Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Influenza Reagent
Influenza virus infectious IVR-155
NIBSC code: 09/304
Instructions for use
(Version 1.0, Dated 11/03/2010)

1. INTENDED USE

The influenza reference virus IVR-155 is a reassortant prepared by CSL Ltd using classical reassortant methodology from A/Victoria/210/2009 H3N2 virus and A/PR/8/34 virus. Reagent 09/304 is prepared from IVR-155 and 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-155 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 handled only in appropriate containment facilities by fully trained competent staff. It should be used and disposed of in accordance with national safety guidelines and your laboratory's safety procedures.

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 freeze dried 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

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 with surface proteins derived from H1N1v 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 and waste disposal procedures should follow those outlined in your facility standard laboratory operating procedures. Appropriate disinfectants would include Chlorine based chemicals, 70% Ethanol and phenolic compounds when used according to manufacturer's specified recommendations.

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-155

Passage level	Lot	Laboratory
E1-E4		CSL, Melbourne, Australia
E5	VI-1534	CSL, Melbourne, Australia
E6	32410	NIBSC, Hertfordshire, UK

E = SPF eggs

Attached derivation as received from CSL

CSL Limited
45 Poplar Road Parkville
Victoria 3052 Australia

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www.csl.com.au

Derivation of IVR-155
A/Victoria/210/2009 (H3N2) – like High Growth Reassortant

PREPARATION

Preparation of IVR-155, lot VI-1534, an A/Victoria/210/2009 (H3N2)-like high growth reassortant influenza virus was conducted in the Influenza Development department, R&D, CSL Limited.

MATERIALS

Virus Isolate: The virus isolate was obtained from the WHO Collaborating Centre for Reference & Research on Influenza, Melbourne (WHO-CC). Supply details are:

A/Victoria/210/2009 (Type A, Subtype H3N2)

WHO-CC Laboratory number:	SL/0906062-1
Passages prior to receipt at WHO-CC:	Nil
Passages undertaken in WHO-CC:	E2, HA=32

Eggs: SPF Premium Plus eggs were used for all passages.

TSE's: No materials of biological origin, other than SPF Premium Plus eggs, were used during the preparation of IVR-155.

PASSAGE HISTORY

Mixed infection passage: A/Victoria/210/2009 (H3N2) @10^{-3} x A/Puerto Rico/8/34 (H1N1) @10^{-5}

HA titre 520

↓

1st Antiserum Passage Inoculum @ 10^{-3} with A/Puerto Rico/8/34 antiserum — HA titre 260

↓

2nd Antiserum Passage Inoculum @ 10^{-3} with A/Puerto Rico/8/34 antiserum — HA titre ≥ 1810

↓

3rd passage (limit dilution) Inoculum @ 10^{-8} — HA titre ≥ 1576

↓

4th passage (limit dilution) Inoculum @ 10^{-8} — HA titre ≥ 1576

↓

5th passage Inoculum @ 10^{-5} — mean HA titre ≥ 1052

IVR-155, Lot VI-1534

Total number of passages post mixed infection = 5
Total number of passages since this virus was received from an approved laboratory = 6
HA titres were determined using chicken red blood cells at room temperature.

TESTING OF INFLUENZA VIRUS IVR-155, LOT VI-1525:

Test	Result	
Sterility (EP 2.6.1 membrane filtration method)	No contamination detected at 5 day read.	
Genotype (by real time RT-PCR)	5:3 i.e. 5 internal genes from PR-8	
	A/Victoria/210/2009	**PR8**
	H3 N2 PB1	PB2 PA NP M NS
Antigenicity (HI serology assay)	A/Perth/16/2009 H3N2-like See WHO report attached	
Infectivity EID50 (log_{10}/0.2mL)	8.75	
Appearance (Electron Microscopy)	The following morphologies were reported (in order of abundance): Small spheres, small kidneys, small dumb-bells, short filaments.	

Disclaimer:

The material i.e. high growth reassortant virus IVR-155 and the information provided in this derivation report are provided on an "as is" basis and as such without any warranty or representation of any kind (express or implied) including, without limitation, of satisfactory quality or fitness for a particular purpose.

Prepared by: Peter Schoofs
Influenza Development, R&D, CSL Limited
Tuesday, 8 February 2010

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WHO COLLABORATING CENTRE FOR REFERENCE AND RESEARCH ON INFLUENZA

MELBOURNE AUSTRALIA 10 Wreckyn St, North Melbourne, Victoria, 3051, Australia
Phone: +61 3 9342 3900 Fax: +61 3 9342 3939

Influenza Virus Seed Lot

Identity Test Report for: CSL Limited

Sample ID No.	999403	Test Code	CSL: QA 0050
Seed Lot No.	VI-1534	Date submitted	29.01.2010
Sample name	IVR-155(A/Victoria/210/2009)	WHO ID No.	1001298

Test applied	**Haemagglutination Inhibition Assay**	Assay Date	29 Jan 2010
Assay performed by		T. Mastorakos	

	HI titre with reference antisera						
Reference antigen	A1	A2	A3	A4	B VIC	B YAM	H1
A/BRISBANE/10/2007 A(H3)	**1280**	<20	20	20	<20	<20	<20
A/SINGAPORE/37/2009 A(H3)	20	**640**	320	640	<20	<20	<20
A/PHILIPPINES/16/2009 A(H3)	40	160	**160**	160	<20	<20	<20
A/PERTH/16/2009 A(H3)	<20	640	640	**640**	<20	<20	<20
B/VICTORIA/304/2006	<20	<20	<20	<20	**640**	<20	<20
B/FLORIDA/4/2006	<20	<20	<20	<20	40	**640**	<20
A/BRISBANE/59/2007 A(H1)	<20	<20	<20	<20	<20	<20	**320**
A/VICTORIA/210/2009 (WT)	40	1280	640	320	<20	<20	<20
Test antigen							
VI-1534	20	1280	1280	320	<20	<20	<20

Actual antisera used were raised to:		
	A1	A/BRISBANE/10/2007
	A2	A/SINGAPORE/37/2009
	A3	A/PHILIPPINES/16/2009
	A4	A/PERTH/16/2009
	B VIC	B/VICTORIA/304/2006
	B YAM	B/FLORIDA/4/2006
	H1	A/Brisbane/59/2007

Conclusion: Seed lot VI-1534 (IVR-155) has a HI reactivity pattern that is consistent with an A/Perth/16/2009-like virus.

Pass ✓	Fail	Warn

Ian Barr
Deputy Director
29.01.2010

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