EXPLANATORY MEMORANDUM TO THE

MEDICINES (MARKETING AUTHORISATIONS AND MISCELLANEOUS AMENDMENTS) REGULATIONS 2004

2004 No.3224

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 the Department for Environment, Food and Rural Affairs is laid before Parliament by Command of Her Majesty.

2. Description

2.1 The instrument amends the regulations which implement the EU legislation relating to marketing authorisations for medicinal products, for both human and veterinary use. It implements certain provisions of Directive 2004/27/EC which relate to the provision of information by marketing authorisation holders for medicines for human use, the package leaflets that accompany such medicines and decisions by the competent authority as to the supply classification of such medicines. The instrument makes amendments to the regulations and to other enactments as a consequence of the coming into force of Title IV of Regulation (EC) No. 726/2004, which establishes the European Medicines Agency, and makes provision for the operation of that Agency and its committees.

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

3.1 None

4. Legislative Background

4.1 The instrument is made under section 2(2) of the European Communities Act 1972 and implements certain provisions of Directive 2004/27/EC ("the 2004 Directive"), which amends Directive 2001/83/EC on the Community code relating to medicinal products for human use ("the 2001 Directive"). Directive 2001/83/EC is the main piece of EC legislation governing medicinal products for human use and consolidated most of the previous EC legislation in this area. The provisions of the 2001 Directive relating to the authorisation of such products are implemented in the UK by the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 ("the 1994 Regulations"). The 2004 Directive is part of a legislative package designed to implement the proposals of the 2001 Review of EU medicines legislation.

4.2 The final date for transposition of the 2004 Directive is 30th October 2005. This instrument, however, amends the 1994 Regulations so as to implement the following provisions early–

(a) Article 1(21) of the 2004 Directive, which amends Article 23 of the 2004 Directive so as to impose on marketing authorization holders additional obligations to provide information to the competent authority (in the UK, the licensing authority under the Medicines Act 1968, which acts by the MHRA);

(b) Article 1(44) and (45)), which amend Articles 59 and 61(1) of the 2004 Directive, so as to provide that package leaflets accompanying medicinal products for human use must be drawn up in accordance with certain new requirements, in particular that the leaflet must reflect the results of consultations with target patient groups; and

(c) Article 1(54)), which inserts a new Article 74a of the 2001 Directive, so as to provide that where a change of classification of such a product (e.g. from prescription only supply to supply without prescription) has been authorised on the basis of significant pre-clinical tests or clinical trials, the competent authority may not refer to the results of those tests or trials, when examining a change of classification for the same substance within one year of the initial change.

4.3 Article 1(21) and (54) are to be implemented as of 1st January 2005; Article 1(44) and (45) as of 1st July 2005 (but with transitional provisions for existing products). A Transposition Note in relation to the 2004 Directive is attached as an Annex to this memorandum.

4.4 The instrument also amends section 63C of the Terrorism Act 2000 and various regulations, as a consequence of the coming into force of Title IV of Regulation (EC) No. 726/2004, another part of the 2001 Review legislative package. This Regulation makes provision for a centralised Community procedure for authorising medicinal products (for both human and veterinary use) and establishes a European Medicines Agency. Most of its provisions do not apply until 20 November 2005, but Title IV came into force on 20th May 2004. The effect of Title IV is to establish and make provision for the operation of the Agency (which is the successor to the European Agency for the Evaluation of Medicinal Products established by Regulation (EEC) No. 2309/93), and to make provision for the membership and operations of the Committee for Medicinal Products for Human Use and the Committee for Medicinal Products for Veterinary Use (which are the are successors to the Committee on Proprietary Medicinal Products and the Committee on Veterinary Medicinal Products, respectively). The changes were made as a result of the accession of 10 new Member States to the EU in May. This instrument makes amends UK legislation so as to replace references to the old Agency and committee with references to the new Agency and committees.

5. Extent

5.1 This instrument applies to all of the United Kingdom

6. European Convention on Human Rights

The Parliamentary Under Secretary of State, Lord Warner, has made the following statement regarding Human Rights:

In my view the provisions of the Medicines (Marketing Authorisations and Miscellaneous Amendments) Regulations are compatible with the Convention rights.

7. Policy background

Data Exclusivity and Switching

Directive 2001/83/EC requires Member States to classify products as prescription or non-prescription. A company may wish to use the results of tests or trials to demonstrate, for example, that the product may safely be switched to non-prescription supply. But if they do so, other companies with similar products may also switch their products, gaining the

benefit of the original MA holder's investment; there is currently no "data protection" period for the test and trial results. The new provision would have the effect that where a company submits data from tests or trials to support a switch, the MHRA will be prevented from relying on that data when considering a switch application by another company in relation to the same substance. In effect, the original MA holder gains a year's data protection period. Implementing the provision early would enable companies considering a switch for their medicines to benefit from this incentive as soon as possible. This would, therefore encourage the earlier availability of such medicines.

User testing
The EU requirements for patient information leaflets are intended to enable users safely to use the medicines they are taking. Although it is current good practice voluntarily to test leaflets, to judge whether they are clear and easy to use, there is no obligation to do so. Implementing the provision will mandate "user testing" to support the safe use of medicines. Implementing the provision early will ensure that patient information reflects the results of "user testing" sooner than it would otherwise and maximises the benefit of the provision for patient safety.

Pharmacovigilance provision
The new provision makes it explicit that a MA holder must notify the competent authority immediately of any information that might affect the terms of their MA, including any restrictions placed on it by another Member State. It also emphasises that the competent authority may at any time ask for data to support a risk-benefit analysis. This might include post-authorisation safety studies, clinical trials for the same or other indications or different patient groups. The primary purpose of this provision is to provide further safeguards aimed at increasing the safety of patients. Implementing the measure early will ensure the safeguards are in place as soon as is practicably possible.

The proposals were subject to public consultation. The non-industry responses broadly supported early implementation of all three provisions. Responses from the industry did not oppose the switching and pharmacovigilance provisions but were opposed to early implementation of user testing of patient information. Following consultation the proposed date for implementation has been amended from 1 April 2005 to 1 July 2005 to reflect concerns raised and to allow for preparations for the new requirements to take place.

8. Impact

8.1 A Regulatory Impact has been placed in the Library.

8.2 The impact on the public sector
There will be no negative impact on the public sector. Implementation of the data exclusivity and switching provision will provide an incentive for companies to make more innovative switches which will increase the availability of medicines for the public. The user testing and pharmacovigilance provisions will act to increase patient safety. Early implementation of all three provisions will ensure these benefits are gained as soon as possible.

9. Contact

Jeremy Mean at the Medicines and Healthcare products Regulatory Agency, Department of Health, Tel: 020 7084 2494 or e-mail: Jeremy.mean@mhra.gsi.gov.uk can answer any queries regarding the instrument.

Transposition Note for Directive 2004/27/EC amending Directive 2001/83/EC on the Community code relating to medicinal products for human use

Directive			
Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use.			
Articles	**Objectives**	**Implementation**	**Responsibility**
1 (except paragraphs (21), (44), (45) and (54)) and 2 to 5	To amend Directive 2001/83/EC on the Community code relating to medicinal products for human use ("the 2001 Directive")	Not yet implemented – final date for transposition is 30 October 2005	Secretary of State for Health.
1(21)	To amend Article 23 of the 2001 Directive so as to impose on holders of marketing authorisations for medicinal products for human use additional obligations to provide information to the competent authority relevant to the evaluation of the risks and benefits of their product	The Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 ("the 1994 Regulations") provide that the licensing authority established by the Medicines Act 1968 ("the Licensing Authority") must carry out the responsibilities of the competent authority under the 2001 Directive (regulation 3). The Regulations also provide that marketing authorisation holders must comply with obligations imposed by "the relevant Community provisions", including the 2001 Directive (regulation 7). Regulation 3(2)(a)(i) and (ii) of the Medicines (Marketing Authorisations and Miscellaneous Amendments) Regulations 2004 ("the Amending Regulations") amends the definition of the 2001 Directive in the 1994 Regulations so as to ensure that marketing authorisation holders must comply with the obligations set out in Article 23 of the 2001 Directive as amended. Regulation 3(4) amends Schedule 3 to the 1994 Regulations so as to create new criminal offences for failure to comply with these obligations.	Regulations made by the Secretary of State for Health. Licensing Authority (which acts by the Medicines and Healthcare products Regulatory Agency (MHRA)) responsible for carrying out functions of UK competent authority. Marketing authorisation holders responsible for complying with obligations under the 2001 Directive. Responsibility for enforcement rests with the "enforcement authority", i.e. the Secretary of State in relation to England, the National Assembly for Wales in relation to Wales, the Scottish Ministers in relation to Scotland, and the Department of Health, Social Services and Public Safety in relation to Northern Ireland. In relation to England, Wales and

			Scotland, the functions of the enforcement authorities are performed by the MHRA.
1(44) and (45)	To substitute a new Article 59 of the 2001 Directive and amend Article 61(1) of that Directive, so as to require package leaflets for medicinal products to be drawn up in accordance with the substituted Article 59 and to require applicants for marketing authorisation to submit the results of consultations with target patient groups to ensure that such leaflets are clear, legible and easy to use	The 1994 Regulations provide that marketing authorisation holders must comply with obligations imposed by "the relevant Community provisions", including the 2001 Directive (regulation 7). Regulation 3(2)(a)(i) and (ii) of the Amending Regulations amends the definition of the 2001 Directive so as to ensure that marketing authorisation holders must comply with the obligations set out in the amended Articles 59 and 61(1) of the 2001 Directive. Regulation 3(5) of the Amending Regulations amends Schedule 6 to the 1994 Regulations so as to make transitional provision for the application of these obligations to products on the market before 30 July 2005 (or 30 October 2005 in the case of products authorised under the centralised Community procedure) Paragraphs 11 and 12 of Schedule 3 to the 1994 Regulations make it a criminal offence for marketing authorisation holders and, in certain circumstances, other persons, to supply a medicinal product if the package leaflet does not comply with the requirements of the 2001 Directive.	As above
1(54)	To insert new Article 74a of the 2001 Directive, so as to provide that where a change of classification of a medicinal product has been authorised on the basis of significant pre-clinical tests or clinical trials, the competent authority may not refer to the results of those tests or	The 1994 Regulations provides that the Licensing Authority must carry out the responsibilities of the competent authority under the 2001 Directive (regulation 3) and must determine applications for the grant, renewal or variation of a marketing authorisation in accordance with the provisions of the 2001 Directive (regulation 4). Regulation 3(2)(a)(i) and (ii) of the Amending Regulations amends the definition of the 2001 Directive so as	Regulations made by the Secretary of State for Health. Licensing Authority (which acts by the Medicines and Healthcare products Regulatory Agency (MHRA)) responsible for carrying out functions of UK competent authority.

	trials, when examining a change of classification for the same substance within one year of the initial change.	to ensure that the licensing authority must comply with the obligation set out in the new Article 74a of the 2001 Directive.	