Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Influenza Reagent
Influenza virus infectious IVR-148
NIBSC code: 08/300
Instructions for use
(Version 1.0, Dated 30/04/2009)

1. INTENDED USE

Reagent 08/300 is prepared from IVR-148 (A/Brisbane/59/2007 (H1N1)x A/Texas/1/77 (H3N2) hgr) which was processed for freeze drying in 250µl volumes as described by Campbell, PJ, Journal of Biological Standardisation, 1974, 2,249-267. The known passage history of IVR-148 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 SPF embryonated 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 cultivation.

8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities. 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 ampoule contents should be taken up with absorbent material wetted with a virucidal agent. Rinse area with 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

Derivation of IVR-148

Post mixed infection passages*	Lot	Laboratory
E- E5 (SPF)		CSL Ltd, Melbourne, Aus
E6 (SPF)	VI 1515	CSL Ltd, Melbourne, Aus
E7 (SPF)	29570	NIBSC, Hertfordshire, UK
E8 (SPF)	30830	NIBSC, Hertfordshire, UK

*****NB Passages in this document are counted post the mixed infection event**.** In the accompanying CSL derivation they are numbered to include the mixed infection event**.**

Pages 5 and 6, along with the information they contain, are as received from CSL Ltd.

Page 7, along with the information it contains, is as received from WHO Collaborating Centre, Melbourne.

CSL

Research and Development

REPORT ON THE PREPARATION AND TESTING OF:

Influenza virus Reassortant Nº IVR-148, SPF LOT Nº VI-1515
A/Brisbane/59/2007-like, (H1N1)

PREPARATION OF SPF LOT:
Preparation of SPF influenza virus IVR-148, lot VI-1515 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 was documented on Batch Process Sheets: RDB0914, RDB0939, RDB0913, RDB0916, RDB0917 and RDB0936. All Lot No. 197.

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/59/2007 (Type A, Subtype H1N1)
WHO-CC Storage lot: SL/0707062-1
Passages prior to receipt at WHO-CC: nil
Passages undertaken in WHO-CC: E2

Derivation of A/Brisbane/59/2007:

Mixed Infection passage:	A/Brisbane/59/2007 (H1N1) Wild Type Virus @ 10^{-5} x A/Texas/1/77(H3N2) @ 10^{-3}	HA Titre 1154
	↓	
1st Antiserum passage:	Inoculum @ 10^{-3} with A/Texas/1/77 antiserum	HA titre ≥1325
	↓	
2nd Antiserum passage:	Inoculum @ 10^{-3} with A/Texas/1/77 antiserum	HA titre 905
	↓	
1st Clone passage:	Inoculum @ 10^{-9}	HA titre 422
	↓	
2nd Clone passage:	Inoculum @ 10^{-9}	HA titre 1114
	↓	
6th Passage:	Inoculum @ 10^{-8}	HA titre ≥1325
	↓	
Preparation of SPF Lot VI-1515:	Inoculum @ 10^{-5}	mean HA titre ≥1108

Total number of passages since this virus was received from an approved laboratory = 7

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TESTING OF INFLUENZA VIRUS SPF LOT VI-1515:

Routine testing on SPF lot VI-1515 has been performed as follows:

LIMS Id. PKV-PR-08000393 (Sample No. 855137)

Sterility	***QA Test Code 2572***
Pending	
Mycoplasma	***QA Test Code 2703***
Pending	
Mycoplasma	***QA Test Code 2705***
Pending	
Mycoplasma (H-Stain)	***QA Test Code 1591***
Pending	
Haemagglutinin Identity	***QA Test Code 0050***
Pending	
EM Appearance	***QA Test Code 0072***
Pending	
Neuraminidase Identity	***QA Test Code 0051***
Pending	
Egg Infectivity	***QA Test Code 0052***
Pending	

CONCLUSION:
Pending.

Prepared by:
Andrew Stalder/Prue Thomas
Influenza Development, R&D, CSL Limited
Thursday, 23 January 2008

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Influenza Virus Seed Lot
Identity Test Report for: CSL Limited

Sample ID No.	855137	Test Code	CSL: QA 0050
Seed Lot No.	VI-1515	Date submitted	22.1.2008
Sample name	IVR-148 (A/BRISBANE/59/2007 reassortant)	WHO ID No.	0801088

Test applied	**Haemagglutination Inhibition Assay**	Assay Date	25.1.2008
Assay performed by	T. Mastorakos		

	HI titre with reference antisera					
Reference antigen	A1	A2	A3	A4	H3	B
A/NEW CALEDONIA/20/99 A(H1)	**640**	160	640	80	<40	<20
A/SOLOMON ISLANDS/3/2006 A(H1)	160	**320**	320	320	<40	<20
A/MALAYSIA/100/2006 A(H1)	640	160	**1280**	80	<40	<20
A/BRISBANE/59/2007 A(H1)	80	160	20	**160**	<40	<20
A/WISCONSIN/67/2005 A(H3)	<20	<20	<20	<20	**320**	<20
B/MALAYSIA/2506/2004	<20	<20	<20	<20	<40	**1280**
Test antigen						
VI-1515 (IVR-148 A/Brisbane/59/2007)	160	160	40	320	<40	<20

Actual antisera used were raised to:	A1	A/NEW CALEDONIA/20/99
	A2	A/SOLOMON ISLANDS/3/2006
	A3	A/MALAYSIA/100/2006
	A4	A/BRISBANE/59/2007
	H3	A/WISCONSIN/67/2005
	B	B/MALAYSIA/2506/2004

Conclusion: Seed lot VI-1515 (IVR-148) has a HI reactivity pattern that is consistent with a reassortant of A/Brisbane/59/2007.

Pass	Fail	Warn
■	□	□

Ian Barr
Deputy Director
25.1.2007
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