ANNEX I

MEDICINAL PRODUCTS TO BE AUTHORISED BY THE UNION

1. Medicinal products developed by means of one of the following biotechnological processes:
   - recombinant DNA technology,
   - controlled expression of genes coding for biologically active proteins in prokaryotes and eukaryotes including transformed mammalian cells.

2. Advanced therapy medicinal products as defined in Article 2 of Regulation (EC) No 1394/2007

3. Medicinal products for human use containing **an** active substance **which on 20 May 2004** was not authorised in the Union**. This shall not apply to allergen products or herbal medicinal products.**

4. Medicinal products that are designated as orphan medicinal products pursuant to this Regulation.

5. Medicinal products authorised in accordance with a paediatric use marketing authorisation.

6. Priority antimicrobial medicinal products as referred to in Article 40.

ANNEX II

LIST OF THE OBLIGATIONS REFERRED TO IN ARTICLE 166

(1) the obligation to submit complete and accurate particulars and **documentation** in an application for marketing authorisation submitted to the Agency or in response to obligations laid down in this Regulation to the extent that the failure to comply with the obligation concerns a material particular;

(2) the obligation to comply with conditions or restrictions included in the marketing authorisation and concerning the supply or use of the medicinal product for human use, as referred to in **Article 12 (4),** point (b) and in **Error! Reference source not found.** Article 13 second subparagraph;

(3) the obligation to comply with conditions or restrictions included in the marketing authorisation with regard to the safe and effective use of the medicinal product for human use as referred to in **Article 12(4)**, points (b), (d), (e), (f) and (g) and in **Article 13(1)**;

(4) the obligation to introduce any necessary variation to the terms of the marketing authorisation to take account of technical and scientific progress and enable the medicinal products for human use to be manufactured and checked by means of generally accepted scientific methods, as provided for in **Article 44(1)**;

(5) the obligation to supply any new information which may entail a variation to the terms of the marketing authorisation, to notify any prohibition or restriction imposed by the competent authorities of any country in which the medicinal product for human use is marketed, or to supply any information that may influence the evaluation of the risks and benefits of the product, as provided for in **Article 44(2)**;

(6) the obligation to keep product information up to date with current scientific knowledge, including the conclusions of the assessment and recommendations made public on the European medicines web-portal, as provided for in **Article 44(3)**;

(7) the obligation to provide, at the request of the Agency, any data demonstrating that the **benefit-risk** balance remains favourable, as provided for in **Article 44(4)**;

(8) the obligation to place the medicinal product for human use on the market in accordance with the content of the summary of the product characteristics and the labelling and package leaflet as contained in the marketing authorisation;

(9) the obligation to comply with the conditions referred to in **Article 18(1) and Article 19**;

(10) the obligation to notify the Agency of the dates of actual marketing and of the date when the medicinal product for human use ceases to be on the market, and to provide to the Agency data relating to the volume of sales and the volume of prescriptions of the medicinal product for human use, as provided in **Article 16(4)**;

(11) the obligation to operate a comprehensive pharmacovigilance system for the fulfilment of pharmacovigilance tasks, including the operation of a quality system, maintenance of a pharmacovigilance system master file and performance of regular audits, in accordance with **Article 100** in conjunction with Article 104 of [revised Directive 2001/83/EC];

(12) the obligation to submit, at the request of the Agency, a copy of the pharmacovigilance system master file, as provided for in **Article 44(4)**;

(13) the obligation to operate a risk management system as provided for in **Article 22 and Article 100(2)** in conjunction with Article 104(3) of [revised Directive 2001/83/EC];

(14) the obligation to record and report suspected adverse reactions for medicinal products for human use, in accordance with Article 23(1) of this Regulation in conjunction with Article 107 of [revised Directive 2001/83/EC];

(15) the obligation to submit periodic safety update reports, in accordance with **Article 108(2)** in conjunction with **Article 104** of [revised Directive 2001/83/EC];

(16) the obligation to conduct post-marketing studies, including post-authorisation safety studies and post-authorisation efficacy studies, and to submit them for review, as provided for in **Article 20**;

(17) the obligation to ensure that public announcements relating to information on pharmacovigilance concerns are presented objectively and are not misleading and to notify them to the Agency, as provided for in **Articles 101 and 102** of [revised Directive 2001/83/EC];

(18) the obligation to comply with the time limits for initiating or completing measures specified in the Agency's decision on deferral following the initial marketing authorisation of the medicinal product for human use concerned and in accordance with the definitive opinion referred to in **Article 85(7)**;

(19) **the obligation to submit to the Agency an updated version of the paediatric investigation plan in accordance with the agreed timing as provided for in Article 75(3) and Article 75(4);**

(20) the obligation to place the medicinal product for human use on the market within two years of the date on which the paediatric indication is authorised, as provided for in **Article 89**;

(21) **the obligation to notify the Agency the intention to discontinue the placing on the market of the product no less than six months before the discontinuation as provided for in Article 90;**

(22) the obligation to transfer the marketing authorisation or to allow a third party to use documentation contained in the file of the medicinal product, as provided for in **Article 90**;

(23) **The obligation to notify the Agency of the intention to discontinue the conduct of and agreed paediatric investigation plan and provide the reasons for such discontinuation no less than six months before the discontinuation as provided in Article 91;**

(24) the obligation to submit paediatric studies to the Agency or to the member States, including the obligation to enter information on third country clinical trials into the European database, as provided for in **Articles 95 and Article 97**.

(25) **the obligation to submit to the Agency a paediatric investigation plan with a request for agreement or an application for a waiver from it, not later than upon completion of the human pharmaco-kinetic studies in adults, except in duly justified cases, as provided for in Article 76.**

ANNEX III

PROCEDURE AND CRITERIA GOVERNING INSPECTIONS CARRIED OUT BY THE AGENCY

Reasoned request by the competent authority

The supervisory authority may submit after consultation with the Agency, a reasoned request to the Agency to carry out an inspection or to participate with its inspectors to an inspection carried out of a site located in a third country. The reasoned request specify:

- **The precise identification of the site, the scope of the inspections and if relevant the concerned products ;**
- **The timeline for this inspection to be completed ;**
- **The reasons for requesting the support of the Agency, by reference to the criteria set out in this Annex.**

The Agency may refuse an inspection request after consideration of the request, the scope and availability of internal inspection capacity.

Assessment by the Agency

The Agency decides whether it accepts to carry out such inspection or to participate with its inspectors in such inspection, based on the following criteria:

- **The site is located in a non-EU/EEA country;**
- **The inspection is in the interest of the Union, when one or more of the following situations apply to ensure faster or continuous access to medicines of patients:**
  - **to prevent, mitigate or address shortages of medicinal products or their active substances or other supply issues;**
  - **to prevent, mitigate or address a possible threat to public health, a public health emergency or a major event which requires immediate action;**
  - **to address a suspicion of non-compliance of the manufacturing site;**
  - **to enable the process of granting of the marketing authorisation for centrally authorised products/emergency use authorisation and for their active substance master files.**
  - **to improve the oversight of medicines production worldwide;**
  - **to address serious challenges of an unexpected and temporary nature with inspections capacities at national level;**
  - **other relevant situations.**

The compilation of Union procedures on inspections and exchange of information referred to in Article 3(1) of Directive 2017/1572 might be updated to cover rules applicable to situations where the Agency may be requested to carry out an inspection or to participate in a joint inspection.

In the context of inspections referred under Article 78 of Regulation (EU) 536/2014, the above criteria apply mutatis mutandis.

ANNEX IV

SPECIAL CRITERIA FOR ORPHAN DESIGNATION AS REFERRED TO IN ARTICLE 60(2)