ACTS ADOPTED BY BODIES CREATED BY INTERNATIONAL AGREEMENTS

DECISION No 1/2017

of 1 March 2017

of the Joint Committee established under Article 14 of the Agreement on Mutual Recognition between the European Community and the United States of America, amending the Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs) [2017/382]

THE JOINT COMMITTEE,

Having regard to the Agreement on Mutual Recognition between the European Community and the United States of America (the 'Agreement') done in 1998, and in particular its Articles 14 and 21, and

Whereas the Joint Committee is to take a decision to amend the Sectoral Annex on GMPs pursuant to Article 21(2) of the Agreement;

HAS DECIDED AS FOLLOWS:

1. Attachment A to this Decision is the United States — European Union Amended Sectoral Annex for Pharmaceutical Good Manufacturing Practices ('Amended Sectoral Annex') which amends the Sectoral Annex for Pharmaceutical Good Manufacturing Practices (GMPs) done in 1998 and replaces it with a consolidated version.
2. Attachment A has been agreed by the Parties.

This Decision, done in duplicate, shall be signed by representatives of the Joint Committee who, pursuant to Article 21(2) of the Agreement are authorized to act on behalf of the Parties for purposes of amending the Annexes. This Decision shall be effective from the date of the later of these signatures.

Signed in Washington DC, 19 January 2017.

On behalf of the United States of America

Michael B. G. FROMAN

Signed in Brussels, 1 March 2017.

On behalf of the European Union

Cecilia MALMSTRÖM

ATTACHMENT A

United States — European Union amended sectoral annex for pharmaceutical good manufacturing practices (GMPs)

PREAMBLE

This Annex constitutes a Sectoral Annex to the Agreement on Mutual Recognition between the United States and the European Union, amending the Sectoral Annex for Pharmaceutical Good Manufacturing Practices done in 1998.

CHAPTER 1

DEFINITIONS, PURPOSE, SCOPE AND PRODUCT COVERAGE

Article 1

Definitions

For purposes of this Annex:

1. 'Assessment pursuant to this Annex' means:

   for the European Union (EU), an equivalence assessment; and

   for the United States, a capability assessment.

   An assessment pursuant to this Annex includes a reassessment.

2. 'Recognized authority' means:

   for the EU, an equivalent authority; and

   for the United States, a capable authority.

3. 'Capable authority' means an authority that the Food and Drug Administration (FDA) FDA has determined is capable according to the criteria and procedures specified in Appendix 4 and referred to in the U.S. laws, regulations and administrative provisions listed in Appendix 1. For greater certainty, a finding that a regulatory authority is 'capable' does not require that the authority maintain procedures for conducting inspections and overseeing manufacturing facilities that are identical to FDA's procedures.

4. 'Equivalent authority' means an authority in respect of which the EU has made a positive equivalence determination according the criteria and procedures specified in Appendix 4 and as referred to in the EU laws, regulations and administrative provisions listed in Appendix 1.

5. 'Equivalence' means that the regulatory system under which an authority operates is sufficiently comparable to assure that the process of inspection and the ensuing official GMP documents will provide adequate information to determine whether respective statutory and regulatory requirements of the authorities have been fulfilled. For greater certainty, 'equivalence' does not require that the respective regulatory systems have identical procedures.

6. 'Enforcement' means an action taken by an authority to protect the public from products of suspect quality, safety and efficacy or to assure that products are manufactured in compliance with appropriate laws, regulations, standards and commitments made as part of the approval to market a product.

7. 'Good Manufacturing Practices' (GMPs) means systems that assure proper design, monitoring, and control of manufacturing processes and facilities, the adherence to which assures the identity, strength, quality, and purity of pharmaceuticals. GMPs include strong quality management systems, obtaining appropriate quality raw materials (including starting materials) and packaging materials, establishing robust operating procedures, detecting and investigating product quality deviations, and maintaining reliable testing laboratories.

8. 'Inspection' means an on-site evaluation of a manufacturing facility to determine whether such manufacturing facility is operating in compliance with Good Manufacturing Practices and/or commitments made as part of the approval to market a product.

9. 'Inspection Report' means a report written by an investigator or inspector of an authority listed in Appendix 2 concerning an inspection of a manufacturing facility that the investigator or inspector conducted that describes the purpose and scope of an inspection and includes written observations and findings bearing on the manufacturing facilities conformance to applicable GMP requirements set out in the laws, regulations and administrative procedures listed in Appendix 1 and any commitments made as part of the approval to market a product.

10. 'Official GMPs document' means a document issued by an authority listed in Appendix 2 following an inspection of a manufacturing facility. Examples of official GMPs documents include inspection reports, certificates issued by an authority attesting the compliance of a manufacturing facility with GMPs, GMPs non-compliance statement issued by authorities of the EU, and notice of observations, untitled letters, warning letters, and import alerts issued by the FDA.

11. 'Pharmaceuticals' includes drugs and medicinal products as defined in the laws and regulations listed in Appendix 1.

12. 'Post-approval inspections' means GMP surveillance inspections during the marketing of products.

13. 'Pre-approval inspections' means pharmaceutical inspections of manufacturing facilities carried out in the territory of a Party as part of the review of an application before marketing approval is granted.

14. 'Regulatory System' means the body of legal requirements for Good Manufacturing Practices, inspections, and enforcements that ensure public health protection and legal authority to assure adherence to these requirements.

Article 2

Purpose

This Annex facilitates the exchange of official GMPs documents between the Parties and reliance on the factual findings in such documents. This Annex seeks to facilitate trade and benefit public health by allowing each Party to leverage and to reallocate its inspection resources, including by avoiding duplication of inspections, so as to improve oversight of manufacturing facilities and better address quality risk and prevent adverse health consequences.

Article 3

Scope

1. The provisions of this Annex apply to pharmaceutical inspections of manufacturing facilities carried out in the territory of a Party during the marketing of products (hereafter referred to as 'post-approval inspections') and, to the extent provided for in Article 11, before products are marketed (hereafter referred to as 'pre-approval inspections'), as well as, to the extent provided for in Article 8(3), to pharmaceutical inspections of manufacturing facilities carried out outside the territory of either Party.

2. Appendix 1 names the laws, regulations and administrative provisions governing these inspections and the GMPs requirements.

3. Appendix 2 lists all the authorities responsible for the oversight of facilities that manufacture products within the product coverage of this Annex.

4. Articles 6, 7, 8, 9, 10 and 11 of the Agreement do not apply to this Annex.

Article 4

Product coverage

1. These provisions apply to marketed finished pharmaceuticals for human or animal use, intermediates (for the EU as defined in EU legislation) and in-process materials (for the United States as defined under U.S. law), certain marketed biological products for human use, and active pharmaceutical ingredients, only to the extent they are regulated by the authorities of both Parties as listed in Appendix 2 and subject to Article 20.

2. Human blood, human plasma, human tissues and organs, and veterinary immunologicals are excluded from the scope of this Annex.

3. Appendix 3 contains the list of products covered by this Annex.

CHAPTER 2

DETERMINATION OF RECOGNITION

Article 5

Assessments

1. Each Party shall conduct assessments of authorities listed in Appendix 2 pursuant to this Annex on the request of the other Party as expeditiously as possible, including for authorities added to Appendix 2 after the effective date of this Annex and as regards products listed in Appendix 3 (including those that are included in the scope of this Annex pursuant to Article 20 after the effective date of this Annex).

2. Each Party shall use the criteria and procedure specified in Appendix 4 to conduct assessments pursuant to this Annex.

Article 6

Participation in and completion of assessments

Each Party with respect to the authorities listed in Appendix 2 shall participate in the procedure as described in Appendix 4. Each Party shall exercise good faith efforts to complete assessments pursuant to this Annex as expeditiously as possible. To this end:

(a) The EU shall complete an assessment of the FDA for human pharmaceuticals under this Annex no later than by 1 July 2017.

(b) The FDA shall complete an assessment under this Annex of each EU Member State authority for human pharmaceuticals listed in Appendix 2 as set out in Appendix 5.

Article 7

Recognition of authorities

1. Each Party shall determine whether to recognize an authority according to the criteria specified in Appendix 4. Each Party shall promptly notify the Joint Sectoral Committee of any determination to recognize an authority of the other Party. The Joint Sectoral Committee shall maintain a list of recognized authorities and shall keep the list up-to-date. The list shall be made publicly available by each Party.

2. The assessing Party shall promptly notify the other Party and the relevant authority of any deficiencies identified in the course of the assessment. In the event of a negative determination, the assessing Party shall notify the other Party and the relevant authority of the reasons for the negative determination and provide sufficient detail to allow the authority to understand corrective measures that must be taken to attain a positive determination. A Party may request the other Party to conduct a reassessment of any authority for which the other Party has made a negative determination once the authority has taken necessary corrective measures in accordance with Article 5.

3. An assessing Party shall, upon request of the other Party, promptly discuss with the other Party in the Joint Sectoral Committee the reasons for a negative determination. In case of a negative determination, efforts shall be made by the Joint Sectoral Committee to discuss within 3 months the appropriate timeframe and exact steps to be taken to reassess the relevant authority.

CHAPTER 3

OPERATIONAL ASPECTS

Article 8

Recognition of inspections

1. A Party shall recognize pharmaceutical inspections and accept official GMPs documents issued by a recognized authority of the other Party for manufacturing facilities located in the territory of the issuing authority, except as provided in paragraph 2.

2. A Party may in specific circumstances opt not to accept an official GMPs document issued by a recognized authority of the other Party for manufacturing facilities located in the territory of the issuing authority. Examples of such circumstances include the indication of material inconsistencies or inadequacies in an inspection report, quality defects identified in the post-market surveillance or other specific evidence of serious concern in relation to product quality or consumer safety. A Party opting not to accept an official GMPs document issued by a recognized authority of the other Party shall notify the other Party and the relevant authority of the reasons for not accepting the document and may request clarification from that authority. The authority shall endeavour to respond to the request for clarification in a timely manner and shall normally provide the clarification based on input from one or more members of the inspection team.

3. A Party may accept official GMPs documents issued by a recognized authority of the other Party for manufacturing facilities located outside the territory of the issuing authority.

4. Each Party may determine the terms and conditions under which it accepts official GMPs documents issued under paragraph 3.

5. For purposes of this Annex, to accept an official GMPs document means to rely on the factual findings in such document.

Article 9

Batch testing

In the EU, as provided in Article 51 paragraph 2 of Directive 2001/83/EC of the European Parliament and of the Council ([1]) and in Article 55 paragraph 2 of Directive 2001/82/EC of the European Parliament and of the Council ([2]), the qualified person will be relieved of responsibility for carrying out the controls laid down in Article 51 paragraph 1 of Directive 2001/83/EC and in Article 55 paragraph 1 of Directive 2001/82/EC provided that these controls have been carried out in the United States, the product was manufactured in the United States and that each batch/lot is accompanied by a batch certificate (in alignment with the WHO certification scheme on the quality of medicinal products) issued by the manufacturer certifying that the product complies with requirements of the marketing authorization and signed by the person responsible for releasing the batch/lot.

([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]) Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products (OJ L 311, 28.11.2001, p. 1).

Article 10

Transmission of official GMPs documents

If an importing Party requests a recognized authority of the other Party for a post-approval official GMPs document, the recognized authority shall transmit the document to the Party within 30 calendar days of the date of the request. If, based on that document, the importing Party determines that a new inspection of the manufacturing facility is needed, the importing Party shall notify the relevant recognized authority of the other Party and request, in accordance with Article 11, the recognized authority of the other Party to conduct a new inspection.

Article 11

Requests for pre-approval and post-approval inspections

1. A Party or a recognized authority of a Party may request in writing that a recognized authority of the other Party conduct a pre-approval or post-approval inspection of a manufacturing facility. The request shall include the reason for the request and identify the precise issues to be addressed in the inspection and the requested timeline for completing the inspection and transmitting the official GMPs documents.

2. In the EU, requests shall be sent directly to the relevant recognized authority, with a copy to the European Medicines Agency (EMA).

3. Within 15 calendar days of receipt of the request, the recognized authority shall acknowledge receipt and confirm whether it will conduct the inspection in accordance with the requested timelines. Where the authority receiving the request is of the opinion that official GMPs documents relevant to the request are already available or are pending, it should inform the requesting authority accordingly and share these documents upon request.

4. For greater certainty, if the recognized authority indicates that it will not conduct the inspection, the requesting authority has the right to conduct its own inspection of the manufacturing facility and the requested authority has the right to join the inspection.

Article 12

Maintenance

Each Party shall maintain ongoing activities to monitor that recognized authorities in its territory maintain the criteria for recognition. For the purpose of such monitoring activities, each Party shall rely on established programmes that include regular audits or assessments of authorities based on the criteria specified in Appendix 4. The frequency and nature of such activities shall be consistent with international best practices. A Party may invite the other Party to participate in these monitoring activities at the other Party's expense. Each Party shall notify the other Party of any significant changes to its monitoring programmes.

Article 13

Suspension of a recognized authority

1. Each Party has the right to suspend recognition of a recognized authority of the other Party. This right shall be exercised in an objective and reasoned manner and communicated in writing to the other Party and the recognized authority.

2. A Party suspending recognition of a recognized authority of the other Party shall, upon request of the other Party or the authority whose recognition was suspended, promptly discuss in the Joint Sectoral Committee the suspension, the reason therefore, and corrective actions that would need to be taken for the suspension to be lifted.

3. Upon the suspension of an authority previously listed as a recognized authority, a Party is no longer obligated to accept official GMPs documents of the suspended authority. A Party shall continue to accept official GMPs documents of that authority prior to suspension, unless the Party decides otherwise based on health or safety considerations. The suspension shall remain in effect until the Parties decide to lift the suspension or until a positive determination of recognition has been made in accordance with Article 7 pursuant to a reassessment.

CHAPTER 4

JOINT SECTORAL COMMITTEE

Article 14

Role and composition of the Joint Sectoral Committee

1. A Joint Sectoral Committee is set up to monitor the activities performed under this Annex.

2. The Committee shall be co-chaired by a representative of the FDA for the United States and a representative of the EU who each shall have one vote in the Joint Sectoral Committee. The Joint Sectoral Committee shall make its decision by unanimous consent. The Joint Sectoral Committee shall determine its own rules and procedures.

3. The Joint Sectoral Committee's functions include in particular:

(a) developing and keeping up to date the list of recognized authorities, including any limitation in terms of inspection type or products, and the list of authorities in Appendix 2 and communicating the lists to all authorities listed in Appendix 2 and the Joint Committee,

(b) providing a forum to discuss issues relating to this Annex, including relating to disagreements as regards determinations of recognition or suspension and timelines for completing assessments under this Annex of authorities listed in Appendix 2;

(c) in accordance with Article 20 and Appendix 3, considering the status, and taking decisions on the inclusion, of the products referred to in Article 20; and

(d) adopting, where necessary, appropriate complementary technical and administrative arrangements for the effective implementation of this Annex.

4. The Joint Sectoral Committee shall meet at the request of either Party with respect to issues relating to disagreements as regards to determinations of recognition or suspension and otherwise at such times as the Parties may agree. The Joint Sectoral Committee may meet in person or by other means.

CHAPTER 5

REGULATORY COOPERATION AND INFORMATION EXCHANGE

Article 15

Regulatory cooperation

The Parties shall inform and consult one another, as permitted by law, on proposals to introduce new controls or to change existing technical regulations or significant changes to pharmaceutical inspection procedures and to provide the opportunity to comment on such proposals.

Article 16

Exchange of information

The Parties shall establish appropriate arrangements, including access to relevant databases, for the exchange of official GMPs documents and other appropriate information related to the inspection of a manufacturing facility and the exchange of information concerning any confirmed problem reports, corrective actions, recalls, rejected import consignments and other regulatory and enforcement problems for products subject to this Annex.

Article 17

Alert System

Each Party shall maintain an Alert System that permits authorities of the other Party when relevant to be made aware proactively and with the appropriate speed in case of quality defect, recalls, counterfeit or falsified products, or potential serious shortages and other problems concerning quality or non-compliance with GMP, which could necessitate additional controls or suspension of the distribution of the affected products.

CHAPTER 6

SAFEGUARD CLAUSE

Article 18

Safeguard clause

1. Each Party recognizes that the importing country has a right to fulfil its legal responsibilities by taking actions necessary to ensure the protection of human and animal health at the level of protection it deems appropriate. An authority of a Party has the right to conduct its own inspection of a manufacturing facility in the territory of the other Party.

2. An authority of a Party conducting its own inspection of a manufacturing facility in the territory of the other Party should be an exception from the normal practice of a Party as of the date on which the Articles referred to in Article 19(2) become applicable.

3. An authority of a Party, prior to conducting an inspection under paragraph 1, shall notify the other Party in writing and the authority of the other Party has the right to join the inspection conducted by the Party.

CHAPTER 7

FINAL PROVISIONS

Article 19

Entry Into Force

1. This Annex shall enter into force on the date on which the Parties have completed an Exchange of Letters confirming completion of any respective procedures for the entry into force of this Annex.

2. Notwithstanding paragraph 1, Articles 8, 10, 11 and 12 of this Annex shall not apply until 1 November 2017, except as provided in paragraph 4.

3. Notwithstanding paragraph 1, Article 9 of this Annex shall not apply until the date on which all the EU Member State authorities for human pharmaceuticals listed in Appendix 2 have been recognized by the FDA.

4. If, by 1 November 2017, the FDA has not completed assessments under this Annex of at least eight Member State authorities for human pharmaceuticals listed in Appendix 2, despite having received complete capability assessment packages from those authorities as specified in paragraph II.A.1 of Appendix 4 in accordance with the schedule set out in Appendix 5, application of the Articles referred to in paragraph 2 shall be postponed to the date on which the FDA has completed assessments of at least eight such authorities.

Article 20

Transitory Provisions

1. No later than by 15 July 2019, the Joint Sectoral Committee shall consider whether to include veterinary products within the product coverage of this Annex. The Joint Sectoral Committee shall exchange views on the organisation of the assessment of respective authorities by 15 December 2017.

2. No later than 15 July 2022, the Joint Sectoral Committee shall consider whether to include vaccines for human use and plasma derived pharmaceuticals within the product coverage of this Annex. Without prejudice to this consideration, as of the effective date of this Annex, a Party shall notify the relevant authority of the other Party in advance of conducting a post-approval inspection of a manufacturing facility of such products located in the territory of the Party and give the authority the option of joining the inspection. In order to support the inclusion of vaccines for human use and plasma derived pharmaceuticals within the product coverage of this Annex, the Joint Sectoral Committee shall take into account, in particular, the experience gained through such joint inspections.

3. No later than 15 July 2019, the Joint Sectoral Committee shall review experience gained in order to decide whether the provisions on pre-approval inspections provided in Article 11 shall be reviewed.

4. Products referred to in paragraphs 1 and 2 shall be included within the product coverage of this Annex only once the Joint Sectoral Committee so decides pursuant to paragraphs 1 and 2.

5. Where the FDA identifies the need for a post-approval inspection of a manufacturing facility in a territory of a Member State authority of which an assessment under this Annex is pending or that the FDA has otherwise not recognized, the FDA shall notify that authority and the EMA in writing.

(a) No later than 30 calendar days of the date it receives a notification pursuant to paragraph 5, the authority in whose territory the manufacturing facility is located or EMA on behalf of this authority shall inform the FDA whether it has opted to request a recognized authority of the EU to conduct the inspection and, if so, whether such recognized authority of the EU will conduct the inspection by the date specified in the notification. The authority in whose territory the manufacturing facility is located shall be allowed to join the inspection.

(b) In the case that a recognized authority of the EU will conduct the inspection, the recognized authority or EMA on behalf of this authority shall inform the FDA of the date(s) on which it will conduct the inspection and submit the official GMPs documents relevant to the inspection to the FDA and the authority of the territory in which the inspection has been conducted by the date specified in the notification in accordance with the applicable laws, regulations and administrative provisions listed in Appendix 1. The FDA shall have the option to participate in the inspection.

(c) In the case that a recognized authority of the EU will not conduct the inspection and the FDA conducts the inspection, the authority of the territory in which the inspection has been conducted has the right to participate in the inspection and the FDA shall submit the official GMPs documents relevant to the inspection to this authority.

Article 21

Termination

1. The Annex shall terminate on 15 July 2019 in the event that the FDA, by that date, has not completed an assessment under this Annex of each EU Member State authority for human pharmaceuticals listed in Appendix 2, provided that the FDA has received complete capability assessment packages as specified in paragraph II.A.1 of Appendix 4 from each Member State authority in accordance with the schedule set out in Appendix 5.

2. The date specified in paragraph 1 shall be extended by 90 calendar days for each authority that provides a complete capability assessment package as specified in paragraph II.A.1 of Appendix 4 after the applicable deadline set out in Appendix 5 but before 15 July 2019.

3. The FDA shall, on request, discuss any disagreement raised by the EU regarding an assessment in the Joint Sectoral Committee. If the Joint Sectoral Committee cannot agree on resolution of the disagreement, the EU may notify in writing to the FDA its formal disagreement and the Annex shall terminate three months from the date of such notification or on such other date as the Joint Sectoral Committee may agree.

Appendix 1

List of Applicable Laws, Regulations and Administrative Provisions

FOR THE UNITED STATES

Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 301 et seq. Of particular relevance: 21 USC 351(a)(2)(B) (drug adulterated if not manufactured in conformance with current good manufacturing practice); 21 U.S.C. 355(d)(3); 21 U.S.C. 355(j)(4)(A) (approval of human drug contingent on adequacy of methods, facilities, and controls for manufacturing, processing, and packing to preserve the identity, strength, quality, and purity of drug); 21 U.S.C. 360b(c)(2)(A)(i); 360b(d)(1)(C) (approval of animal drug contingent on contingent on adequacy of methods, facilities, and controls for manufacturing, processing, and packing to preserve the identity, strength, quality, and purity of drug); 21 U.S.C. 374 (inspection authority); 21 U.S.C. 384(e) (recognition of foreign government inspections)

Public Health Service Act Section 351, 42 U.S.C. 262. Of particular relevance: 42 U.S.C. 262(a)(2)(C)(i)(II) (licensing of biologic contingent on demonstration that the facility in which it is manufactured, processed, packed, or held meets standards designed to assure that the product continues to be safe, pure, and potent); 42 U.S.C. 262(j) (Federal Food, Drug, and Cosmetic Act applies to biologic products)

21 CFR Part 210 (Current Good Manufacturing Practice in Manufacturing, Processing, Packing or Holding Drugs; General)

21 CFR Part 211 (Current Good Manufacturing Practice for Finished Pharmaceuticals)

21 CFR Part 600, Subpart B (Establishment Standards); Subpart C (Establishment Inspection)

FOR THE EUROPEAN UNION

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;

Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products;

Directive 2001/20/EC of European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use;

Regulation (EU) No 536/2014 of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC;

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;

Commission Directive 2003/94/EC of 8 October 2003 laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use;

Commission Directive 91/412/EEC of 23 July 1991 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products;

Commission delegated Regulation (EU) No 1252/2014 of 28 May 2014 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;

Current version of the Guide to good manufacturing practices contained in volume IV of Rules governing medicinal products in the European Union and compilation of the community procedures on inspections and exchange of information.

Appendix 2

LIST OF AUTHORITIES

UNITED STATES

The Food and Drug Administration

EUROPEAN UNION

Country	For medicinal products for human use	For medicinal products for veterinary use
Austria	Austrian Agency for Health and Food Safety/Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH	See responsible authority for human medicinal products
Belgium	Federal agency for medicines and health products/Federaal Agentschap voor geneesmiddelen en gezondheidsproducten/Agence fédérale des médicaments et produits de santé	See responsible authority for human medicinal products
Bulgaria	Bulgarian Drug Agency/ИЗПЪЛНИТЕЛНА АГЕНЦИЯ ПО ЛЕКАРСТВАТА	Bulgarian Food Safety Agency/Българска агенция по безопасност на храните
Cyprus	Ministry of Health — Pharmaceutical Services/Φαρμακευτικές Υπηρεσίες, Υπουργείο Υγείας	Ministry of Agriculture, Rural Development and Environment-Veterinary Services/Κτηνιατρικές Υπηρεσίες- Υπουργείο Γεωργίας, Αγροτικής Ανάπτυξης και Περιβάλλοντος
Czech Republic	State Institute for Drug Control/Státní ústav pro kontrolu léčiv (SÚKL)	Institute for State Control of Veterinary Biologicals and Medicaments/Ústav pro státní kontrolu veterinárních biopreparátů a léčiv (ÚSKVBL)
Croatia	Agency for Medicinal Products and Medical Devices/Agencija za lijekove i medicinske proizvode (HALMED)	Ministry of Agriculture, Veterinary and Food Safety Directorate/Ministarstvo Poljoprivrede, Uprava za veterinarstvo i sigurnost hrane
Denmark	Danish Medicines Agency/Laegemiddelstyrelsen	See responsible authority for human medicinal products
Germany	Federal Institute for Drugs and Medical Devices/Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) Paul-Ehrlich-Institute (PEI), Federal Institute for Vaccines and Biomedicines/Paul-Ehrlich-Institut (PEI) Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel Federal Ministry of Health/Bundesministerium für Gesundheit (BMG)/Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten (ZLG) [1]	Federal Office for Consumer Protection and Food Safety/Bundesamt für Verbraucherschutz und Lebensmittelsicherheit (BVL) Federal Ministry of Food and Agriculture, Bundesministerium für Ernährung und Landwirtschaft

Country	For medicinal products for human use	For medicinal products for veterinary use
Estonia	State Agency of Medicines/Ravimiamet	See responsible authority for human medicinal products
Greece	National Organisation for Medicines/Ethnikos Organismos Farmakon (EOF) — (ΕΘΝΙΚΟΣ ΟΡΓΑΝΙΣΜΟΣ ΦΑΡΜΑΚΩΝ))	See responsible authority for human medicinal products
Spain	Spanish Agency of Medicines and Medical Devices/Agencia Española de Medicamentos y Productos Sanitarios (2)	See responsible authority for human medicinal products
Finland	Finnish Medicines Agency/Lääkealan turvallisuus- ja kehittämiskeskus (FIMEA)	See responsible authority for human medicinal products
France	French National Agency for Medicines and Health Products Safety Agence nationale de sécurité du médicament et des produits de santé (ANSM)	French agency for food, environmental and occupational health safety — *National Agency for Veterinary Medicinal Products*/Agence Nationale de Sécurité Sanitaire de l'alimentation, de l'environnement et du travail-Agence Nationale du Médicament Vétérinaire (Anses-ANMV)
Hungary	Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet/National Institute of Pharmacy and Nutrition	National Food Chain Safety Office, Directorate of Veterinary Medicinal Products/Nemzeti Élelmiszerlánc-biztonsági Hivatal, Állatgyógyászati Termékek Igazgatósága (ÁTI)
Ireland	Health Products Regulatory Authority (HPRA)	See responsible authority for human medicinal products
Italy	*Italian Medicines Agency*/Agenzia Italiana del Farmaco	Direction General for Animal Health and Veterinary Medicinal Products Ministero della Salute, Direzione Generale della Sanità Animale e dei Farmaci Veterinari
Latvia	State Agency of Medicines/Zāļu valsts aģentūra	Assessment and Registration Department of the Food and Veterinary Service/Pārtikas un veterinārā dienesta Novērtēšanas un reģistrācijas departaments
Lithuania	State Medicines Control Agency/Valstybinė vaistų kontrolės tarnyba	State Food and Veterinary Service/Valstybinės maisto ir veterinarijos tarnyba
Luxembourg	Minìstere de la Santé, Division de la Pharmacie et des Médicaments	See responsible authority for human medicinal products
Malta	Medicines Regulatory Authority	Veterinary Medicines and Animal Nutrition section VMANS) (Veterinary Regulation Directorate (VRD) within The Veterinary and Phytosanitary Regulation Department (VPRD)

Country	For medicinal products for human use	For medicinal products for veterinary use
Netherlands	Healthcare Inspectorate/Inspectie voor de Gezondheidszorg (IGZ)	Medicines Evaluation Board/Bureau Diergeneesmiddelen, College ter Beoordeling van Geneesmiddelen (CBG)
Poland	The Main Pharmaceutical Inspectorate/ Główny Inspektorat Farmaceutyczny (GIF)	See responsible authority for human medicinal products
Portugal	National Authority of Medicines and Health Products/INFARMED, I.P Autoridade Nacional do Medicamento e Produtos de Saúde, I.P	General Directorate of Food and Veterinary/ DGAV — Direção Geral de Alimentação e Veterinária (PT)
Romania	National Agency for Medicines and Medical Devices/Agenția Națională a Medicamentului și a Dispozitivelor Medicale	National Sanitary Veterinary and Food Safety Authority/Autoritatea Națională Sanitară Veterinară și pentru Siguranța Alimentelor
Sweden	Medical Products Agency/Läkemedelsverket	See responsible authority for human medicinal products
Slovenia	Agency for Medicinal Products and Medical Devices of the Republic of Slovenia/Javna agencija Republike Slovenije za zdravila in medicinske pripomočke (JAZMP)	See responsible authority for human medicinal products
Slovak Republic (Slovakia)	State Institute for Drug Control/Štátny ústav pre kontrolu liečiv (ŠÚKL)	Institute for State Control of Veterinary Biologicals and Medicaments/Ústav štátnej kontroly veterinárnych biopreparátov a liečiv (USKVBL)
United Kingdom	Medicines and Healthcare products Regulatory Agency	Veterinary Medicines Directorate

(1) For the purpose of this Annex, and without prejudice to the internal division of competence in Germany on matters falling within the scope of this Annex, ZLG shall be understood as covering all the competent Laender authorities issuing GMP documents and conducting pharmaceutical inspections.

(2) For the purpose of this Annex, and without prejudice to the internal division of competence in Spain on matters falling within the scope of this Annex, Agencia Española de Medicamentos y Productos Sanitarios shall be understood as covering all the competent regional authorities issuing GMP documents and conducting pharmaceutical inspections.

Appendix 3

LIST OF PRODUCTS COVERED BY THE ANNEX

Recognizing that precise definition of medicinal products and drugs are to be found in the laws, regulations and administrative provisions referred to in Appendix 1, an indicative list of products covered by the Annex is given below. This applies to processing, packaging, testing and sterilizing facilities, including contract facilities performing these functions.

1. Marketed finished pharmaceuticals for human use in various pharmaceutical dosage forms such as tablets, capsules, ointments, and injectables, including:

   (a) Medical gases;

   (b) Radiopharmaceuticals or radioactive biological products;

   (c) Herbal (botanical) products (*); and

   (d) Homeopathic products;

2. Marketed biological products:

   (a) Vaccines for human use (**);

   (b) Plasma derived pharmaceuticals (**);

   (c) Therapeutic biotechnology-derived biological products; and

   (d) Allergenic products.

3. In process materials (for the United States as defined under U.S. law) and intermediates (for the European Union as defined in EU legislation);

4. Active pharmaceutical ingredients or bulk drug substance;

5. Investigational products (clinical trial material) (***); and

6. Veterinary products (**):

   (a) veterinary pharmaceuticals, including prescription and non-prescription drugs, with the exclusion of veterinary immunologicals;

   (b) pre-mixes for the preparation of veterinary medicated feeds (EU), Type A medicated articles for the preparation of veterinary medicated feeds (US);

(*) These are included to the extent that they are regulated as drugs by the FDA and medicinal products by the EU.

(**) These products are only included within the product coverage of this Annex to the extent the Joint Sectoral Committee decides to include them pursuant to Article 20.

(***) The FDA does not routinely conduct GMP inspections for investigational medicinal products. Inspection information on these products will be provided to the extent that they are available and resources allow. These products are only included within the product coverage of this Annex to the extent the Joint Sectoral Committee decides to include them.

Appendix 4

CRITERIA AND PROCEDURE FOR ASSESSMENTS UNDER THIS ANNEX

I. CRITERIA FOR ASSESSMENTS UNDER THIS ANNEX

Each Party will apply the following criteria to determine whether to recognize an authority listed in Appendix 2:

(i) The authority has the legal and regulatory authority to conduct inspections against a standard for GMP (as defined in Article 1).

(ii) The authority manages conflict of interest in an ethical manner.

(iii) The authority has the ability to evaluate risks and mitigate them.

(iv) The authority maintains appropriate oversight of manufacturing facilities within its jurisdiction.

(v) The authority has and uses sufficient resources.

(vi) The authority employs trained and qualified inspectors with the skills and knowledge to identify manufacturing practices that may lead to patient harm.

(vii) The authority has the tools necessary to take action to protect the public from harm due to poor quality drugs or medicinal products.

II. PROCEDURES FOR ASSESSMENTS UNDER THIS ANNEX

A. **Assessment of EU authorities by FDA**

1. To receive a capability assessment for an authority listed in Appendix 2, each Member State authority shall submit capability assessment packages containing the following materials before the FDA will initiate an assessment:

   (i) a finalized Joint Audit Programme audit report of an audit, where the FDA has been given three months advance notice to be an observer, that includes the full report of the observed inspection, any associated corrective measures, and all documents cited by the auditors in the report for the indicators as identified by FDA in the Joint Audit Programme audit checklist as essential for the assessment and for any indicators that required the authority to propose a corrective and preventative action;

   (ii) a completed conflicts of interest questionnaire established by the FDA signed by a principal of the authority;

   (iii) a total of four inspection reports including the report from the inspections observed during the Joint Audit Program audit;

   (iv) standard operating procedures or a description on how the authority finalizes inspection reports;

   (v) standard operating procedures related to training and inspector qualification, including training files for all inspectors who conducted the inspections in the reports provided to the FDA (pursuant to subparagraph (iii)); and

   (vi) its most recent inventory of manufacturing facilities within its territory and under the authority's jurisdiction, including type of manufacturing facility of products falling within the product coverage of this Annex, and upon request, completion of a table provided by the FDA detailing types of manufacturing facilities.

2. During a capability assessment, the FDA may require additional information or further clarification from the Member State authority.

3. The FDA may waive the requirement to submit certain information listed under II.A.1 and may request alternative information from the Member State authority. The decision to waive any assessment materials will be made by the FDA on a case by case basis.

4. Upon receipt of all requisite information specified in paragraph II.A from a Member State authority, the FDA intends to submit such information for official translation into English within a reasonable timeframe. The FDA will complete assessments and determine capability of the Member State authority no later than 70 calendar days from the date the FDA receives a translation of all requisite information specified in paragraph II.A for the Member State authority. The FDA will dedicate two capability assessment teams; therefore, the FDA shall conduct assessments of two Member State authorities at any given time.

B. **Assessment of FDA by the EU**

The EU will carry out its assessment of FDA based on:

(i) The performance of an audit in line with the elements of the Joint Audit Programme taking into account audits performed in the framework of the Pharmaceutical Inspection Convention/Scheme (PIC/S) and audits performed in the context of Article 111(b)(1) of Directive 2001/83/EC.

(ii) An assessment of the equivalence of legislative and regulatory GMP requirements.

C. **Reassessment of authorities**

In the event an assessing Party issues a negative determination or suspension of an authority of the other Party, it may reassess the authority. The scope of the reassessment shall relate to the reasons for the negative determination or suspension.

III. MAINTAINING RECOGNITION

To maintain recognition, it is required that the authority continue to meet the criteria set out in paragraph I.A and remain subject to the monitoring activities described in Article 12 which for Member State authorities the FDA requires monitoring through an audit program that includes an audit (that the FDA has the option to observe) of each recognized Member State authority every five to six years. In case an authority has not been subject to an audit for a period of 6 years, the other Party shall have the right to audit such authority.

Appendix 5

SCHEDULE FOR INITIAL ASSESSMENT OF MEMBER STATE AUTHORITIES

1. Member State authorities for human pharmaceuticals listed in Appendix 2 shall submit complete capability assessment packages containing the information specified in paragraph II.A.1 of Appendix 4 according to the following schedule:

   — No later than January 1, 2017: capability assessment packages from four Member State authorities

   — No later than February 15, 2017: capability assessment packages from three additional Member State authorities

   — No later than April 1, 2017: capability assessment packages from two additional Member State authorities.

   — No later than May 15, 2017: capability assessment packages from two additional Member State authorities

   — No later than September 15, 2017: capability assessment packages from two additional Member State authorities

   — No later than December 15, 2017: capability assessment packages from four additional Member State authorities

   — No later than March 15, 2018: capability assessment packages from four additional Member State authorities

   — No later than June 15, 2018: capability assessment packages from seven additional Member State authorities

2. The FDA shall complete assessments under this Annex of Member State authorities for human pharmaceuticals listed in Appendix 2 as set out in paragraph II.A.4 and according to the following schedule, provided that the FDA receives complete capability assessment packages for such authorities containing the information specified in paragraph II.A.1 of Appendix 4 according to the schedule set out in paragraph 1:

   — November 1, 2017: eight assessments

   — March 1, 2018: four additional assessments

   — June 1, 2018: two additional assessments

   — December 1, 2018: six additional assessments

   — July 15, 2019: eight additional assessments

3. For each Member State authority:

   (a) The EU shall submit a final audit report to the FDA no later than 60 days before the due date of the capability assessment package for the authority.

   (b) The FDA shall provide a finalized capability assessment package checklist to the authority no later than 20 days after the FDA receives the audit report.

   (c) The authority shall submit the capability assessment package to FDA no later than 40 days after the authority receives the capability assessment package checklist.