National Authority of Medicines and Health Products, I.P.

CERTIFICATE NUMBER: ***F053/S1/ME/001/2020***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER [1, 2]

Part 1

Issued following an inspection in accordance with :
Art. 15 of Directive 2001/20/EC

The competent authority of Portugal confirms the following:
The manufacturer: ***GenIbet Biopharmaceuticals, S.A.***
Site address: ***Edifício da Instalação Piloto do IBET - 4.º Piso - Av. da República, Quinta do Marquês, Oeiras, 2780-157, Portugal***

Has been inspected under the national inspection programme in accordance with Art. 13 of Directive 2001/20/EC transposed in the following national legislation:
Art. 29 of Law n. º 46/2004, de 19 of August

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2019-07-11*** , it is considered that it complies with :

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC [3]

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

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[1] *The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.*

[2] *Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.*

[3] *These requirements fulfil the GMP recommendations of WHO.*

Part 2

Human Investigational Medicinal Products

1 MANUFACTURING OPERATIONS	
1.1	**Sterile products**
	1.1.1 Aseptically prepared (processing operations for the following dosage forms) 1.1.1.4 Small volume liquids
	1.1.3 Batch certification
1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell
	1.2.2 Batch certification
1.3	**Biological medicinal products (list of product types)**
	1.3.1 Biological medicinal products (list of product types) 1.3.1.2 Immunological products 1.3.1.3 Cell therapy products 1.3.1.4 Gene therapy products 1.3.1.5 Biotechnology products Special Requirements 7 Other: Human origin(en)
	1.3.2 Batch Certification (list of product types) 1.3.2.2 Immunological products 1.3.2.3 Cell therapy products 1.3.2.4 Gene therapy products 1.3.2.5 Biotechnology products Special Requirements 7 Other: Human origin(en)
1.6	**Quality control testing**
	1.6.4 Biological

2020-04-20

Name and signature of the authorised person of the Competent Authority of Portugal

Maria Fernanda Ralha Henriques Matos

Assinado de forma digital por Maria Fernanda Ralha Henriques Matos
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National Authority of Medicines and Health Products, I.P.

CERTIFICATE NUMBER: ***F053/S1/SA/001/2020***

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER [1, 2]

Part 1

Issued following an inspection in accordance with :
Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of Portugal confirms the following:
The manufacturer: ***GenIbet Biopharmaceuticals, S.A.***
Site address: ***Edifício da Instalação Piloto do IBET - 4.º Piso - Av. da República, Quinta do Marquês, Oeiras, 2780-157, Portugal***

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation:
Art.176.º n.º 1 a) of Decree-Law n.º 176/2006, 30 of August

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2019-07-11*** , it is considered that it complies with :

- The principles of GMP for active substances [3] referred to in Article 47 of Directive 2001/83/EC .

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

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[1] *The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.*

[2] *Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.*

[3] *These requirements fulfil the GMP recommendations of WHO.*

Part 2

Manufacture of active substance. Names of substances subject to inspection :
POLYSACCHARIDES(en)
RECOMBINANT PROTEINS(en)
PLASMID DNA(en)
VIRUS AND VIRUS LIKE PARTICLES(en)
CELL BANK(en)
VIRAL BANK(en)
IN VITRO TRANSCRIBED RNA(en)
LIVE MICROBIAL PRODUCTS(en)
VACCINES AND OTHER IMMUNOLOGICAL PRODUCTS(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : POLYSACCHARIDES

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.2 Cell Culture : bacterial 3.3.3 Isolation / Purification
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

Active Substance : RECOMBINANT PROTEINS

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.2 Cell Culture : e.g. mammalian/bacterial 3.3.3 Isolation / Purification 3.3.4 Modification
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:*

	3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

Active Substance : PLASMID DNA

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.2 Cell Culture : bacterial 3.3.3 Isolation / Purification
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

Active Substance : VIRUS AND VIRUS LIKE PARTICLES

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.2 Cell Culture : e.g. mammalian 3.3.3 Isolation / Purification 3.3.5 Other : Viral propagation
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification

3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : CELL BANK

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.2 Cell Culture : e.g. mammlian/bacterial
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

Active Substance : VIRAL BANK

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.2 Cell Culture : e.g. mammalian 3.3.3 Isolation / Purification 3.3.5 Other : Viral propagation
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)

Active Substance : IN VITRO TRANSCRIBED RNA

3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.5 Other : Reverse transcription of plasmid DNA
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

Active Substance : LIVE MICROBIAL PRODUCTS

3.2	**Extraction of Active Substance from Natural Sources**
	3.2.5 Modification of extracted substance Human
3.3	**Manufacturing of Active Substance using Biological Processes**
	3.3.1 Fermentation 3.3.2 Cell Culture : bacterial 3.3.3 Isolation / Purification
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing

Active Substance : VACCINES AND OTHER IMMUNOLOGICAL PRODUCTS

3.3	**Manufacturing of Active Substance using Biological Processes**

	3.3.1 Fermentation 3.3.2 Cell Culture : mammalian, bacterial 3.3.3 Isolation / Purification 3.3.5 Other : viral propagation
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared *Special Requirements:* 3. Live Cells 7. Other : Batch certification
3.5	**General Finishing Steps**
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing 3.6.2 Microbiological testing excluding sterility testing 3.6.4 Biological Testing

2020-04-20

Name and signature of the authorised person of the Competent Authority of Portugal

Maria Fernanda Ralha Henriques Matos

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