model contracts for the NHS to work from, there would be need for each entity to consider legal advice to make sure that the contracts are legally enforceable and equitable. We have canvassed costs from a number of firms that specialise in the production and processing of contracts, but it is difficult to estimate how much would be charged, as a solicitor's work is charged on an hourly basis. At best guess, we calculate that the production of a contract will cost between £1,500 and £2,500 to prepare. The agent would also need to put aside some time to consider and sign these contracts – we expect this to take at least five hours of time at the standard UK wage of £25,500 p/a (£21 an hour including non-salary costs), plus time to be signed by a senior member of the organisation (at least two hours) at an estimated £50,000 p/a (£40 an hour including non-salary costs), with a total of £2,183 per contract.

Non-Pharmacy entities affected by the changes

Table 3: Estimates of UK healthcare providers and other UK businesses users') indirectly affected by the repeal of the Section 10(7) exemption

Individual/business	Private practitioners	NHS entities (England only)	Totals	Calculation notes
NHS Primary Care Trusts	n/a	145	145	England only
NHS non-acute trusts	n/a	55	55	England only
Podiatrists/chiropodists	1,793 sites†	3,330 sites†	5,123 sites†	According to a 2010 HPC headcount, there are 12,704, of which 50% work solely for the NHS. With others their time is split – it is assumed a 65/35 split.
Dispensing opticians	15 sites	85 sites	100 sites	There are very few dispensing opticians - less than 100. Most use NHS pharmacies for supplies.
Midwives	250	2,000	Approx 2,250	The NMC estimates that around 250 midwives operate independently. We assume a further 2,000 work for the NHS.
Dentist Practices	4,500 sites	4,500 sites	9,000 sites	Around 1,000 Dentists are exclusively private, and the same number work exclusively for the NHS. Others split their time evenly, so the remaining 7,000 are split between the two columns.
Paramedics	3,334 sites†	3,334 sites	6,668 sites†	According to a 2010 HPC headcount, 16,562 paramedics operate in the UK. We have assumed a 50/50 split between the NHS and private ambulances.
Fire Services	1,439 stations 3,261 vehicles	n/a	4,700	Figures for England only (from DCLG) – not clear whether both fire stations and vehicles carry prescription medicines, but numbers of both included for completeness.
Lifeboat services	150 sites	n/a	150 sites	RNLI figures for lifeguard stations in the UK - not clear whether lifeguards carry prescription medicines, but numbers included for completeness.
Police forces	400	n/a	400	Numbers of police stations in the UK as a rough estimate - not clear whether police stations carry prescription medicines, but numbers included for completeness.
Armed Forces	n/a	n/a	n/a	The armed forces source directly from AAH.

Prison services	144 prisons	n/a	144	Not clear whether prisons carry prescription medicines, although this is highly likely.
Totals	**15,286**	**13,449**	**28,735**	

† Northern Ireland matrix of 2.48 has been applied to estimate the number of sites in these circumstances – please see risks and assumptions section below for further information

Small firms

Data received from the National Pharmacy Association indicates that 3,909 community pharmacies are either small or micro businesses. For other private sector entities, we have assumed that all podiatrists/chiropodists, dispensing opticians, private sector midwives and private sector dentists are small and micro businesses. This yields a figure of 6,558.