Medicines & Healthcare products Regulatory Agency

NIBSC Confidence in Biological Medicines

Influenza Reagent
Influenza virus infectious IVR-142
NIBSC code: 06/164
Instructions for use
(Version 2.0, Dated 04/04/2008)

1. INTENDED USE

Reagent 06/164 is prepared from IVR-142 (A/Hiroshima/52/2005 (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-142 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-142 (post mixed infection)

Passage level	Lot	Laboratory
E1-E5		CSL, Melbourne, Australia
E6	VI 1489	CSL, Melbourne, Australia
E7	24810	NIBSC, Hertfordshire, UK

Documents as Received from CSL and WHO CC, Melbourne, Australia

CSL Research and Development

REPORT ON THE PREPARATION AND TESTING OF
A/Hiroshima/52/2005 SPF LOT NO VI-1489 (IVR-142)

PREPARATION OF SPF LOT:
Preparation of the SPF lot VI-1489 (IVR-142) 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 Product Development R&D, D823, CSL Ltd.
This work is documented on Batch Process Sheets: RDB 0916 Lot 175 and RBD0936 Lot VI-1489

VIRUS ISOLATE FROM WHO-CC
Virus originally obtained from NIID, Tokyo, Japan
A/Hiroshima/52/2005
Passages prior to receipt at WHO-CC E3
Passages undertaken in WHO-CC E1 HA 32 (Turkey cells)

A brief description of the preparation of the SPF lot follows:
Mixed infection: A/Hiroshima/52/2005 Wild Virus @10-3 x A/PR/8/34@ 10-3
HA=394
⇓
1st Antiserum Passage @ 10-3 with A/PR/8/34 Antiserum Lot 4430 HA=43
⇓
2nd Antiserum Passage @ 10-3 with A/PR/8/34 Antiserum Lot 4430 HA=160
⇓
1st Clone @ 10-9 HA=355
⇓
2nd Clone @ 10-7 HA=190
⇓
3rd Clone @ 10-8 HA=453
⇓
Preparation of SPF Lot VI-1489 @ 10-5 mean HA>525

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

TESTING OF SPF LOT VI-1489
Routine testing on SPF lot VI-1489 has been performed as follows:
LIMS Id. 06004547

Sterility QA Test Code 2572
Pass

Mycoplasma QA Test Code 2703
Pending

Haemagglutinin Identity QA Test Code 0050
Pending

EM Appearance QA Test Code 0072
Appearance: short and medium filaments, small and medium spheres, kidney shapes, some long filaments and large spheres, some irregular shaped particles.
Micrograph numbers CM1107-1 to CM1107-8.

Neuraminidase Identity QA Test Code 0051
Pending

Egg Infectivity QA Test Code 0052
Pending

CONCLUSION:
Pending

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www.influenzacentre.org

INFLUENZA HIGH-YIELD REASSORTANT IVR-142 A/Hiroshima/52/2005 (H3N2)
DATE OF DERIVATION REPORT: 6 March 2006.
SOURCE:
The reassortant virus IVR-142 (the 'Reassortant') has been made available to the WHO Collaborating Centre (the 'Centre'), by CSL Limited ACN 051 588 348 ('CSL'), for distribution. It is requested that in any citations the origin of the reassortant should be acknowledged as: CSL Limited, Parkville, Australia.

DERIVATION:
The Reassortant was prepared from the A/Hiroshima/52/2005 virus which was isolated at the NIID WHO Collaborating Centre in Tokyo, Japan and passaged at the Melbourne WHO Collaborating Centre in chicken eggs from healthy disease-free flocks, before being reassorted by CSL Limited. The derivation history of IVR-142 is attached.

TESTING:
Haemagglutinin Identity.
In reciprocal haemagglutination-inhibition tests conducted at the Centre using reference reagents, SPF Lot VI-1489 (IVR-142) was antigenically equivalent to A/Hiroshima/52/2005.

HI titre with reference antisera
Reference antigen A1 A2 A3 B H1
A/California/7/2004 (Egg) **320** 40 80 <40 <40
A/Brisbane/3/2005 (Egg) 640 **640** 320 <40 <40
A/Hiroshima/52/2005 (Egg) 160 40 **640** <40 <40
B/Malaysia/2506/2005 – B (Egg) <40 <40 <40 **640** <50
A/New Caledonia/20/99 H1 (Egg) <40 <40 <40 <40 **160**

Test antigen
VI-1489 (IVR 142; A/Hiroshima/52/2005) 160 40 640 <40 <40
A1 A/California/7/2004 (H3)
A2 A/Brisbane/3/2005 (H3)
A3 A/Hiroshima/52/2005 (H3)
B B/Malaysia/2506/2005
Actual antisera used were raised to:
H1 A/New Caledonia/20/99

Infectivity Titre:
Pending

Sterility:
CSL SPF lot VI-1489 has been tested and shown to be free of bacterial contaminants.

CAUTION
IVR-142 (VI-1489) is a living biological preparation and should be regarded as potentially hazardous to humans. Appropriate safety procedures should be employed for avoiding exposure and for discarding infectious materials or contaminated equipment. It is the recipient's responsibility for ensuring that it complies with all laws and regulations for the handling and use of the Reassortant

LIABILITY:
1. CSL and the Centre take all reasonable care and skill in preparing the viral isolate and the Reassortant and compiling any information provided herewith and have used reasonable endeavours to ensure that the Reassortant complies with the specification set out in this Information Sheet.
2. However, CSL and the Centre disclaim all warranties, express or implied, concerning the Reassortant including any warranty that it is accurate, complete, safe, merchantable or fit for any purpose such as a basis for preparing vaccines or reagents.
3. The recipient is solely responsible for ensuring that the Reassortant is fit for the use to which (s)he puts same.
4. CSL and the Centre accept no liability whatsoever for any loss, damage or liability which arise as a result of or in connection with the use of the Reassortant including any loss, damage or liability that:
· arises from CSL's or the Centre's negligence or wilful default; or
· relates to any product derived from use of the Reassortant; or
· relates to any results obtained from use of the Reassortant; or
· results in direct, indirect, special or consequential damages.

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