Medicines & Healthcare products Regulatory Agency



#### Influenza Reagent Influenza virus infectious NIB-79 NIBSC code: 11/222 Instructions for use (Version 1.0, Dated 26/03/2012)

#### 1. INTENDED USE

Reagent 11/222 is prepared from NIB-79 (A/Victoria/361/2011 (H3N2) x A/Puerto Rico/8/34 (H1N1) ) which was processed for freeze drying in 250  $\mu l$  volumes as described by Campbel, PJ, Journal of Biological Standardisation, 1974, 2, 249-267. The passage history of NIB-79 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 freeze dried allantoic fluid from embryonated SPF premium plus hen's eggs.

#### 5. STORAGE

Store in the dark at -20°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

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Potters Bar, Hertfordshire, EN6 3QG. T +44 (0)1707 641000, nibsc.org WHO International Laboratory for Biological Standards, UK Official Medicines Control Laboratory

#### 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 appeara<br>White powder | nce:           | Corrosive:                      | No |  |  |  |  |  |  |
| Stable:                          | Yes            | Oxidising:                      | No |  |  |  |  |  |  |
| Hygroscopic:                     | No             | Irritant:                       | No |  |  |  |  |  |  |
| Flammable:                       | No             | Handling:See caution, Section 2 |    |  |  |  |  |  |  |
| Other (specify):                 | Live influenza | 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

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http://www.nibsc.org/About\_Us/Terms\_and\_Conditions.aspx or upon 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 NIB-79

| Passage | Lot   | Laboratory               |
|---------|-------|--------------------------|
| E1 – E4 |       | NIBSC, Hertfordshire, UK |
| E5      | 34540 | NIBSC, Hertfordshire, UK |

### Derivation of NIB-79 A/Victoria/361/2011 (H3N2)-like High Growth Reassortant

Strain: A/Victoria/361/2011



Received from WHO Melbourne # SL/1110498-1, E3 Passage undertaken at NIBSC #34320, E4



Total number of passages since mixed infection= E5

SPF eggs were used for all passages.

RT-PCR/RFLP analysis indicates that NIB-79 has HA and NA genes from A/Victoria/361/11 and M, NP, PB1, PB2, PA and NS genes from A/PR/8/34 making it a 6:2 reassortant.

Results of one way HI test provided by National Institute of Medical Research, Mill Hill, London



| Antigenic analyses of influenza A H3N2 viruses (Guinea Pig RBC with 20nM Oseltamivir) (29/02/2012) |                             |            |       |          |                      |            |        |          |         |       |       |                     |         |               |       |                    |
|--|-----------------------------|------------|-------|----------|----------------------|------------|--------|----------|---------|-------|-------|---------------------|---------|---------------|-------|--------------------|
|  |                             |            |       |          |                      |            |        |          |         |       |       |                     |         |               |       |                    |
|  |                             |            |       |          |                      |            |        |          |         |       |       |                     |         |               |       |                    |
|  | Viruses                     | Collection |       | Passage  | A/Perth              | A/Vic      | A/Ala  |          | A/HK    | A/S   | tock  | A/lowa              | A/Fin   | A             | /Eng  | A/Norway           |
|  |                             | Date       |       | History  | 16/09                | 208/09     | 5/10   | 3        | 3969/11 | 18/   | 2011  | 19/2010             | 190/11  | 25            | 9/11  | 1/89/11            |
|  |                             |            |       |          | F35/11               | F7/10      | F27/10 |          | F27/11  | F2    | 28/11 | F15/11              | F01/12  | FO            | )2/12 | F03/12             |
| Vir  | uses                        | Colle      | ction | Pa       | ssage                | A/Vic      | Gro    | Gr       | oup 🏹   | Vičou | p 3A  | NIBº79 <sup>6</sup> |         | 1 <b>6</b> 4u | p 3B  | VRº165             |
|  | REFERENCE VIRUSES           |            | Date  |          |                      | 361/11     | 361/1  | 1        | 361     | /11   | N     | ic/361)             | (Bris/2 | 00)           | 0     | (ic/361)           |
|  | A/Perth/16/2009             | 2009-07-04 | Care  | E3/E2    | isto <b>ny</b> 80    | 80         | 320    |          | 640     |       | 320   | 320                 | 320     |               | 320   | 640                |
|  | A/Victoria/208/2009         | 2009-06-02 |       | E3/E1    | 1280                 | E05/120    | 1280   | 2        |         |       | 2560  | NB0                 | 5120    | NIB :         | 2560  | NHBO               |
|  | A/Alabama/5/2010            | 2010-07-13 | MK1/I | M2/SIAT2 | 40                   | 40         |        | 2        | F320    | 2     | 160   | F9/1120             | F60     | /12           | 160   | F11/820            |
| RE   | FERENCE VIRUSES             | 2011-05-19 | MDC   | K2/SIAT4 | 160                  | 160        | 320    |          | 1280    |       | 640   | 320                 | 1280    |               | 640   | 1280               |
|  | A/Stockholm/18/2011         | 2011-03-28 | MDC   | K2/SIAT3 | 80                   | 80         | 160    |          | 640     |       | 640   | 320                 | 320     |               | 320   | 640                |
| A/V  | iontonalias/36/1b/2011      | 2010-12-30 |       | E3/E1    | F3/F <sup>2≨60</sup> | 5120       | 2560   | 0        | 5120    | 60    | 5120  | 25 <b>600</b>       | 5120    | 640 :         | 5120  | 12 <del>3</del> 00 |
| NIE  | A/Finland/190/2011          | 2011-11-25 |       | Cx/SIAT3 | (SPE)60              | 2568       | 1320   | n        | 1280,   | 280   | 640   | 1280                | 1280    | 160           | 640   | 1280               |
|  | A/Ehdiana/258/2011'/        | 2011-11-16 |       | C×/SIATZ |                      | 2000       | 180    |          | 320     | 240   | 160   | - <u>160</u>        | 640     | 100           | 320   | 640                |
|  | 2/NB5twl.49/1/78/9/2074(11) | 2011-08-02 |       | Cx/SIATS | D0/E320              | 0344       | 690    | 0        | 1280    | 040   | 640   | 040                 | 1280    | 120           | 640   | 0(180              |
| IVR  | -165 (Vic/361/11)           |            |       | E3/      | D6/E1                | 640        | 64     | 0        | 12      | 280   |       | 320                 |         | 160           |       | 1280               |
|  | TEST VIRUSES                |            |       |          |                      |            |        |          |         |       |       |                     |         |               |       |                    |
|  | NIR-79                      |            |       | E5       | 160                  | 320        | 160    |          | 640     |       | 80    | 320                 | 320     |               | 160   | 640                |
|  | A //ictoria/361/2011        | 2011-10-24 |       | E3/E1    | 160                  | 520<br>640 | 320    |          | 640     |       | 80    | 640                 | 640     |               | 320   | 640                |
|  | A VICIONA/301/2011          | 2011/10-24 |       | L3/L1    | 100                  | 040        | 520    | <u> </u> | 040     |       | 00    | 040                 | 040     |               | 520   | 040                |



Results of two way HI test provided by National Institute of Medical Research, Mill Hill, London

Antigenic analyses of influenza A H3N2 viruses (Guinea Pig RBC with 20nM Oseltamivir) (15/03/2012)

Dr. John McCauley, BSc PhD Director, WHO Collaborating Centre For Reference and Research on Influenza Division of Virology



Monday, 19 March 2012

Medicines & Healthcare products Regulatory Agency



Dear Othmar,

Thank you for sending your reassortant to us for characterisation and for sharing ferret sera with us.

The results with your reassortant NIB-79 was that it reacted well with three post-infection ferret sera raised against the wild-type A/Victoria/361/2011 virus and the serum raised against NIB-79 reacted well with wild-type A/Victoria/361/2011. The results of this two-way test indicate that NIB-79 is A/Victoria/361/2011-like in HI assays.

As you know, we carry out analyses in the presence of oseltamivir to circumvent any influence of the NA mediated agglutination of the red cells that are used (see Yi Pu Lin's paper in J.Virol in 2010, (http://www.ncbi.nlm.nih.gov/pubmed/20410266))

With best wishes,

John McCauley.