EXPLANATORY MEMORANDUM TO

THE HUMAN MEDICINES REGULATIONS 2012

2012 No. 1916

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.

2. Purpose of the instrument

2.1. The Human Medicines Regulations 2012 ("the Regulations") repeal or revoke most existing United Kingdom legislation regulating the authorisation, sale and supply of medicinal products for human use – comprising an Act and a large number of statutory instruments – and consolidate their effect in one place and in rationalised form.

2.2. During the consolidation exercise, the MHRA also reviewed the legislation to identify policy changes that would help ensure that the regulatory framework for medicines remains fit for purpose. Those changes are summarised below.

2.3. In addition, the Regulations remove an existing exemption from wholesale dealing licensing requirements in order to ensure compliance with EU law, and implement an EU Directive introducing modified requirements for the monitoring of the safety of medicines in clinical use and taking appropriate action to minimise risk ("pharmacovigilance").

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

3.1. None

4. Legislative Context

4.1. United Kingdom medicines legislation establishes a comprehensive regime for the authorisation of medicinal products for human use, for the manufacture, import, distribution, sale and supply of those products, for their labelling and advertising, and for pharmacovigilance. It provides for the protection of public health by ensuring that medicines meet appropriate standards of safety, quality and efficacy. Most of the topics covered by the legislation are now the subject of EU enactments, most notably Directive 2001/83/EC of the European Parliament and of the Council on the Community code relating to medicinal products for human use ("the Directive").

4.2. The legislation being consolidated comprises the greater part of the Medicines Act 1968 ("the Act"), many principal statutory instruments and an even greater number of amending instruments, some made under the Act and some under the European Communities Act 1972. These have reflected developments in pharmaceuticals, wholesale trade, regulatory practice and

EU harmonisation. This has resulted in a legislative framework that is fragmented, complex, poorly structured and in places obsolete. The Regulations consolidate the effect of nearly all this legislation, mostly under powers in the European Communities Act 1972. The Regulations also provide for the enforcement in the United Kingdom of Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. Regulation (EC) No 726/2004 covers much the same topics as the Directive, but in relation to products based on new active substances for treatment of certain major diseases, and to certain advanced or biological medicines.

4.3. The Regulations leave parts of the Act in place. This principally concerns Part IV of the Act, which deals with the registration and conduct of pharmacies. Also retained are certain powers to make secondary legislation in areas that fall outside the scope of the Directive. Enforcement and other ancillary provisions of the Act are retained with appropriate amendments to support these.

4.4. Certain pieces of medicines legislation have not been consolidated. Legislation concerning clinical trials, the administration of radioactive medicinal products and fees charged by the MHRA for the administration of procedures under the provisions being consolidated are left in place. They have been, or will be, subject to changes as part of separate policy initiatives, so it would have been unhelpful to consolidate them at this point; in addition, the administration of radioactive medicinal products and fees are governed by Directives other than Directive 2001/83/EC. Consideration will however be given to consolidating them in the future. Various orders made under section 62 of the Act to prohibit the sale, supply and importation of products containing particular substances will also remain in force along with section 62, because prohibitions of this sort are outside the scope of the Directive.

4.5. The Regulations implement for the first time Directive 2010/84/EU of the European Parliament and of the Council amending as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use ("Directive 2010/84/EU"). Directive 2010/84/EU introduces a strengthened, clarified and more proportionate regime for pharmacovigilance (monitoring the safety of medicines in clinical use) in the EU market. Provisions implementing it are mainly in Part 11 of the Regulations.

4.6. The Commons and Lords EU Committees were consulted on the proposed UK negotiating position on this set of proposals and kept informed as negotiations on the Directive progressed. The final texts were cleared by both Committees.

4.7. Finally, the Regulations repeal section 10(7) of the Medicines Act 1968 without consolidating it. This exempts pharmacists from the need for a

wholesale dealer's licence if wholesale dealing forms only an inconsiderable part of their business, but is not compatible with the Directive.

5. Territorial Extent and Application

5.1. This instrument applies to all of the United Kingdom

6. European Convention on Human Rights

The instrument is subject to the negative resolution procedure but amends primary legislation.

Earl Howe has made the following statement regarding Human Rights: In my view the provisions of the Human Medicines Regulations 2012 are compatible with the Convention rights.

7. Policy background

7.1. The Regulations aim to simplify medicines legislation and improve its accessibility for users. As has been the case with the existing legislation, it will be necessary to update the new legislation over time to reflect changes in practice and scientific advances. The MHRA will keep the legislation and subsequent amendments under review and consolidate the legislation again in the future when it becomes appropriate to do so. It will also publish interim informal consolidations on its website.

7.2. The Regulations also introduce the following policy changes, identified during the consolidation exercise as improvements to help ensure that the regulatory framework remains fit for purpose.

Removal of statutory warnings

7.3. Legislation has hitherto required that standardised warnings in prescribed form, known as "'statutory warnings", were included on labelling and in patient information leaflets for certain over the counter medicines to ensure patients received clear warnings, and that these warnings were consistent across products with the same active ingredient. The Regulations remove most statutory warnings. In their place, the MHRA will rely on the inclusion of warnings specific to products or classes of medicinal products as terms of marketing authorisations. This will allow warnings to reflect the results of user testing and be changed without the need for legislative action, and will avoid the burden of recalling medicines from the supply chain when warning requirements in legislation are changed.

7.4. The Regulations retain statutory warnings for paracetamol, which poses particular dangers in relation to overdose, in order to ensure that consistent warnings are employed across the wide range of products. The Regulations update these warnings to reflect the findings of user testing undertaken by the British National Formulary.

Changes to membership criteria for the review process of licensing decisions

7.5. The Regulations require the licensing authority to appoint a panel to review their licensing decisions at the request of applicants in certain circumstances. Legislation has hitherto excluded former members of the medicines advisory bodies[1] from the membership of this panel. This restriction was intended to address the risk of members having a conflict of interest, but responses to consultation agreed that this went beyond what was necessary to address that risk. The Regulations accordingly revise the restriction so that former members of medicines advisory bodies can be appointed providing that one year has elapsed since their term of office on any such body has expired.

Sale, supply and administration exemptions

7.6. Medicines legislation provides exemptions to the requirements that certain medicines may only be supplied in response to a prescription by a person entitled to prescribe, or may only be administered by injection by such person; that other medicines may only be sold or supplied in a registered pharmacy; and that even medicines on general sale may only be sold in certain premises and on certain conditions. The Regulations remove a number of obsolete exemptions, amend or extend some current exemptions, and introduce some new exemptions in order to reflect modern clinical practice.

Patient group directions

7.7. Patient group directions ("PGDs") are written directions for the sale, supply or administration of a description or class of medicines to persons generally in a defined clinical situation. A PGD must be signed by a doctor or dentist and a pharmacist, and be authorised by a relevant body as defined in the legislation. The PGD will contain other requirements relating to the groups of registered health professionals who can use it and the circumstances in which they apply. The Regulations update the process by which independent hospitals, clinics and agencies are able to continue using PGDs to ensure processes reflect changes to the registration requirements for organisations.

7.8. The Health and Social Care Act 2012 includes changes to the structure of the NHS which have implications for the PGD regime. Amendments will be made to the Regulations after they come into force to ensure that the PGD regime can continue to operate fully when the 2012 Act takes effect.

Optimisation of medicines use

7.9. Legislation has hitherto provided that if, in the exercise of professional skill and judgement they believe it is appropriate to do so, a pharmacist may make changes to a prescription relating to the name of the product or its common name; directions for use of the product; and precautions relating to the use of the product. This allows pharmacists to change prescriptions in order to "optimise" patients' use of medicines, for example by changing the

[1] The Commission on Human Medicines or any of its Expert Advisory Groups; and the Advisory Board on the Registration of Homeopathic Products, the Herbal Medicines Advisory Committee and the British Pharmacopoeia Commission or any of their sub-committees.

dose or duration for which the medicines is taken, but keeping within the overall ceiling of the dosage or timeframe originally prescribed. The legislation has stated that the pharmacist can only make such changes if they have attempted to contact the prescriber but have been unable to do so. The Regulations remove this requirement, with the aim of enabling pharmacists to use their expertise and professional judgement to make such changes in a more timely way.

Section 10(7) of the Medicines Act 1968

7.10. The Regulations repeal section 10(7) of the Act. Section 10(7) allows pharmacists to wholesale deal medicines without a wholesale dealer's licence where that dealing constitutes no more than an inconsiderable part of that business. It is not compatible with Directive 2001/83/EC, which requires that anyone wholesaling medicines must hold a wholesale dealer's licence. The provision is therefore being repealed, but the MHRA has provided advice to the pharmacy profession to ensure that appropriate supply of medicines within the healthcare service can continue. Pharmacists will however incur additional costs if they wish to trade commercially in medicines, because they will be required to become licensed wholesale dealers in order to ensure compliance with EU law.

Directive 2010/84/EU

7.11. Directive 2010/84/EU amends the pharmacovigilance framework in the Directive. The amendments made by Directive 2010/84 /EU are intended to establish clear roles and responsibilities for authorisation holders and for regulators; introduce greater involvement of patients and healthcare professionals in reporting safety issues arising from the use of medicines; and strengthen authorisation holders' pharmacovigilance systems whilst reducing administrative burdens, providing the means for a greater focus on collective EU decision making on safety issues.

7.12. Directive 2010/84/EU is implemented by Part 11 (Pharmacovigilance) of the Regulations in the main. Where the changes made by Directive 2010/84/EU apply to other areas of the Regulations, they are reflected in the relevant Part. For example, provisions which (i) require that risk management plans are submitted as part of the authorisation application process; and (ii) allow authorisations to be granted subject to pharmacovigilance-based conditions are both implemented in Part 5 (Marketing Authorisations). The transposition note for Directive 2010/84/EU is attached.

8. Consultation outcome

8.1. The MHRA held a number of consultations on the Regulations and the changes they introduce. In addition, other government departments and the devolved administrations have been closely involved in the development of the proposals. The Regulations were notified in draft to the European Commission under the Technical Standards and Regulations Directive 98/34/EC. No concerns were raised.

Consolidation

8.2. The MHRA published a concept paper in January 2009 that described the consolidation and solicited topics for review. In 2010 and 2011 it published a number of informal consultations on an early draft of the Regulations and ideas for potential policy changes. From 25 October 2011 to 17 January 2012 it ran a formal 12 week consultation, *MLX 375: Consolidation and Review of UK Medicines legislation*. This presented a further draft of the Regulations; explained the drafting approach; asked whether the Regulations successfully met the aims of consolidation; and set out proposals for policy changes.

8.3. The MHRA made the formal consultation document publicly available on its website and alerted over 700 stakeholders by email. These included pharmaceutical industry bodies; professional, trade and negotiating pharmacy bodies; the NHS; Royal Colleges; and patient associations. The consultation received 204 responses, of which 199 gave specific comments and the remaining five gave general support and/or no comments. A full analysis of the consultation is available on the MHRA's website.

8.4. Overall, the responses demonstrated broad support among stakeholders for the approach to consolidation and the structure of the Regulations. A number of drafting changes were made in response to those comments to ensure that the Regulations accurately consolidate existing law or to improve clarity where possible. In addition, the MHRA will update guidance to clarify the meaning of the Regulations in a number of cases.

8.5. There was generally support for the proposed policy changes outlined above. The most notable change made by the MHRA as a result of the consultation was to retain statutory warnings for paracetamol due to the specific dangers it poses in relation to overdose. The other changes were some small adjustments to the proposals on sale, supply and administration exemptions and PGDs, in order to ensure that changes reflected healthcare delivery arrangements and did not inadvertently disadvantage those who currently benefit from the provisions.

8.6. Some concerns were raised – mostly from the pharmaceutical industry – that the optimisation proposal would enable pharmacists to substitute generic medicines for branded versions detailed in the original prescription, and that there would be safety risks if pharmacists made other substantive changes to the prescription without consulting the prescriber. The MHRA and the Department for Health, which has policy responsibility for this area, have clarified with industry bodies that the change is not intended to, and does not, facilitate the substitution of generic medicines. The Department of Health will work with the relevant regulatory and professional bodies to ensure that guidance is in place to support the decisions made by pharmacists.

8.7. Many responses provided commented on issues related to medicines legislation but on which the consultation was not specifically seeking views, and the MHRA will address these in detail in its published response. Of

particular note were concerns expressed by the homeopathic medicines sector (103 responses) that the consolidation should allow the continuation of pharmacy supply of unlicensed homeopathic medicines by present routes. The MHRA has clarified with homeopathic interests that the consolidation does not, and is not intended to, change either the current regulatory status or the longstanding regulations governing the sale and supply of homeopathic products. Any reforms to provisions for homeopathy would require further consideration and consultation after the Regulations come into force.

Section 10(7) of the Medicines Act 1968

8.8. The issue of section 10(7) of the Act and compliance with EU obligations was subject to two formal consultations – *MLX 357: Consultation on measures to strengthen the supply chain and reduce the risk from counterfeit medicines* (published December 2008) and *MLX 365: Measures to strengthen the medicines' supply chain and reduce the risk from counterfeit medicines* (published December 2009). The MHRA set out its intention to remove the exemption in MLX 375. A number of responses set out concerns that this would restrict the supply of medicines to other bodies for public health needs (as opposed to commercial purposes). As set out above, the MHRA has subsequently provided advice to the pharmacy profession to ensure that appropriate supply of medicines within the healthcare service can continue.

Directive 2010/84/EU

8.9. The draft Regulations consulted on in MLX 375 did not include provisions implementing Directive 2010/84/EU. Instead, a separate 12 week public consultation on implementation of Directive 2010/84/EU was held between 6 December 2011 and 28 February 2012 – *MLX 374: Transposition of Pharmacovigilance Directive 2010/84/EU.* A full analysis of the consultation is available on the MHRA's website.

8.10. A concern raised in response to this consultation was the approach the MHRA had taken to define what is meant by "regular" with respect to undertaking audits – i.e. stating that for audit by marketing authorisation holders "regular" means at least once every 2 years. Respondents were concerned that this timeframe was not stated in the Directive nor in line with the idea of a risk based approach. This frequency had been proposed in line with the first draft of the related EU Implementing measures. However, those measures have since been amended to state that a risk-based approach should be taken, and the MHRA has amended the Regulations accordingly.

8.11. Another concern was that one of the proposed offences should not have been so designated, as it described an opportunity rather than an obligation. This was as the result of an incorrect cross-reference in the draft text. The cross reference has now been amended.

8.12. There was also a concern that the MHRA had applied a definition of post-authorisation study when one had not been agreed at EU level. The definition has been retained in the Regulations to ensure clarity. However, the MHRA has raised this issue for discussion within Europe so that a

common definition can be agreed, and will amend the Regulations in due course if necessary.

8.13. In many of the responses, further information or clarification was sought on the following issues:

- audit of pharmacovigilance systems (9 responses)
- risk management systems (6 responses)
- infringement notice (6 responses)
- penalties (5 responses)
- requirements for periodic safety update reports (5 responses)
- transition to the new pharmacovigilance system master file (3 responses)
- reporting of suspected adverse drug reactions during transition (2 responses)

8.14. Guidance being developed at European level will address many of these requests for clarification. In addition, a dedicated page on Directive 2010/84/EU has been established on the MHRA website and will be updated with questions and answers over the coming months. The MHRA has also set up a dedicated email address for further questions and comments. This will ensure that there is clarity on all these matters.

8.15. All the consultations above are available on the MHRA website: www.mhra.gov.uk.

9. Guidance

9.1. As the Regulations are predominantly a consolidation exercise, they largely contain the same provisions as in existing law, but in a different place. The MHRA will publish tables of origins and destinations so that the movement of these provisions can be tracked, and will also ensure that legislative references in existing guidance are updated where necessary. The MHRA will also publish a briefing document explaining the few instances where consolidation has changed the meaning of the law and setting out any new obligations in plain English.

9.2. In relation to implementation of Directive 2010/84/EU, which introduces new provisions, the EU will publish guidance to accompany the new EU legislative provisions on pharmacovigilance. This guidance is currently being developed and will aim to ensure consistent application across the EU. It will also explain the obligations imposed by Directive 2010/84/EU in non-legal terms. The MHRA will only supplement this guidance if further clarity is requested by marketing authorisation holders.

9.3. All guidance documents will be available on the MHRA website.

10. Impact

10.1. The impact on business, charities or voluntary bodies is as follows:

	Net Present Value[2] (£ million)
Consolidation	8.6
Implementation of Directive 2010/84/EU	-39.7
Repeal of section 10(7)	-28.3

10.2. The impact on the public sector is as follows:

	Net Present Value (£ million)
Consolidation	0.4
Implementation of Directive 2010/84/EU	22.7
Repeal of section 10(7)	0

10.3. Impact Assessments are attached to this memorandum and will be published alongside the Explanatory Memorandum on www.legislation.gov.uk. The Regulatory Policy Committee has rated the impact assessments fit for purpose.

11. Regulating small business

11.1. The legislation applies to small business.

11.2. The MHRA consulted with bodies representing small businesses about the impact of the consolidated medicines legislation and the policy changes identified in review of the legislation. Consolidation is a de-regulatory measure that will deliver benefits to businesses of all sizes, including small businesses.

11.3. There was in principle an option to exempt such businesses from consolidation – that is, to retain the existing legislation and apply it just to such businesses – and also from the policy changes. However, this was discounted on the basis that it would disadvantage them to be exempted from de-regulatory measures.

11.4. The MHRA consulted extensively with the pharmacy sector on the implications of the necessary repeal of section 10(7) and explored a number of scenarios. The approach that the MHRA have taken has been broadly welcomed by those on whom it impacts as being the most pragmatic and least burdensome solution to the problem. Its main impact will fall on small businesses such as independent pharmacies if they wish in the future to trade commercially in medicines.

11.5. There is no scope for exempting small businesses from provisions in the pharmacovigilance Directive, as EU medicines legislation is based on the principle that harmonised requirements applying to all medicines in all Member States provides the basis for free movement of medicines throughout the EU. Any exemption from these provisions would be contrary

[2] The Net Present Value is the value (benefits less costs) of the intervention over a ten year period and discounted at the HM Treasury social discount rate of 3.5%.

to EU law and would commercially disadvantage these businesses. Furthermore, the EU impact assessment for this legislation – although it does not provide an in-depth analysis of the impacts on small firms – does conclude that SMEs will disproportionately benefit from the cost-saving measures as it specifically reduces some of the regulatory burdens on them.

12. Monitoring & review

12.1. The MHRA will monitor how successfully the Regulations meet the goal of simplifying the structure of the law and improving its accessibility for users. This will include recording any comments and queries that interested parties raise, and any issues or areas for improvement identified within the MHRA.

12.2. As set out above, the MHRA also intends to remake the Regulations periodically to consolidate amendments that have been made to them. As part of this process, we will seek to address issues identified internally and externally, and when consulting on the draft legislation will seek further suggestions to simplify or improve the accessibility of the legislation.

12.3. The MHRA will carry out reviews of the policies contained in the legislation as part of the MHRA's Regulatory Excellence programme, which will aim to ensure that the MHRA fully meets better regulation principles. The MHRA will publish the results of these reviews, and will consult fully with interested parties on any proposed policy changes

12.4. In accordance with the Government guidance on sunsetting, the Regulations contain a provision requiring that the provisions implementing Directive 2010/84/EU and repealing section 10(7) of the Medicines Act 1968 are reviewed within five years of the Regulations coming into force.

13. Contact

Daniel Markson at the MHRA Tel: 020 3080 6405 or email: daniel.markson@mhra.gsi.gov.uk can answer any queries regarding the instrument.

TRANSPOSITION NOTES

Directive 2010/84/EU of the European Parliament and of the Council of 15th December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use.

The new Directive amends Directive 2001/83/EC on the Community code relating to medicinal products for human use (the Medicines Directive) as regards pharmacovigilance. Pharmacovigilance is the monitoring of the safety of medicines.

The new Directive makes substantial changes to existing pharmacovigilance requirements to strengthen public health protection. The UK government is required to implement these changes in law by July 2012.

The main changes to the Medicines Directive introduced by the new Directive are:

- providing for clear roles and responsibilities for key responsible parties and clear obligations against which they perform their roles in relation to pharmacovigilance;
- rationalising EU decision-making on drug safety issues in order to deliver measures that are equally and fully implemented for all relevant products and across the community with a view to preventing unnecessary patient exposure to risks;
- strengthening medicines safety transparency and communication to increase the understanding and trust of patients and health professionals in the safety of medicines and improve the penetration of key warnings;
- strengthening companies' pharmacovigilance systems, allowing companies to improve their systems constantly while reducing administrative burden;
- ensuring the proactive and proportionate collection of high-quality data relevant to the safety of medicines through risk management systems and structured data collection in the form of post authorisation safety studies, together with rationalised reporting of suspected adverse drug reactions (ADRs);
- involving stakeholders in pharmacovigilance including through direct patient reporting of suspected ADRs and inclusion of patients and heath-care professionals in decision-making; and
- simplifying the current community pharmacovigilance procedures with efficiency gains for both the pharmaceutical industry and medicines regulators.

The new Directive is transposed by the Human Medicines Regulations 2012 which also serve to consolidate the majority of medicines legislation in the United Kingdom.

Article of Directive 2010/84	Article of Directive 2001/83 affected	Objective	Implementation (references are to the Human Medicines Regulations 2012 unless otherwise stated)
1(1)	1	Amends defined terms	Regulation 8 [j002] (general interpretation)
1(2)	8(3)	Amends list of documents that must accompany an application for a marketing authorisation (MA) or traditional herbal registration (THR)	Schedule 8, Part 1 in relation to MAs; Schedule 12, Part 1 in relation to THRs

1(3)	11	Amends material that must be included in the summary of product characteristics (SPC) in relation to MAs & THRs	Schedule 8, Part 2 in relation to MAs; Schedule 12, Part 2 in relation to THRs
1(4)	16(g)(1)	Amends provision applying provisions of the 2001 Directive to THRs to include Title IX provisions.	Part 7 (traditional herbal registrations) Part 11 (pharmacovigilance)
1(5)	17	Corrects an erroneous cross reference	No transposition needed
1(6)	18	Corrects an erroneous cross reference	No transposition needed
1(7)	21	Amends obligations on national competent authorities (NCAs) relating to assessment reports and the publication of product information	Regulation 64 [J190] (duties of licensing authority in connection with determination)
1(8)	21a	Enables MAs to be granted subject to conditions	Regulation 59 [j106B] (conditions of a UK marketing authorisation: general)
1(9)	22	Enables MAs to be granted subject to conditions in exceptional circumstances	Regulation 60 [j106A] (conditions of UK marketing authorisation: exceptional circumstances) in relation to MAs; Regulation 105 [j310] (conditions of certificate of registration) in relation to HCR
1(10)	22a	Enables the licensing authority to impose obligations on MAH in relation to conducting efficacy or safety studies	Regulation 61 [j106C] (conditions of UK marketing authorisations: new obligations post-authorisation)
Article 1(10)	22b	Enables the Commission to adopt implementing measures	No transposition needed
1(10)	22c	Creates an obligation on MAH and Member States (MS) arising from grant of conditions	Regulations 59(6) [J106B], (conditions of a UK marketing authorisation: general), 60(11) [j106A] (conditions of UK marketing authorisation: exceptional circumstances) and 61(14) [j106C] (conditions of UK marketing authorisations: new obligations post-authorisation) in relation to the obligation on MAH Regulations 59(5), 60(10), 61(13) in relation to the obligation on MS
1(11)	23	Amends post-authorisation obligations on MAH	Regulations 75 [j116C] (obligation to provide information relating to safety etc) & 76 [j116D] (obligation in relation to product information) in relation to MAs; regulations 115 [j315]

			and 116 [j315A] in relation to HCRs; and regulations 145 [j418] & 146 [418A] in relation to THRs In relation to last paragraph of article 23, regulation 182(5) [j455] (obligation on holder to operate pharmacovigilance system).
1(12)	24	Amends provisions relating to renewal of a MA.	Regs 65 [j107] (validity of UK marketing authorisation) and 66 [j107A] (application for renewal of authorisation) in relation to MAs; regulations 107 [j306] (validity of certificate of registration) & 108 [j307] (application for reneal of certificate) in relation to HCRs; and regulations 132 [j408] (validity of traditional herbal registration) & 133 [j409] (application for renewal of registration) in relation to THRs
1(13)		Removes a heading	No transposition needed
1(14)	27	Establishes an EU co-ordination group	No transposition needed
1(15)		Inserts a heading	No transposition needed
1(16)	31(1)	Amends EU aspects of mutual recognition and de-centralised procedures	No transposition needed
1(17)	36	Omits article 36	No transposition needed
1(18)	59	Amends the requirements in relation to package leaflets	Regulation 260 [j602] (package leaflets) and Schedule 27 [j602s] (package leaflets)
1(19)	63(3)	Creates exemptions to labelling and leaflet requirements	Regulation 266 [j604A] (language requirements etc)
1(20)		Substitutes a new title IX into Directive 2001/83	
1(20)	101(1) to (3)	Confers obligations on MS in relation to operation of pharmacovigilance system (PvS)	Regulation 179 [j452] (obligations on licensing authority to operate pharmacovigilance system)
1(20)	101(3):	Confers obligation on MS to designate competent authority for pharmacovigilance tasks	Regulation 6(4) [j013] (the licensing authority and Ministers)
1(20)	101(4):	Enables Commission to request MS participation	No transposition needed
1(20)	102	Confers obligations on MS in relation to pharmacovigilance	Regulation 178 [j451] (general obligations of licensing authority)

1(20)	102, second paragrap h	Enables MS to impose obligations on doctors, pharmacists and healthcare professionals (HCP)	No transposition needed - the UK does not wish to exercise this discretionary power as its exercise would impose additional burdens on healthcare professionals
1(20)	103	Enables and Confers obligations on MS in relation to the delegation of Title IX functions to other MS	Regulation 181 [j454] (delegation of obligations under this Part)
1(20)	104(1) to (3):	Confers obligation on holders relating to the operation of PvS, how to use PvS; audit of the PVS; and what must be delivered as part of the PvS.	Regulation 182 [j455] (obligations on holders to operate pharmacovigilance system) and regulation 185 [j457] (obligation on holder to audit pharmacovigilance system)
1(20)	104(4):	Enables NCA to request holders to have a national contact person for Pv.	No transposition needed - the UK is not exercising this power as exercise of the power would increase burden on industry
1(20)	104a	Creates an exception to obligation under article 104 that holders must operate risk management system (RMS); and discretionary power for NCA to impose obligation to do so (with procedural provisions)	Regulation 183 [j456] (exception to obligation to operate risk management plan)
1(20)	105	Makes provision for fund management	No transposition needed
1(20)	106	Confers obligations on MS in relation to national medicines web-portal	Regulation 203 [j473] (obligations on licensing authority in relation to national medicines web-portal)
1(20)	106a	Confers obligations in relation to public announcement	Regulation 204 [j474] (obligations on licensing authority in relation to public announcements) and regulation 205 [j475] (obligations on holders in relation to public announcements). Also Data Protection Act and common law of confidentiality.
1(20)	107	Confers obligations on holders in relation suspected adverse reaction	Regulations 187 [j444] (recording obligations on holders) and 188 [j445] (reporting obligations on holders)
1(20)	107a	Confers obligations on MS in relation to suspected adverse reactions reports; and a discretionary power for MS to involve to holders in the follow up of reports	Regulation 185 [j458] (recording obligations on licensing authority) and regulation 186 [j459] (reporting obligations on the licensing authority) in relation to the obligations No transposition needed for article 107a(5), second paragraph (obligation to ensure that authorities responsible for medicinal products within MS are informed); in the UK the

			licensing authority is the only UK authority responsible for medicinal products. No transposition needed in relation to the discretionary power – it will not be exercised in the UK as to do so would increase burdens on holders.
1(20)	107b	Confers obligations in relation to periodic safety update reports (PSURs)	Regulation 191 [j446] (obligation on holder to submit periodic safety update reports: general requirements) and regulation 192 [j462] (obligation on holder to submit periodic safety update reports: derogation from general requirements)
1(20)	107c	Makes procedural provisions on the frequency and date of PSUR submission; confers obligations on holders in relation to PSUR submissions and varying authorisations; obligation on EMA to make public harmonised frequency of PSUR submission; enables holders to request harmonised frequency and date of PSUR .	Regulation 191 [j446] (obligation on holder to submit periodic safety update reports: general requirements) and regulation 193 [j463] (harmonisation of PSUR frequency or date of submission)
1(20)	107d	Confers obligation on NCA in relation to assessment PSURs (where EU procedure does not apply)	Regulation 195 [j465] (obligation on licensing authority to assess PSURs where EU single assessment procedure does not apply)
1(20)	107e	Makes procedural provisions in relation to EU single assessment of PSURs	No transposition needed
1(20)	107f	Confers obligation on NCA post-PSUR assessment (where EU procedure does not apply)	Regulation 195 [j465] (obligation on licensing authority to assess PSURs where EU single assessment procedure does not apply)
1(20)	107g	Makes procedural provisions in relation to post-EU single assessment of PSURs; obligation on CA to implement EU agreed position post PSUR-assessment	No transposition needed for EU procedural matters. Regulation 194 [j464] (responding to a single assessment of PSUR under article 107e of the 2001 Directive).
1(20)	107h	Confers obligations on MS/NCA, PRAC, EMA and holders in relation to signal detection.	Regulation 189 [j460] (signal detection: licensing authority obligations) and regulation 190 [j461] (signal detection: holder obligation)

1(20)	107i	Confers obligations on MS, Commission and EMA in relation to urgent EU procedure; discretionary power to MS to take (urgent) action to protect public health pending EU determination	Regulation 196 [j466] (urgent action)
1(20)	107j	Confers obligation on EMA to announce initiation of EU urgent procedures on EU web port; discretionary power for MS to announce in parallel on national web portal; mandatory content of the announcement; provision on the EU procedure	Regulation 197 [j467] (EU urgent action procedure)
1(20)	107k	Creates an EU urgent action procedure in relation to safety concerns; obligation on MS to implement EU agreement; Confers obligation on holder to submit variation application (if variation required under agreement)	Regulation 197 [j467] (EU urgent action procedure). No transposition required for EU procedural matters & obligations on EU bodies
1(20)	107l	Confers obligation on EMA to make public EU determinations under urgent action procedure through EU web portal	No transposition needed
1(20)	107m	Makes provision in relation to specified post authorisation safety studies provisions	Regulation 198 [j468] (post-authorisation safety studies: general provisions)
1(20)	107n	Makes provision in relation to submission of protocol for mandatory post authorisation safety studies	Regulation 199 [j469] (submission of draft study protocols for required studies)
1(20)	107o	Makes provision in relation to protocol amendments for mandatory post authorisation safety studies	Reg 200 [j470] (amendment to study protocols for required studies)
1(20)	107p	Makes provision in relation to completed mandatory post authorisation safety studies	Regulation 201 [j471] (submission and evaluation of final study reports for required studies)
1(20)	107q	Enables PRAC to make post-study recommendations; EU procedure for dealing with	Regulation 202 (follow-up of final study reports).

		PRAC recommendation & reaching agreement; Confers obligation on MS to implement EU agreement; Confers obligation on holder to submit application for variation (where required by EU agreement)	No transposition needed for EU procedure and obligations on EU bodies.
1(20)	108	Confers obligation on Commission to adopt implementing measures to harmonise the performance of pharmacovigilance activities under 2001 Directive	No transposition required
1(20)	108a	Confers obligation on EMA to draw up guidance	No transposition required
1(20)	108b	Confers obligation on Commission to report on MS performance of pharmacovigilance tasks	No transposition required
1(21)	111	Amends inspection provisions	Regulations 327 [j706] (powers of inspection, sampling and seizure) and 331 [j710A] (finding and reports of inspections)
1(22)	116	Amends the circumstances in which an authorisation or registration may be suspended, varied or revoked.	Regulation 68 [j111] (revocation, variation and suspension of marketing authorisation) in relation to MAs, regulation 110 [j309] (revocation, variation and suspension of registration) in relation to HCRs and regulation 135 [j412] (revocation, variation and suspension of traditional herbal registration) in relation to THRs
1(23)	117	Amends the circumstances in which supply may be prohibited.	Regulation 69 [j112] (suspension of use etc of relevant medicinal product) in relation to MAs; and regulation 138 [j413] (suspension of use etc of traditional herbal registration) in relation to THRs.
1(24)	121a	Enables Commission to adopt delegated acts	No transposition needed
1(24)	121b	Enables European Parliament and Council to revoke Commission's power to make delegated acts.	No transposition needed
1(25)	121c	Makes provision in relation to delegated acts	No transposition needed
1(25)	122	Requires that inspection reports are sent electronically and can be requested by EMA.	No transposition required

1(26)	123(4)	Transfers responsibility for making public information on prohibited and withdrawn medicinal products from Commission to EMA.	No transposition needed
1(27)	126a	Amends provision relating to article 126a authorisations	Regulations 157 [j187A] (requests from other member states) and 266 [j604A] (language requirements etc)
1(28)	127a	Amends the Commission's power to adopt decisions addressed to MS in relation to centralised products	No transposition required.
2	n/a	Transitional provisions	Regulation 212 [j480] (transitional arrangements) and Schedule 33 [j480s] (transitional arrangements: pharmacovigilance)
3	n/a	Transposition	No transposition needed
4	n/a	Entry into force	No transposition needed.
5	n/a	Addressee	No transposition needed