Medicines and Healthcare products Regulatory Agency

CERTIFICATE NUMBER : UK GMP 12546 Insp GMP 12546/6212631-0001[H]

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER*(1),(2)*

Part 1

Issued following an inspection in accordance with :
Regulation 331A of The Human Medicines Regulations 2012 (SI 2012/1916)

The competent authority of United Kingdom confirms the following :

The Manufacturer : ISIS PHARMACEUTICALS INCORPORATED

Site address : ISIS PHARMACEUTICALS INCORPORATED, BUILDING 2282 FARADAY AVENUE, CARLSBAD, 92008, UNITED STATES

Has been inspected in connection with marketing authorisation(s) listing manufacturers located outside of the European Economic Area in accordance with of The Human Medicines Regulations 2012 (SI 2012/1916)

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 25/04/2012, it is considered that it complies with

- The principles and guidelines of Good Manufacturing Practice laid down in Regulation B17 of the Human Medicines Regulations 2012 (as amended)

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 MHRA-GMDP. If it does not appear, please contact the issuing authority.

- *(1) Guidance on the interpretation of this template can be found in the Help menu of MHRA-GMDP database.*
- *(2) These requirements fulfil the GMP recommendations of WHO.*

Part 2

Human Medicinal Products

1. MANUFACTURING OPERATIONS

[1.2] Non-sterile products

[1.2.1] Non-Sterile Products (processing operations for the following dosage forms)

[1.2.1.17] Other non-sterile medicinal products
RNA produced by Chemical synthesis

[1.3] Biological medicinal products

[1.3.1] Biological medicinal products

[1.3.1.8] Other biological medicinal products

RNA produced by Chemical synthesis

[1.4] Other products or manufacturing activity

[1.4.1] Manufacture of:

[1.4.1.3] Other

Low bioburden API from chemical synthesis

[1.6] Quality control testing

[1.6.1] Microbiological: sterility

[1.6.2] Microbiological: non-sterility

[1.6.3] Chemical/Physical

[1.6.4] Biological

Restrictions or Remarks

This inspection was performed for a biological molecule API produced via chemical synthesis. Although the product is biological in nature the site is not approved for biological processes such as fermentation and cell banking and would require further inspection prior to authorisation of this type of product

Any restrictions related to the scope of this certificate:

Building	Room	Line/equipment	QC Testing	Products
2282 Faraday road used for testing, manufacturing and processing 2280 used for storage and stability chambers only	2280 rooms 145 158 159 171 180 182 185 and 190 2282 Rooms Tank Yard 108 109 122 130 131 133 136 140 150 151			

14/06/2012	Name and signature of the authorised person of the Competent Authority of United Kingdom Confidential Medicines and Healthcare products Regulatory Agency Tel : Confidential