EXPLANATORY MEMORANDUM TO THE

MEDICINES (PROVISION OF FALSE OR MISLEADING INFORMATION AND MISCELLANEOUS AMENDMENTS) REGULATIONS 2005

2005 No. 1710

1. This explanatory memorandum has been prepared by the Department of Health and is laid before Parliament by Command of Her Majesty.

2. Description

2.1 The instrument introduces new criminal offences of providing false or misleading information (or of failing to provide relevant information) to the Licensing Authority in support of an application for the grant, renewal, or variation of a marketing authorisation for a medicinal product, and in specified circumstances during the currency of a marketing authorisation or in relation to the sale or supply of unlicensed medicinal products. The instrument also makes it a condition of a manufacturer's and wholesale dealers' licence that holders of these licences take reasonable steps to ensure that information provided to the Licensing Authority is not false or misleading and imposes an additional record-keeping requirement on manufacturers of biological medicinal products for human use

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

3.1 None.

4. Legislative Background

4.1 As a result of circumstances surrounding the withdrawal of Oral Polio Vaccine in 2000, recommendations were made by the Chief Medical Officer that the Medicines Control Agency (MCA – predecessor to the Medicines and Healthcare products Regulatory Agency), review its procedures for checking the validity of information supplied to the licensing authority by pharmaceutical companies.

Enquiries carried out by the MCA determined that companies had, at the time, provided incorrect or misleading information in their returns to the Agency - yet, due to deficiencies in the legislation, no offence was committed and no action could be taken by the regulator against the companies concerned.

Accordingly, the proposed regulations will provide an effective sanction and will serve to reassure the public that the Medicines and Healthcare products Regulatory Agency (MHRA) possesses the necessary enforcement powers against potentially serious breaches or omissions in the application process for a marketing authorization, or for the provision of relevant data during the currency of a licence.

5. Extent

5.1 This instrument applies to all of the United Kingdom.

6. European Convention on Human Rights

The Minister of State, The Rt. Hon Jane Kennedy MP, has made the following statement regarding Human Rights:

In my view the provisions of the Medicines (Provision of False or Misleading Information and Miscellaneous Amendments) Regulations 2005 are compatible with the Convention rights.

7. Policy background

7.1 In accordance with the requirements of the Medicines Act 1968 and Council Directive 2001/83/EC, the MHRA operates a system of licensing before the marketing of medicines in the UK. The MHRA, as the Licensing Authority for the UK, carries out pre-marketing assessment of a medicines safety, quality and efficacy, examining all the research and test results in detail, before a decision is made on whether the product should be granted a marketing authorisation. Once granted, the marketing authorisation is the signal to the healthcare professional and patient that the product has been thoroughly tested and analysed before being placed on the market.

The MHRA also licenses manufacturers and wholesale dealers of medicinal products. These licences cover all the main activities associated with manufacture or distribution of medicinal products. This system of licensing is intended to ensure that manufacturers and wholesale dealers have the necessary staff, premises, equipment and facilities to carry out their activities and that they do so to appropriate standards of quality, in accordance with the principles of good manufacturing or good distribution practice.

The changes being made by this Statutory Instrument strengthen the MHRA's position to take action if the relevant licence holder(s) do not provide correct information to the Licensing Authority and to bring into effect the following measures to improve the Licensing Authority's enforcement powers. The Regulations have been drafted to:

[i] Require manufacturers of biological medicinal products for human use to keep records relating to intermediate medicinal products;

[ii] Introduce offences for failing to provide relevant information to the licensing authority:

- during the course of an application for the grant, variation or renewal of a marketing authorisation;
- for providing false or misleading information to the Licensing Authority in specified circumstances during the currency of an authorisation;
- or in relation to the sale or supply, or provision of a specification for an unlicensed medicinal product supplied in accordance with Schedule 1 of the Marketing Authorisations Regulations[1].

[iii] Extend the Standard Provisions to make it an offence for holders of manufacturers or wholesale dealers' licences to provide false or misleading information in relation to medicinal products for human use to the Licensing Authority during the currency of their licence.

8. Impact

8.1 A Regulatory Impact Assessment is attached to this memorandum. This includes an analysis of the consultation exercise.

8.2 The impact on the public sector is judged to be low – the new offences will, in the main, apply to pharmaceutical companies in the private sector.

9. Contact

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FULL REGULATORY IMPACT ASSESSMENT

Title of regulatory proposal

The Medicines (Provision of False or Misleading Information and

Miscellaneous Amendments) Regulations 2005

1. Purpose and intended effect of measure

Policy objective

1.1 To introduce Regulations establishing new criminal offences of failing to provide or providing false or misleading information to the Licensing Authority in support of an application for the grant, renewal, or variation of a marketing authorisation for a medicinal product, and in specified circumstances during the currency of a marketing authorisation or in relation to the sale or supply of unlicensed medicinal products ("specials").

1.2 It is also proposed to extend the Standard Provisions[2] to make it an offence to provide false or misleading information during the currency of a manufacturer's or wholesale dealers licence in relation to medicinal products for human use, and introduce an additional record-keeping requirement on manufacturers of biological medicinal products for human use.

Background

1.3 The MHRA operates a system of licensing before the marketing of medicines. Medicines, which meet the standards of safety, quality and efficacy, are granted a marketing authorisation (previously a product licence), which is normally necessary before they can be prescribed or sold. This authorisation covers all the main activities associated with the marketing of a medicinal product. The MHRA carries out pre-marketing assessment of the medicines safety, quality and efficacy, examining all the research and test results in detail, before a decision is made on whether the product should be granted a marketing authorization.

1.4 Once granted, the marketing authorisation is the signal to the healthcare professional and patient that the product has been thoroughly tested and analysed before being placed on the market. It is important, therefore, that the licensing authority has the appropriate regulatory means to call a pharmaceutical company to account if the application for a marketing authorization is deficient in any way.

[2] The Medicines (Standard Provision for Licences and Certificates) Regulations 1972 (S.I. 1972/972)

1.5 Similarly, the MHRA licences manufacturers and wholesale dealers of medicinal products. These licences cover all the main activities associated with manufacture or distribution of medicinal products. This system of licensing is intended to ensure that manufacturers and wholesale dealers have the necessary staff, premises, equipment, facilities to carry out their activities and that they do so to appropriate standards of quality, in accordance with the principles of good manufacturing or good distribution practice.

1.6 At the present time, it is an offence for a company to provide false or misleading information in response to an Agency request, in the context of an application for the grant, variation or renewal of a manufacturer's or wholesale dealer's licence. However, perhaps due to an oversight in the original drafting of the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994, the same does not apply to a marketing authorisation (product licence) application.

1.7 This position is at odds with provisions in the Good Laboratory Practice Regulations, the new Clinical Trials Regulations and the pharmacovigilance requirements from Council Directive 2001/83/EC, where the supply of false or misleading information creates an offence in its own right. This inconsistency constitutes a significant weakness in medicines regulation and the Government intends ending this discrepancy.

Risk Assessment

1.8 The key risks associated with these regulatory proposals were demonstrated within the context of the Oral Polio Vaccine withdrawal in 2000, where false or misleading information relating to the manufacturing process was provided to the Agency by pharmaceutical companies. This incorrect information was used to inform Government on an issue of clear public health interest, yet, due to the aforementioned deficiencies in Regulations, the Agency was unable to take any action against the companies concerned.

1.9 Recommendations were made by the Chief Medical Officer that the MCA (predecessor to the MHRA) review both the governing legislation and the Agency's procedures for checking the validity of information supplied to the licensing authority by pharmaceutical companies. The proposed regulations will provide an effective sanction, should the need arise and will serve to reassure the public that the Agency possesses the necessary enforcement powers against potentially serious breaches or omissions in the application process for a marketing authorization, or for the provision of relevant data during the currency of a licence.

Detail

1.10 The Medicines (Provision of Misleading Information and Miscellaneous Amendments) Regulations 2005 bring into effect the following offences:

Regulation 2

1.11 Regulation 2 amends the Medicines (Standard Provisions for Licences and Certificates) Regulations 1971 (the "Standard Provisions"). Paragraphs 3(a) and (b) introduce the requirement for holders of manufacturers' licences that hold intermediate products for use in the manufacture of biological medicinal products for human use to keep records on the detail of the manufacture of these intermediate products. Failure to keep these records in the correct form or destruction of these

records would be a breach of a condition of the manufacturer's licence, hence a breach of section 8(2) of the Medicines Act 1968 and an offence under section 45(1) of the Act.

1.12 Paragraphs 3(c) and 4(b) make it a condition of manufacturers' and wholesale dealers' licences that licence holders do not provide the licensing authority with information which is relevant to an evaluation of the safety, quality or efficacy of a medicinal product for human use (or, for manufacturers, such information about starting materials or intermediate products for use in manufacture of products for human use as well) which is false or misleading. Breach of this condition would be a breach of sections 8(2) or 8(3A) of the Medicines Act 1968 and again an offence under section 45(1) of the Act.

Regulation 3

1.13 Regulation 3 introduces new offences in relation to marketing authorisations but also in relation to "specials" - i.e. unlicensed medicinal products.

1.14 Paragraph 10(A)(1) makes it an offence to fail to provide, or to provide false or misleading information, which is relevant to an evaluation of the safety, quality or efficacy of a product in the course of an application for the grant, variation or renewal of a marketing authorisation for that product. This means that an offence will have been committed if an applicant for a marketing authorisation either doesn't supply all the information which is relevant to an evaluation of that medicinal product or if they supply information which is false or misleading in a material particular. The offence covers information provided "in the course of an application" so applies both to information presented with the initial application and any requested by the licensing authority as part of considering that application.

1.15 Paragraph 10A(2) deals with information provided to the licensing authority not in the course of an application. The offence could be committed by anyone responsible for placing a product on the market - by an MA holder or by a QP (pharmacovigilance). The offence is not restricted to only applying during the currency of a marketing authorisation, although in practice this is when it will apply since products cannot be placed on the market without authorisation.

1.16 Paragraph 13A deals with information supplied in relation to unlicensed products. Schedule 1 (of the Marketing Authorisations etc Regulations) provides an exemption from the requirement that to place products on the market they must have a Marketing Authorisation.

1.17 The reason for adding an offence of supplying false and misleading information relating to "specials" is that there is already a record keeping requirement (see paragraph 6 of Schedule 1) and a requirement to make these records available to the licensing authority (paragraph 7). So there is a separate category of information which might be supplied to the licensing authority in relation to "specials".

2 Options

2.1 The MHRA's primary objective is to safeguard public health by ensuring that all medicines on the UK market meet appropriate standards of safety, quality and efficacy. Safety aspects cover potential or actual harmful effects; quality relates to development and manufacture; and efficacy is a measure of the beneficial effect of the medicine on patients.

2.2 Given this heavy responsibility and the clear public health interest in ensuring that medicines are placed on the market only when they have been thoroughly tested and analysed, there are essentially only two options to consider:

Option 1 – Do nothing and rely, as now, on the existing legislation.

Option 2 – Introduce strengthened legislation to bring the application process relating to marketing authorizations and the provision of relevant data during the currency of a licence more into line with the requirements of other parts of the licensing system.

2.3 A third option would normally be the consideration of a non-regulatory solution but the context of these proposals and the fact that they relate to the public health issues of medicines licensing and enforcement make this an undesirable alternative.

3 Benefits

3.1 **Option 1** – This would require no action on the part of the regulatory authority but equally, would provide no additional benefits or safeguards for the patient or end user of medicines placed on the market. Not recommended.

3.2 **Option 2** – The aim of these proposals is to ensure probity in the application process for a marketing authorization and maintenance of a licence, which currently allow applicants to submit potentially false or misleading information without penalty or sanction.

3.3 The public interest around medicines licensing is best served by legislation that is both effective and enforceable. The existence of offences in other medicines legislation for dealing with the supply of false or misleading information, and the Agency Enforcement Group's capability for dealing with offenders has an obvious deterrent effect. It is, therefore, a logical move to extend these requirements to the provision of information relevant to applications for marketing authorisations.

3.4 The proposed Regulations are sensible, proportionate and achievable. They will plug potentially serious loopholes in current provisions and allow enforcement staff in the Agency to deal effectively with false or misleading representations, so protecting the patient or end user.

4 Costs

4.1 The regulatory proposals amount to an additional record-keeping requirement for companies manufacturing biological products and the creation of new offences around applying for a marketing authorization and maintaining manufacturing or wholesale dealer licences.

Record keeping

4.2 Due to the very low numbers of companies involved in the manufacture of biological products, the administrative impact of this additional record keeping requirement is judged to be extremely low. Indeed, in order to ensure proportionality, there is no requirement to provide documentation routinely to the Agency to demonstrate compliance. The requirement would instead be a matter for inspection – or, in exceptional circumstances, following a request from the Agency.

New offences

4.3 The application process itself (in terms of what companies are asked to do and submit in support of an application for a marketing authorization) is not changing as a result of the proposals. As such, the Government considers that there are no costs directly attributable to companies (financial, administrative or otherwise) in bringing these proposals into force at the earliest opportunity.

4.4 Similarly, the impact on pharmaceutical companies of submitting relevant data – either routinely or in response to an Agency request – is not expected to be unduly onerous, because such information should already be available within the company in support of manufacturing or distribution processes.

4.5 Of course, there may be cost implications in terms of fines if companies submitting incomplete, false or misleading information to the licensing authority are found to be in breach of the Regulations. However, since pharmaceutical companies control what is presented to the licensing authority the risk of this happening should be very low if the application, supporting evidence or other information relevant to the safety, quality and efficacy of a medicinal product is collated and submitted in the correct way.

5 Equity and fairness

5.1 There are no distributional impacts to the regulatory proposals. The Regulations relate to the pharmaceutical industry and will not disproportionately affect vulnerable or already disadvantaged groups.

6 Business Sectors Affected

6.1 Currently there are 785 Marketing Authorisation Holders, 48 Manufacturers of Biological medicinal products, 222 Manufacturers and 1168 Full Wholesale Dealers in the UK market who will be affected by the implementation of these regulations.

7 Consultation with small businesses: The small firms impact test

7.1 The regulatory proposals will apply equally to small, medium and large businesses. A "significant impact" can be both a high cost and/or a disproportionate cost on small firms, relative to other sized businesses. Neither applies in this case because the process of applying for a marketing authorisation is not changing. Similarly, the administrative task of providing information to the licensing authority, which is relevant to the safety, quality or efficacy of any medicinal product, is unlikely to create a "significant impact" on small businesses. Accordingly, there are no implementation or compliance costs – other than the creation of an offence if the application or information is deficient in the ways already described.

7.2 The Government has tested these assumptions with the public, industry and across interested Government Departments including the Small Business Service, the Regulatory Impact Unit, the Home Office and the Office of Fair Trading, all of whom confirmed that they were content with the approach.

8 Competition assessment

The market

8.1 It is necessary to consider the impact on competition within UK markets and to analyse the impacts of the proposed Regulations on UK businesses in the relevant markets and on importers into the UK. The proposed Regulations will apply to all applications for a marketing authorization in the UK, and information submitted to the licensing authority which is relevant to the safety, quality or efficacy of a medicinal product, including those dealt with through the Mutual Recognition and Centralised Procedures (in cases where the UK acts as Rapporteur) as well as those products considered for licences as part of the parallel import scheme. That is, the UK would apply whatever domestic legislation is applicable and this would be binding on all such applications where the relevant assessment work is undertaken in the UK - whether or not the same provisions exist in other Member States.

8.2 The question therefore arises as to whether or not introducing the proposed Regulations would affect decisions in the industry as to which competent authority to select as the Rapporteur for assessment of their products. The Government, for its part, views the regulatory proposals as relating to matters of probity and transparency in the application process rather than of the introduction of a new and unwelcome regulatory burden on businesses.

Restrictions on businesses?

8.3 It is important to consider whether the regulatory proposals will have any detrimental impact on new businesses. The Government's view is that there is unlikely to be any change in the number or size of businesses within the market, and no identifiable change to market shares on the basis of these additional enforcement powers. The prices of end products should be similarly unaffected. New businesses entering the market will not be affected differently from existing businesses – they will be required to observe the same processes and standards as existing companies and will be subject to the proposed regulatory sanctions on that basis. Accordingly, there is unlikely to be any additional set-up or "on" costs for new or potential businesses triggered by the new enforcement powers and, in the Government's view the proposals will not cause any impediment to them competing in the market.

8.4 In view of the above factors the Government considers that the proposals are unlikely to affect significantly the current nature of competition within the affected markets.

9. Enforcement and sanctions

9.1 The Government is mindful not to impose an over-cumbersome regime on the industry whilst, at the same time, ensuring that the provisions are properly enforceable by the MHRA. Accordingly, the new offences will "strict liability offences" but with a due diligence defence. The obligation on holders of manufacturers and wholesale dealers licences will be to "take all reasonable precautions and exercise all due diligence to ensure" that information is not false or misleading. Therefore, if a licence holder provides false or misleading information, but had taken all reasonable precautions and exercised all due diligence to avoid doing so, they will not have committed an offence.

9.2 In the interests of proportionality, it is proposed that an offence will only be committed if information that is false or misleading is relevant to the safety, quality or efficacy of medicinal products - where there is a clear public health justification for these offences.

9.3 Offences relating to the provision of other false information about a medicine - e.g. in respect of patent or company law issues - are not primarily the responsibility of the MHRA and would not be covered by the proposed Statutory Instrument.

9.4 Penalties are consistent with other Medicines Act offences (i.e. on summary conviction a fine not exceeding £5,000 or on conviction on indictment an unlimited fine and/or a 2-year prison sentence).

10. Monitoring and review

10.1 The Government will monitor continuously the impact of the new Regulations and make any necessary changes. Indeed, it is a manifesto commitment to review all new legislation after 3 years. Where significant policy amendments are proposed, there will be further consultation to ensure the views of the industry are represented.

11. Consultation

11.1 The consultation on the proposed False and Misleading Information Regulations was launched on 24 December and sent to 2780 participants. The Agency was committed to seeking views from as many interested parties as possible. In particular, wanting opinions on whether:

- The benefits and costs look reasonable;
- The assessment of competition effects looks reasonable;
- The enforcement issues are reasonable and fair;
- There are any unintended consequences.

11.2 The majority of correspondents supported the measures that strengthen the regulatory procedure to ensure compliance. The breakdown of responses was as follows:

Medical Associations/Groups	8
Pharmaceutical Associations/Groups	7
Charities	1
Scottish Police Associations	1
Individuals/Companies commenting	6
Individuals/Associations/Companies choosing not to comment	5
Total	**28**

11.3 Concerns were expressed about the following:

Liability – It was considered personal liability would be too onerous on an individual.

Comment: The offences, as with all the medicines offences, can be committed either by an individual or a company. The offences refer to the offence being committed by "any person" but a "person" means both individual people and companies (it is defined as such in the Interpretation Act 1978). Therefore, if a licence holder happens

to be an individual they could be guilty of one of these offences but if the licence is held by a company then the company, as licence holder, could be guilty.

11.4 Concerns about particular phrasing e.g. "provide relevant information".

Comment: The language used in the regulations is the same as that in Annex I to Directive 2001/83/EC which requires applicants to supply all data relevant to an evaluation of the medicinal product concerned.

11.5 The ambiguity concerning intentional vs unintentional withholding of data.

Comment: The MHRA is mindful not to impose an over-cumbersome regime on the industry whilst, at the same time, ensuring that the provisions are properly enforceable. It is proposed that offences should be strict liability offences but with a due diligence defence.

11.6 Concern about "applicants" responsibility for third party data.

Comment: In respect of third party data, the due diligence defence would cover licence holders provided they had taken reasonable measures to ensure that the data supplied from a 3rd party was accurate. They could not argue they had exercised "due diligence" if they simply passed the information on to the MHRA.

11.7 Concern about Qualified Persons and insurance.

Comment: The proposed new regulations do not change the relationship between the Qualified Person (QP) and the Licence Holder It is up to licence holders what terms they employ QPs on, provided of course the QPs are not prevented by the contract terms from carrying out their regulatory duties.

12. Summary and recommendation

12.1 The Government proposes to introduce Regulations establishing a new criminal offence of providing false and misleading information to the Licensing Authority in support of an application for a Marketing Authorization for a new medicinal product and for information that is submitted during the currency of a licence that is relevant to the safety, quality or efficacy of medicinal products that are manufactured or distributed. This would be achieved by amendments to the Medicines for Human Use (Marketing Authorisations Etc.) Regulations 1994 and the Medicines (Standard Provision for Licences and Certificates) Regulations 1971 (S.I. 1971/972).

12.2 Option 2, which creates the new offences, is the necessary step that needs to be taken to strengthen the governing Regulations. The new Regulations will plug potentially serious loopholes in current provisions and help companies to comply with the requirements of the application process, while strengthening enforcement action against those who flout the law.

12.3 The Government plans to implement the changes by July 2005.

13. Declaration.

I have read the Regulatory Impact Assessment and I am satisfied that the benefits justify the costs.

Jane Kennedy, 22nd June 2005, Minister of State for Quality and Patient Safety, Department of Health