EXPLANATORY MEMORANDUM TO

THE MEDICINES FOR HUMAN USE (MARKETING AUTHORISATIONS ETC.) AMENDMENT REGULATIONS 2009

2009 No. 2820

1. This explanatory memorandum has been prepared by the Medicines and Healthcare products Regulatory Agency (MHRA), an executive agency of the Department of Health, and is laid before Parliament by Command of Her Majesty.

This memorandum contains information for the Joint Committee on Statutory Instruments.

2. Purpose of the instrument

2.1 This instrument makes amendment to current legislation to make clear that the licensing authority can reject a UK Marketing Authorisation without the need to consult the Commission on Human Medicines (CHM) if there is no response from the applicant to a request for further information to enable the application to be determined, after 6 months following the initial assessment, or after 3 months following assessment of supplementary information.

3. Matters of special interest to the Joint Committee on Statutory Instruments

3.1 None.

4. Legislative Context

4.1 This instrument amends the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 (SI 1994/3144) in order to make provision for the licensing authority (LA) to reject a Marketing Authorisation without the need to consult with the CHM in these circumstances.

5. Territorial Extent and Application

5.1 This instrument applies to all of the United Kingdom.

6. European Convention on Human Rights

6.1 As the instrument is subject to negative resolution procedure and does not amend primary legislation, no statement is required.

7. Policy background

- What is being done and why

7.1 Before a medicine can be sold in the UK, the product must have a licence called a marketing authorisation (MA). Applications for MAs come mainly from the pharmaceutical industry but anyone with the necessary supporting data may apply. Applications are made to the MHRA who act on behalf of the licensing authority (the Secretary of State and the Minister of Health and Social Services for Northern Ireland) (LA).

7.2 The MHRA has a large number of applications for MAs which cannot be progressed or granted because companies do not respond to repeated requests for further information whilst the application is still in the assessment process.

7.3 Current legislation states that the licensing authority can reject an MA application on grounds of quality, safety or efficacy only after the Commission on Human Medicines (CHM) has been consulted on the matter. Since the information is requested in order to assess quality, safety or efficacy, rejection of an application on the grounds of inadequacy of information thus requires CHM consultation.

7.4 This situation is not satisfactory as:

- These applications continue to demand unnecessary resources each time they are picked up for evaluation and may cause delays to other applications in house.
- Referral to the CHM is time consuming and expensive as the experts would need to assess each case and then give their decision to reject on incomplete information supplied.
- There are no time limits set for UK applications to be assessed at present; therefore if a long gap in time occurs before a response is received, the assessment may need to start again from scratch in order for a new assessor to understand the issue and evaluate new data or guidance.
- Companies sometimes submit a premature application but continue to develop the product and testing, using the MHRA's requests for further data and information as a development tool.

7.5 The minor amendment to current legislation effected by the instrument will make clear that the LA can reject an application without the need to consult the CHM if there is no response from the applicant after 6 months following a request for it (after the initial assessment), or after 3 months following a request for it (after assessment of supplementary information). This would help to deter companies submitting their applications before the product was ready for UK use. It would also be consistent with time limits set for other applications under the European procedures (where 3 months extendable to a six months 'clock off' period is permitted). The instrument provides for these periods to be extendable in exceptional circumstances at the request of the applicant.

- Consolidation

7.6 No consolidation, other than what has already been consolidated is anticipated.

8. Consultation outcome

8.1 A 12 week public consultation exercise was carried out with letters being issued to over 1400 companies, individuals, industry associations and licence and Marketing Authorisation holders who were likely to be affected by the proposals or interested in them. The consultation document was placed on the Agency's website.

8.2 A total of 5 responses to the proposals were received. All in favour of the changes. The Agency will respond individually to any queries which were raised.

9. Guidance

9.1 Guidance and information regarding the process followed for applying for a Marketing Authorisation by the pharmaceutical industry can be found on the MHRA website at www.mhra.gov.uk.

10. Impact

10.1 An Impact Assessment has been prepared and is attached to the memorandum. Copies can also be obtained from Karen Salawu, Fees Policy Unit, Room 16-159 Market Towers, 1 Nine Elms Lane London SW8 5NQ, Tel: 020 7084 2216, e-mail: karen.salawu@mhra.gsi.gov.uk.

10.2 The impact on the public sector is minimal. The changes mainly affect the private sector pharmaceutical industry.

11. Regulating small business

11.1 The legislation applies to small business. The MHRA operates a number of provisions to assist smaller companies, such as reduced fees for certain small companies, lower periodic fees for products with low turnover, and extended terms of payment of a number of capital fees. The Agency will consider further assistance and continue to targets small businesses in all its consultation processes each year.

12. Monitoring & review

12.1 The changes will be monitored, and a full review will take place on a yearly basis.

13. Contact

13.1 Tracy Murray at MHRA Tel: 020 7084 2329 or e-mail: tracy.murray@mhra.gsi.gov.uk can answer any queries regarding this instrument.

Summary: Intervention & Options

Department /Agency:	Title:	
Medicines and Healthcare products Regulatory Agency (MHRA)	**Impact Assessment - Marketing Authorisation (MA) Regulations – Latent MA applications**	
Stage: Final	**Version: 2**	**Date: 8 October 2009**
Related Publications:		

Available to view or download at:

http://www.mhra.gov.uk

Contact for enquiries: Tracy Murray **Telephone: 020 7084 2329**

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

Changes are proposed to existing legislation to reject national (UK only) Marketing Authorisation applications (MA) which have been in house with the Licensing Authority (LA) for a long time after requesting further information from a company and receiving no response. The difficulty at present is that a decision to refuse this application – even on the grounds of not supplying the relevant information - would have to be submitted to the Commission on Human Medicines (CHM), which is time consuming and an inappropriate use of expert committee resource and provides no value in terms of public health.

What are the policy objectives and the intended effects?

Make clear that the LA can refuse an application due to lack of information if no response is received six months following the initial full assessment (or 3 months following assessment of supplemental information). This will give a clear timeframe for both the Agency and industry to work to, and will be in line with current European procedures for MA applications.

The objectives are to ensure that the MHRA can recover its full costs in relation to this work and thus continue its role to protect public health in a more efficient manner.

What policy options have been considered? Please justify any preferred option.

1. Do nothing.

2. Make clear that an application can be refused due to lack of information if no response is received six months following the initial full assessment (or 3 months following assessment of supplementary information).

When will the policy be reviewed to establish the actual costs and benefits and the achievement of the desired effects?

On a yearly basis from implementation of these changes.

Ministerial Sign-off For final proposal/implementation stage Impact Assessments:

I have read the Impact Assessment and I am satisfied that, given the available evidence, it represents a reasonable view of the likely costs, benefits and impact of the leading options.

Signed by the responsible Minister:

Mike O'Brien.....Date: ***10th October 2009***

Summary: Analysis & Evidence

Policy Option: 1	Description: Do nothing

COSTS

ANNUAL COSTS	
One-off (Transition)	**Yrs**
£ 664,514	1
Average Annual Cost (excluding one-off)	
£ 196, 086	3

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

Based on the assumption that all outstanding national MAs will continue to accumulate. Working on the assumption that there are already 397 outstanding applications and 61% of these are two or more years with no correspondence- these would need to be re-assessed - at a cost of a 'simple' application of £2,744. Each year 18% more exceed 2 years and need to re-apply.

Total Cost (PV) **£ 1,213,876**

Other **key non-monetised costs** by 'main affected groups' If we continue with this option, the MHRA will be operating at below cost without the ability to rely on any other funding (there is no central Government funding for medicines work). It would restrict the Agency's ability to meet its regulatory requirements and would not be in line with efficiency processes with regards to licensing products, to the detriment of public health.

BENEFITS

ANNUAL BENEFITS	
One-off	**Yrs**
£ 664,514	1
Average Annual Benefit (excluding one-off)	
£ 196, 086	3

Description and scale of **key monetised benefits** by 'main affected groups' Whilst the MHRA would be able to meet most of its commitments with a limited budget, it would be working with fees below actual costs. This would be contrary to Treasury guidance and against the Trading Fund. The income from fees would be countered by the cost to companies and the loss of efficiency. Therefore there are no real benefits in continuing this option.

Total Benefit (PV) **£ 1,213,876**

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

Key Assumptions/Sensitivities/Risks Requirements of the Trading Fund Order to break even taking one year with another. Treasury guidance on ensuring fees match costs; Responsibility of MHRA to protect public health

Price Base Year	Time Period Years	**Net Benefit Range** (NPV) £	**NET BENEFIT** (NPV Best estimate) £ **NIL**

What is the geographic coverage of the policy/option?			UK	
On what date will the policy be implemented?			1 January 2010	
Which organisation(s) will enforce the policy?			MHRA	
What is the total annual cost of enforcement for these organisations?			£ N/A	
Does enforcement comply with Hampton principles?			Yes	
Will implementation go beyond minimum EU requirements?			No	
What is the value of the proposed offsetting measure per year?			£ N/A	
What is the value of changes in greenhouse gas emissions?			£ N/A	
Will the proposal have a significant impact on competition?			No	
Annual cost (£-£) per organisation (excluding one-off)	Micro	Small	Medium	Large
Are any of these organisations exempt?	No	No	No	No

Impact on Admin Burdens Baseline (2005 Prices) (Increase - Decrease)

Key: **Annual costs and benefits:** **(Net) Present**

Summary: Analysis & Evidence

Policy Option: 2	Description: Make clear that an application can be refused due to lack of information if no response is received six months following the initial full assessment (or within 3 months

COSTS

ANNUAL COSTS	
One-off (Transition)	**Yrs**
£ 230,496	1
Average Annual Cost (excluding one-off)	
£ 230,496	3

Description and scale of **key monetised costs** by 'main affected groups' In the event of writing to all companies to confirm their a/f is denied, there would be no additional resource needed as at some time the Agency would need to write to them, either to ask for repeated information or to inform them of their CHM referral. No extra costs to agency. Assume the backlog can be cleared or applications are not re-applied, then only the average 28% of the annual 300 new applications would exceed 6 months and need to re-apply.

Total Cost (PV) **£ 876,262**

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

BENEFITS

ANNUAL BENEFITS	
One-off	**Yrs**
£ 230,496	1
Average Annual Benefit (excluding one-off)	
£ 230,496	3

Description and scale of **key monetised benefits** by 'main affected groups' Given that this is a small activity (average UK MAs a/f in last 4 years average just over 300, 28% are in the latent category) it has not proved possible to establish specific costs and benefits. But benefits would include: more efficient process as it relieves congestion; companies can trade sooner and earn income from their products; public health will gain through early access to new medicines, at least 5000 freed up processing days for the MHRA

Total Benefit (PV) **£ 876,262**

Other **key non-monetised benefits** by 'main affected groups' No backlogs of a/f clogging up the system, releasing around 5000 processing days at the MHRA and gives CHM time freed to spend time on other important areas of work and innovations. A MA process in line with European efficiency procedures within specific timescales to produce a streamlined effective procedure.

Key Assumptions/Sensitivities/Risks Requirements of the Trading Fund Order to break even taking one year with another;. Treasury guidance on ensuring fees match costs; Responsibility to protect public health, Implementing Better Regulation benefits.

Price Base Year	Time Period Years	**Net Benefit Range** (NPV) **£**	**NET BENEFIT** (NPV Best estimate) **5,000 MHRA processing days**

What is the geographic coverage of the policy/option?			UK	
On what date will the policy be implemented?			1 Jan 2010	
Which organisation(s) will enforce the policy?			MHRA	
What is the total annual cost of enforcement for these organisations?			£ N/A	
Does enforcement comply with Hampton principles?			Yes	
Will implementation go beyond minimum EU requirements?			No	
What is the value of the proposed offsetting measure per year?			£ N/A	
What is the value of changes in greenhouse gas emissions?			£ N/A	
Will the proposal have a significant impact on competition?			No	
Annual cost (£-£) per organisation	Micro	Small	Medium	Large
Are any of these organisations exempt?	No	No	No	No

Impact on Admin Burdens Baseline (2005 Prices) (Increase - Decrease)

Increase of £ nil Decrease of £ nil **Net Impact** **£** nil

Key: **Annual costs and benefits: Constant Prices** **(Net) Present Value**

Key: **Annual costs and benefits: Constant Prices** **(Net) Present Value**

Evidence Base (for summary sheets)

[Use this space (with a recommended maximum of 30 pages) to set out the evidence, analysis and detailed narrative from which you have generated your policy options or proposal. Ensure that the information is organised in such a way as to explain clearly the summary information on the preceding pages of this form.]

Background

1.1 The Medicines and Healthcare products Regulatory Agency (MHRA) is an Executive Agency of the Department of Health. It acts on behalf of the Ministers comprising the Licensing Authority (as described in the Medicines Act 1968 as amended[1]), in the regulation of the parts of the pharmaceutical industry concerned with medicines for human use.

1.2 The MHRA is a Government Trading Fund and, as such, is fully funded for its medicines regulatory function by fees in connection with the manufacture, sale and supply of medicines. The fees charged by the MHRA are monitored and reviewed annually to ensure, as far as possible, that the fees charged for a particular service reflect the cost of the work undertaken. This is in line with Treasury guidance on Fees and Charges

Objectives

1.3 These proposed Regulations will make absolutely clear that the Licensing Authority can refuse a National UK marketing authorisation due to lack of information if no response is received six months following the initial full assessment (or within 3 months following assessment of supplementary information).

1.4 The Agency also intends that, through the implementation of these fee proposals, it will support its broader objectives and priorities, including:

- Ensuring that the Agency is adequately funded to fulfil its responsibilities for public health protection;
- Improving efficiency and promptness in the handling of licence applications and variations,
- Ensuring that the Agency has sufficient funding to recruit and retain the staff it needs, in licence assessment and other areas;
- Ensuring that fee levels reflect fairly the costs related to that activity, without cross-subsidy;
- Supporting “Better Regulation” activities, by simplified regulatory processes, with revised and consolidated legislation.

Rationale for Government intervention

1.5 The need for a statutory system for regulating medicines and other healthcare products is well accepted by all parties, and reflects the position followed in all developed countries. The rationale for this is not only to protect the public from unsafe, ineffective or poor quality medicines (although this is the primary purpose of the regulatory system), but also to enable and support a successful industry sector able to develop and market products that can benefit health quickly and efficiently. In the absence of a regulatory system, the lack of public confidence – and the lack of a level playing field - would hamper companies’ ability to do this. These proposals are designed so as to ensure that the MHRA can effectively carry out its responsibilities to safeguard health, through a process that provides sufficient resources for its work.

[1] *Relevant amendments have been made by the Veterinary Medicines Regulations 2006 (S.I 2006/2497). "The Ministers" are the Secretary of State for Health and the Northern Ireland Department of Heath, Social services and Public Safety.*

1.6 It is difficult to quantify precisely the health or economic impact of the Agency having insufficient resources to carry out its work effectively, but examples that are relevant to the proposals being made are:

Health impact – The implementation of this proposal will improve efficiency of the evaluation process, allowing applications to be determined earlier, to the benefit to the industry and Agency and also indirectly allow the public to have earlier access to new medicines.

Economic impact – Unnecessary delay in MHRA approvals can have an impact on pharmaceutical companies through lost earnings. For example, for a branded medicine earning £19m annual revenue in the UK, a delay of two weeks might reduce annual profits by an estimated £36,000 for that one product (this is a crude estimate). By removing the processing constraint on the MHRA, it will provide a more efficient service which will remove the barrier to these earnings for companies.

1.7 It is therefore important that the MHRA is able to gain sufficient income to resource these functions effectively. However, it is also recognised that the Agency must carry out its responsibilities efficiently and in accordance with the Government's principles on Better Regulation, so that regulation is proportionate, targeted and risk-based.

1.8 The Agency also has a role in supporting innovation and enabling businesses to prosper, through handling routine regulatory processes promptly and efficiently. Unnecessary delay in regulatory activity can be costly to companies in terms of delayed product launches, lost revenues from new or revised products, and planning blight from unpredictable timetables.

2. Consultation

2.1 These proposals have been considered by DH lawyers and the MHRA Better Regulations team. Both have approved the proposals and are satisfied that the Agency is making every effort to match fees with costs and that these changes serve to ensure that this is the case.

2.2 A 12 week public consultation exercise was carried out with letters being issued to over 1400 companies, individuals, industry associations and licence and Marketing Authorisation holders who were likely to be affected by the proposals or interested in them. The consultation document was placed on the Agency's website.

2.3 A total of five responses were received all broadly in support of these proposals. We intend to respond to individuals on any points they have raised.

3. Options

3.1 Two options for the main proposals have been identified:

Option 1 Do nothing option i.e. make no changes

This is a "do nothing" option in the pure sense, although it would amount to a real terms cut in Agency funding, leaving the Agency less well resourced. The backlog of applications will continue to rise, and in many cases the assessor may have to begin the assessment again due to the long gap in information and responses from the company.

Option 2 Make clear that an application can be refused due to lack of information if no response is received six months following the initial full assessment (or within 3 months following assessment of supplementary information).

The implementation of this proposal will improve efficiency, allowing applications to be determined much earlier, to the benefit to the industry and Agency and also indirectly allow the public to have earlier access to new medicines.

Option two is the preferred option to take.

4. Sectors and groups affected

4.1 All sectors of the pharmaceutical industry, involved in the marketing of medicinal products for human use.

4.2 It is not possible to identify a "typical" business. Businesses range from small "one-man-band" wholesale dealers, NHS Trusts and hospitals, academic research establishments, up to multi-billion pound international manufacturing businesses. There are no indirect costs, policy costs or additional administrative burden costs as a result of these proposals. These proposals include a measure which will reduce administrative burden.

5 Costs and Benefits

The consultation period will allow the quantification of the costs and benefits to be made with greater accuracy.

Benefits of Option 1: do nothing

5.1 The only benefit of continuing with the current arrangement is the Agency could earn the figures stated in the summary when companies have to re-apply. However these figures do not represent the true cost of the Agency's work, and also represent a cost to the companies.

Benefits of Option 2: 6 month cut off for incomplete applications

5.2 All stakeholders will continue to see benefit from improvements in service levels from the MHRA in terms of speed and predictability of processing of licence applications. The public health will benefit from these measures with early access to new medicines, as the proposal will ensure that the MHRA is adequately resourced for the work it undertakes in ensuring the safety, quality and efficacy of the medicines used by patients in the UK.

5.3 A key concern of pharmaceutical companies is that they receive a prompt and efficient response from the MHRA when they submit applications for the licences that they hold. The Agency recognises that the business costs to companies from slower than expected processing of applications (for example delayed product launches) can greatly outweigh the costs from the fees themselves. The intention of Option 2 is that the process will work in such a way that the resources can be deployed to ensure efficient and prompt handling of such work.

5.4 Companies can then enjoy the income from their products, as a delay of two weeks might reduce annual profits by an estimated £36,000 for a product that would earn £19m annually.

5.5 The Agency would benefit from a more efficient process and the freeing up of valuable man hours. With a complete application for a UK license taking 210 days, and assuming that the incomplete and premature applications take around a tenth of that time, or 25 days, if even half of the backlog is cleared (200) applications) it will see 5,000 processing days freed up.

5.6 Regulatory activity in this sector is in large part demand-led, in that companies choose whether to submit applications for new licences. By setting a clearer process, making it absolutely clear in legislation that there is a 'cut off' date for response to information required by company's, the Agency will be making efficiency gains enabling it to achieve its regulatory requirements and business plans within this resource provision.

Better Regulation benefits

5.7 The new procedure will be a pro-active approach, and will reduce administrative costs in relation to making individual applications and processing individual invoices for each change.

Costs of Option 1: do nothing

5.8 It would hamper the Agency's ability to maintain its operation. It would create a position where costs would be running at a level above income and would result in a deficit. If the Agency was not resourced adequately there could be a long term risk to public health. There would be a direct impact on companies in terms of the speed and efficiency with which work were dealt with, and the loss of potential earnings on drugs that cannot be traded due to the delay in processing. Of the 397 outstanding applications, 61% (242) have had no correspondence for more than two years, and would need to re-apply at a cost to the companies of £664, 514, using the cost of £2, 744 per application.

Costs of Option 2: 6 month cut off for incomplete applications

5.9 Assuming the consultation period could provide sufficient time and incentives for companies to help clear the backlog before the legislation is passed, it is assumed that only the current average of 28% of the 300 new annual applications will exceed 6 months and need to re-apply.

5.10 There are no associated policy costs or administration costs from these proposals.

6. Small Firms Impact Test

6.1 It is recognised that although regulatory fees represent a relatively small element in the annual outgoings of a small pharmaceutical business, it is likely to represent a greater proportion of their outgoings than for larger businesses. The smallest of the businesses in the pharmaceutical industry do not tend to be developmental companies and so costs associated with applications for new products rarely arise.

6.2 The MHRA operates a number of provisions to assist smaller companies, for example:

- reduced fees for certain smaller companies;
- lower periodic fees for products with low turnover;
- extended terms of payment of a number of capital fees.

6.3 The Agency will consider further assistance it is able to offer. However, reducing fees below costs incurred would lead to cross-subsidisation from fees paid by other companies, so it is not possible to offer general fee reductions for smaller companies.

7. Competition Assessment

7.1 The proposed fee increases will affect a number of different markets within the pharmaceutical industry and the NHS. No organisation may operate in the pharmaceutical market in the UK (whether in manufacturing, distribution or sales) without being subject to the regulatory system operated by the MHRA. Regulatory fees are a permanent feature of the market, and we do not anticipate that the proposed changes are likely to have any significant impacts for competition in any of the affected markets.

8. Equality Impact Assessment:

8.1 An initial Equality Impact screening assessment has been carried out, which has shown that a full assessment is not required as the proposed policy has no disproportionate impact on race or other relevant equalities. The proposed policy will not have any disproportionate impact on rural populations.

9. Legal Aid, Sustainable Developments, Carbon assessment, other environmental issues

9.1 There are no impacts on environmental, sustainable development or carbon offsetting from these proposals. There are no implications for Legal Aid from these proposals.

10. Enforcement, Sanctions, and Monitoring

10.1 The new proposals will be enforced by the Licensing Division of the Agency which is responsible for assessment of applications for MAs for the Agency. The measure of whether the policy meets its objectives will be apparent through the year through monitoring the workloads and feedback from industry.

11. Implementation and delivery plan

11.1 The new proposals will apply to all applications. The new proposals will be advertised on the MHRA's website and all those affected will be made aware through the consultation exercise.

12. Post-implementation review

12.1 MHRA licensing processes are subject to continuous rigorous monitoring and review with a view to making annual amendments (where necessary) to ensure that, as far as possible, the cost of the work undertaken by the MHRA is reflected in the fees charged to industry. In addition, the Agency is continuing to seek efficiencies from within its working practices, both to speed up the processes and also to provide a better standard of service from within current resources.

13. Risks, Uncertainties and Unintended consequences

13.1 This proposal may be seen as a barrier to entry. With a stiff penalty – having to repay the full amount if the company fails to meet the information requirement within 6 months - there is the risk of companies refusing to begin the application process or not re-applying in the future, which would be at a financial cost to the Agency and to the economy, and to public health if the companies do not trade in the future. However with sufficient notice, through the consultation before the legislation is passed, companies would be well informed of the proposal to ensure this does not pose much of a risk.

14. Summary and Recommendations

14.1 Option 2 best achieves the objective of ensuring that costs to the pharmaceutical industry reflect the actual cost of the work undertaken by the MHRA in connection with medicines regulation. It will allow the MHRA to undertake its responsibilities for protecting public health. It will provide incentives, and target resources, in a way that supports the Agency's ability to respond to public health threats as well as deliver prompt handling of regulatory business.

14.2 Option 2 represents the most effective option.

Specific Impact Tests: Checklist

Use the table below to demonstrate how broadly you have considered the potential impacts of your policy options.

Ensure that the results of any tests that impact on the cost-benefit analysis are contained within the main evidence base; other results may be annexed.

Type of testing undertaken	*Results in Evidence Base?*	*Results annexed?*
Competition Assessment	Yes	No
Small Firms Impact Test	Yes	No
Legal Aid	Yes	No
Sustainable Development	Yes	No
Carbon Assessment	Yes	No
Other Environment	Yes	No
Health Impact Assessment	Yes	No
Race Equality	Yes	No
Disability Equality	Yes	No
Gender Equality	Yes	No
Human Rights	Yes	No
Rural Proofing	Yes	No

Annexes