



Health Products Regulatory Authority

CERTIFICATE NUMBER: 21434/ASR11378

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 Ireland confirms the following:

The manufacturer: **Pfizer Ireland Pharmaceuticals**

Site address: **Little Island, Co. Cork, Ireland**

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:

Medicinal Products (Control of Manufacture) Regulations 2007 to 2013.

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on **2018-08-31**, it is considered that it complies with :

- The principles of GMP for active substances³ 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.

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.

I certify that that this document is a true and faithful copy of the original document or of the relevant extracts thereto produced to me and which after careful examination I attest

this 17th day of December 2018

Hugh McGroddy, Notary Public,
33 Upper Merrion St., Dublin 2.
Commissioned for Life

HUGH Mc GRODDY
33 Upper Merrion Street
Dublin 2.
Notary Public for the
County and City of Dublin
Commissioned for Life



Part 2

Manufacture of active substance. Names of substances subject to inspection :

ATORVASTATIN CALCIUM(en) - confidential

AXITINIB (EN)(en) - confidential

CRIZOTINIB (EN)(en) - confidential

TEMSIROLIMUS(en) - confidential

VARENICLINE TARTRATE(en) - confidential

VORICONAZOLE(en) - confidential

TOLTERODINE L- TARTRATE(en) - confidential

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : ATORVASTATIN CALCIUM - confidential

3.1 Manufacture of Active Substance by Chemical Synthesis

- 3.1.1 Manufacture of active substance intermediates
- 3.1.2 Manufacture of crude active substance
- 3.1.3 Salt formation / Purification steps :
Crystallisation

3.5 General Finishing Steps

- 3.5.1 Physical processing steps :
Drying & milling
- 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
- 3.5.3 Secondary Packaging (placing the seal material or container. This also includes any identification or traceability (lot numbering))

3.6 Quality Control Testing

- 3.6.1 Physical / Chemical testing

Active Substance : AXITINIB (EN) - confidential

3.1 Manufacture of Active Substance by Chemical Synthesis

- 3.1.1 Manufacture of active substance intermediates
- 3.1.2 Manufacture of crude active substance
- 3.1.3 Salt formation / Purification steps :
Crystallisation

3.5 General Finishing Steps

- 3.5.1 Physical processing steps :
Drying
- 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
- 3.5.3 Secondary Packaging (placing the seal material or container. This also includes any identification or traceability (lot numbering))

3.6 Quality Control Testing

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3.6.1 Physical / Chemical testing	
Active Substance : CRIZOTINIB (EN) - confidential	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Crystallisation
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Drying & milling 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : TEMSIROLIMUS - confidential	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Crystallisation
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Drying 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : VARENICLINE TARTRATE - confidential	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Crystallisation
3.5	General Finishing Steps

	3.5.1 Physical processing steps : Drying & milling
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : VORICONAZOLE - confidential	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.3 Salt formation / Purification steps : Crystallisation of intermediate
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Drying
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : TOLTERODINE L- TARTRATE - confidential	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.3 Salt formation / Purification steps : Crystallisation of Tolterodine L- Tartrate Intermediate 3 (TL3)
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Drying
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

4. Other Activities - Active Substances :

Distribution: Atorvastatin Calcium, Crizotinib, Temsirolimus, Varenicline Tartrate, Axitinib,

Voriconazole, Tolterodine L- Tartrate

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Signatory: Mr. Olsin Daly

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




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