Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Influenza Reagent
Influenza virus infectious IVR-147
NIBSC code: 07/246
Instructions for use
(Version 2.0, Dated 31/03/2008)

1. INTENDED USE

Reagent 07/246 is prepared from IVR-147 (A/Brisbane/10/2007 (H3N2) x A/PR/8/34 (H1N1)) which was processed for freeze drying in 250 µl volumes as described by Campbel, PJ, Journal of Biological Standardisation, 1974, 2, 249-267. The known passage history of IVR-147 is attached

2. CAUTION

This preparation is not for administration to humans or animals in the human food chain.

The material is not of human or bovine origin. As with all materials of biological origin, this preparation should be regarded as potentially hazardous to health. It should be used and discarded according to your own laboratory's safety procedures. Such safety procedures should include the wearing of protective gloves and avoiding the generation of aerosols. Care should be exercised in opening ampoules or vials, to avoid cuts.

3. UNITAGE

No unitage is assigned to this material

4. CONTENTS

Country of origin of biological material: United Kingdom.
Each ampoule contains 250µl (nominal) of infectious influenza virus as allantoic fluid from embryonated SPF hen's eggs.

5. STORAGE

Store in the dark at -20^{0}C or below
Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.

6. DIRECTIONS FOR OPENING

DIN ampoules have an 'easy-open' coloured stress point, where the narrow ampoule stem joins the wider ampoule body. Various types of ampoule breaker are available commercially. To open the ampoule, tap the ampoule gently to collect material at the bottom (labelled) end and follow manufactures instructions provided with the ampoule breaker.

7. USE OF MATERIAL

Reconstitute the contents of one ampoule of reagent with 250µl of sterile distilled water. Leave for a minimum of 5 minutes before use to allow for complete solution of freeze dried material. A range of dilutions (e.g. 10^{-3} to 10^{-5}) should be made in a suitable medium for initial cutivation.

8. STABILITY

Reference Materials should be stored on receipt as indicated on the label.

NIBSC follows the policy of WHO with respect to its reference materials.

9. REFERENCES

NA

10. ACKNOWLEDGEMENTS

NA

11. FURTHER INFORMATION

Further information can be obtained as follows;
This material: enquiries@nibsc.org
WHO Biological Standards:
http://www.who.int/biologicals/en/
JCTLM Higher order reference materials:
http://www.bipm.org/en/committees/jc/jctlm/
Derivation of International Units:
http://www.nibsc.org/standardisation/international_standards.aspx
Ordering standards from NIBSC:
http://www.nibsc.org/products/ordering.aspx
NIBSC Terms & Conditions:
http://www.nibsc.org/terms_and_conditions.aspx

12. CUSTOMER FEEDBACK

Customers are encouraged to provide feedback on the suitability or use of the material provided or other aspects of our service. Please send any comments to enquiries@nibsc.org

13. CITATION

In all publications, including data sheets, in which this material is referenced, it is important that the preparation's title, its status, the NIBSC code number, and the name and address of NIBSC are cited and cited correctly.

14. MATERIAL SAFETY SHEET

Classification in accordance with Directive 2000/54/EC, Regulation (EC) No 1272/2008: Not applicable or not classified

Physical and Chemical properties			
Physical appearance: White powder		Corrosive:	No
Stable:	Yes	Oxidising:	No
Hygroscopic:	No	Irritant:	No
Flammable:	No	Handling:	See caution, Section 2
Other (specify):	Live influenza virus		

Toxicological properties	
Effects of inhalation:	Likelihood of influenza virus infection
Effects of ingestion:	Not established, avoid ingestion
Effects of skin absorption:	Not established, avoid contact with skin

Suggested First Aid	
Inhalation:	Seek medical advice
Ingestion:	Seek medical advice
Contact with eyes:	Wash with copious amounts of water. Seek medical advice
Contact with skin:	Wash thoroughly with water.

Action on Spillage and Method of Disposal

Spillage of contents should be taken up with absorbent material wetted with a virucidal agent. Rinse area with an appropriate virucidal agent followed by water.
Absorbent materials used to treat spillage should be treated as biologically hazardous waste.

15. LIABILITY AND LOSS

In the event that this document is translated into another language, the English language version shall prevail in the event of any inconsistencies between the documents.
Unless expressly stated otherwise by NIBSC, NIBSC's Standard Terms and Conditions for the Supply of Materials (available at http://www.nibsc.org/About_Us/Terms_and_Conditions.aspx or upon

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WHO International Laboratory for Biological Standards,
UK Official Medicines Control Laboratory

request by the Recipient) ("Conditions") apply to the exclusion of all other terms and are hereby incorporated into this document by reference. The Recipient's attention is drawn in particular to the provisions of clause 11 of the Conditions.

16. INFORMATION FOR CUSTOMS USE ONLY

Country of origin for customs purposes*: United Kingdom * Defined as the country where the goods have been produced and/or sufficiently processed to be classed as originating from the country of supply, for example a change of state such as freeze-drying.
Net weight: NA
Toxicity Statement: Non-toxic
Veterinary certificate or other statement if applicable**.** **Attached:** No

Passage history of IVR-147 (post mixed infection)

Passage level	Lot	Laboratory
E1-E6		CSL, Melbourne, Australia
E7	VI 1510	CSL, Melbourne, Australia
E8	29100	NIBSC, Hertfordshire, UK

CSL

Attachment 1

Research and Development

REPORT ON THE PREPARATION AND TESTING OF:

Influenza virus Reassortant Nº IVR-147, SPF LOT Nº VI-1510
A/Brisbane/10/07-like, (H3N2)

PREPARATION OF SPF LOT:
Preparation of SPF influenza virus IVR-147, lot VI-1510 was carried out following procedures set out in Standard Operating Procedure RDS0030, and in accordance with the Australian Good Laboratory Practice guidelines. This work was conducted in the Influenza Development department, R&D, CSL Limited.

This work is documented on Batch Process Sheets: RDB0917 Lot 189C and RBD0936 Lot VI-1510.

VIRUS ISOLATE FROM WHO-CC
Virus was obtained from the WHO Collaborating Centre for Reference & Research on Influenza (WHO-CC).

Virus was originally obtained locally as a clinical sample from Brisbane, Australia

A/Brisbane/10/2007 (Type A, Subtype H3N2)
WHO-CC Storage lot: SL/0703020-1
Passages prior to receipt at WHO-CC: nil
Passages undertaken in WHO-CC: E2

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Attachment 1

Derivation of A/Brisbane/10/07-like influenza virus IVR-147 SPF lot VI-1510:

Mixed infection passage:	A/Brisbane/10/2007 Wild Type Virus@10^{-3} x A/Puerto Rico/8/34 (H1N1) @10^{-5}	HA titre 557
	↓	
1st Antiserum Passage	Inoculum @ 10^{-3} with A/PR/8/34 antiserum	HA titre 190
	↓	
2nd Antiserum Passage	Inoculum @ 10^{-3} with A/PR/8/34 antiserum	HA titre 113
	↓	
1st Clone passage	Inoculum @ 10^{-8}	HA titre 48
	↓	
2nd Clone passage	Inoculum @ 10^{-7}	HA titre 67
	↓	
3rd Clone passage	Inoculum @ 10^{-8}	HA titre 320
	↓	
4th Clone passage	Inoculum @ 10^{-8}	HA titre 394
	↓	
Preparation of SPF Lot VI-1510	Inoculum @ 10^{-5}	mean HA titre ≥ 166

Total number of passages since this virus was received from an approved laboratory = 8

TESTING OF INFLUENZA VIRUS SPF LOT VI-1510:

Routine testing on SPF lot VI-1510 has been performed as follows:

LIMS Id. 07006435 (Sample No. 821189)

Sterility ***QA Test Code 2572***
Pending (satisfactory at 7 days)

Mycoplasma ***QA Test Code 2703***
Pending

Haemagglutinin Identity ***QA Test Code 0050***
Pending

EM Appearance ***QA Test Code 0072***
Appearance: PASS. Small spheres, Medium Spheres, Small Kidneys,
Medium Irregular Particles, Medium Filaments
EM micrographs: Folio No 7-545 CM 1437-1 to CM1437-20

Neuraminidase Identity ***QA Test Code 0051***
Pending

Egg Infectivity ***QA Test Code 0052***
Pending

CONCLUSION:
Pending.

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Friday, 14 September 2007

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WHO COLLABORATING CENTRE FOR REFERENCE AND RESEARCH ON INFLUENZA
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Attachment 2

Influenza Virus Seed Lot

Identity Test Report for: CSL Limited

Sample ID No.	821189	Test Code	CSL: QA 0050
Seed Lot No.	VI-1510	Date submitted	6.9.2007
Sample name	A/BRISBANE/10/2007 (IVR-147)	WHO ID No.	0709053

Test applied	**Haemagglutination Inhibition Assay**	Assay Date	13/9/2007
Assay performed by	T. Mastorakos		

	HI titre with reference antisera					
Reference antigen	A1	A2	A3	A4	B	H1
A/CALIFORNIA/7/2004 A(H3)	**1280**	640	640	320	<20	<20
A/WISCONSIN/67/2005 A(H3)	1280	**1280**	640	640	<20	<20
A/MALAYSIA/753/2005 A(H3)	160	40	**80**	80	<20	<20
A/BRISBANE/10/2007 A(H3)	1280	640	320	**640**	<20	<20
B/MALAYSIA/2506/2004	<40	<40	<40	<40	**1280**	<20
A/NEW CALEDONIA/20/99 A(H1)	<40	<40	<40	<40	<20	**640**
Test antigen						
VI-1510 (IVR-147)	1280	640	320	1280	<20	<20

Actual antisera used were raised to:	A1	A/CALIFORNIA/7/2004
	A2	A/WISCONSIN/67/2005
	A3	A/MALAYSIA/753/2005
	A4	A/BRISBANE/10/2007
	B	B/MALAYSIA/2506/2004
	H1	A/NEW CALEDONIA/20/99

Conclusion: Seed lot VI-1510 (IVR-147) has a HI reactivity pattern that is consistent with a reassortant of A/Brisbane/10/2007.

Pass	Fail	Warn
■	☐	☐

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Attachment 2

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Deputy Director
13.9.2007