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REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL

on the exercise of the delegation conferred on the Commission pursuant to Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use and pursuant to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency

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1. INTRODUCTION

The EU legal framework for medicinal products for human use is intended to ensure a high level of public health protection and to help the internal market function effectively. Moreover, the measures taken should encourage innovation. The framework works on the principle that medicinal products are placed on the market only if granted marketing authorisation by the competent authorities.

The requirements and procedures for authorising the marketing of medicinal products for human use, and the rules on continuous supervision of products after they have been authorised, are laid down principally in Directive 2001/83/EC[1] ('the Medicinal Product Directive') and Regulation (EC) No 726/2004[2] ('the Regulation'). These texts also lay down harmonised provisions in related areas such as the manufacture, wholesale distribution and advertising of medicinal products for human use. They cannot properly be understood in isolation from one another but must instead be considered together.[3]

The Medicinal Product Directive, as amended by Directive 2010/84/EU[4] and Directive 2011/62/EU[5], empowers the Commission to adopt delegated acts on post-authorisation efficacy studies (Article 22b), the principles of good manufacturing practice for active substances (Article 47), criteria to assess the potential falsified character of medicinal products transiting through the EU (Article 52b) and safety features for medicinal products (Article 54a).

The Regulation, as amended by Regulation (EU) No 1235/2010[6], empowers the Commission to adopt delegated acts on post-authorisation efficacy studies (Article 10b).

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1 Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, OJ L 311, 28.11.2001, p. 67.

2 Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency, OJ L 136, 30.4.2004, p. 1.

3 AG Sharpston in Case C-535/11, *Novartis Pharma* v *Apozyt*, ECLI:EU:C:2013:53, paragraph 47.

4 Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 348, 31.12.2010, p. 74.

5 Directive 2011/62/EU of the European Parliament and of the Council of 8 June 2011 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use, as regards the prevention of the entry into the legal supply chain of falsified medicinal products, OJ L 174, 1.7.2011, p.74.

6 Regulation (EU) No 1235/2010 of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance of medicinal products for human use, Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal

2. LEGAL BASIS

The present report is a requirement under Article 121a(1) of the Medicinal Product Directive and Article 87b(1) of the Regulation. These provisions delegate powers to the Commission for five years from January 2011 and require it to report on its exercise of those powers at the latest six months before the end of this period.

3. EXERCISE OF THE DELEGATION

During the period the Commission adopted two delegated acts, one on post-authorisation efficacy studies and the other on the principles of good manufacturing practice for active substances. In both cases, the exercise of the empowerment responds to the need to supplement non-essential elements of a legislative act.

3.1. Delegated act on post-authorisation efficacy studies

Under Article 21a(f) of the Medicinal Product Directive and Article 9(4)(cc) of the Regulation, it may be necessary in specific situations to complement the data available at the time a medicinal product was granted marketing authorisation with additional information on its efficacy, to address concerns that could not be resolved before the authorisation was granted. Moreover, under Article 22a(1)(b) of the Directive and Article 10a(1)(b) of the Regulation, information that becomes available post-authorisation may necessitate significant revision of previous efficacy evaluations and call for additional, confirmatory efficacy data while the marketing authorisation is maintained. In both situations, the national competent authorities, the European Medicines Agency and the Commission may oblige the marketing authorisation holder to conduct a post-authorisation efficacy study.

Under Article 22b of the Medicinal Product Directive and Article 10b of the Regulation, the Commission is empowered to specify the situations in which post-authorisation efficacy studies may be required. The same provisions give the Commission discretionary powers in deciding whether to adopt a delegated act. That said, the Directive and the Regulation require that any post-authorisation efficacy study imposed as an obligation on the marketing authorisation holder 'shall be based on the delegated act'. This implies that a delegated act is a pre-condition for imposing post-authorisation efficacy studies. For the application of the new approach, it was therefore considered necessary to adopt a delegated act.

Moreover, the delegated act increases predictability and transparency regarding situations in which post-authorisation studies may be required.

The Expert Group[7] formed by the Pharmaceutical Committee was consulted on the subject of the draft Commission Delegated Regulation. The consultation took place at the Expert Group's meeting of 4 June 2013 on the basis of a Commission working document. The Commission adopted the delegated act on 3 February 2014 and notified the European Parliament and the Council of it. Neither institution objected to the delegated act within the two-month period provided for in Article 121c of the Directive

products for human and veterinary use and establishing a European Medicines Agency, and Regulation (EC) No 1394/2007 on advanced therapy medicinal products, OJ L 348, 31.12.2010, p. 1.

7 Expert groups that help the Commission in relation to the preparation of delegated acts are listed in the Register of Commission Expert groups: http://ec.europa.eu/transparency/regexpert/.

and Article 87d of the Regulation. Commission Delegated Regulation (EU) No 357/2014 was published in the Official Journal[8] and entered into force on 30 April 2014.

3.2. Delegated act on good manufacturing practice for active substances

Directive 2011/62/EU amends the Medicinal Product Directive by introducing new provisions on the manufacturing of active substances, the active ingredients of medicines. These provisions aim to ensure that only active substances that are safe and of high quality are used in the manufacturing of medicines in the Union.

As a result of this amendment, since 2 January 2013 the manufacturing of active substances has been subject to good manufacturing practice for active substances regardless of whether the substances are manufactured in the Union or imported. In addition, manufacturers of medicinal products are now obliged to use only active substances manufactured in accordance with the principles and guidelines of good manufacturing practice for such substances.

In this context, it is necessary to set EU-wide standards for the manufacturing of active substances and to harmonise the implementation and enforcement of these standards throughout the EU. To this end, Article 47(3) of the Medicinal Product Directive mandates the Commission to adopt, by means of delegated acts, measures supplementing the provisions of that Directive on good manufacturing practice for active substances.

To prepare a Commission delegated regulation 'on the principles and guidelines of good manufacturing practice for active substances in medicinal products for human use', an Expert Group 'on the preparation of delegated acts relating to manufacturing, import and introduction of medicinal products for human use and their active substances' was set up. It was consulted on 21 September 2012 and — in writing — in September 2013. The Commission adopted the delegated act on 28 May 2014 and notified the European Parliament and the Council of it on 17 July 2014. The European Parliament decided to extend the deadline for objections until 17 November 2014, in accordance with Article 121c of the Medicinal Product Directive, but neither it nor the Council issued any objections. Commission Delegated Regulation (EU) No 1252/2014 was published in the Official Journal[9] and entered into force on 15 December 2014.

3.3. Other delegations

As regards the delegation in Article 54a of the Medicinal Product Directive, the Commission intends, before the end of 2015, to adopt a delegated regulation supplementing the Directive 'with regard to the detailed rules for the safety features appearing on the packaging of medicinal products for human use'.

To prepare this delegated regulation, the Commission carried out extensive consultations with interested parties. An Expert Group on the delegated act on safety features for medicinal products for human use was set up and met seven times between December 2011 and January 2015. The Commission met with key European associations

[8] Commission Delegated Regulation (EU) No 357/2014 of 3 February 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council as regards situations in which post-authorisation efficacy studies may be required, OJ L 107, 10.4.2014, p. 1.

[9] Commission Delegated Regulation (EU) No 1252/2014 of 28 May 2014 supplementing Directive 2001/83/EC of the European Parliament and of the Council with regard to principles and guidelines of good manufacturing practice for active substances for medicinal products for human use, OJ L 337, 25.11.2014, p. 1.

representing manufacturers, wholesale distributors and pharmacies in June 2011, December 2012, December 2013 and April 2014. In addition, a public consultation was held from 18 November 2011 to 27 April 2012.

The delegation in Article 52b of the Medicinal Product Directive allows — but does not oblige — the Commission to adopt a delegated act clarifying the criteria to be considered and the verifications to be made when assessing the potential falsified character of medicinal products introduced into the EU but not intended to be placed on the market. To this end, the Commission carried out a public consultation on a concept paper in April 2013. The consultation showed that Member States' and stakeholders' interest in the proposed measures was limited. Consequently, the Commission does not intend to initiate work on a delegated act at this stage.

4. CONCLUSION

To date the Commission has exercised the delegated powers provided for by Regulation (EC) No 726/2004 and in two of the four instances provided for by Directive 2001/83/EC.

The Commission is of the view that the delegated powers conferred by Articles 22b, 47, 52b and 54a of Directive 2001/83/EC, as amended by Directive 2010/84/EU and Directive 2011/62/EU, and by Article 10b of Regulation (EC) No 726/2004, as amended by Regulation (EU) No 1235/2010, should remain in force.