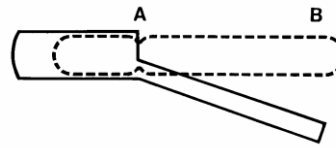




**WHO International Standard**  
**The 1st International Standard for Newcastle Disease Vaccine**  
**(Inactivated)**  
**NIBSC code: NVIA**  
**Instructions for use**  
**(Version 4.0, Dated 26/04/2013)**



Side view of ampoule opening device containing an ampoule positioned ready to open. 'A' is the score mark and 'B' the point of applied pressure.

### 1. INTENDED USE

This material has been prepared and characterised by the Veterinary Laboratories Agency, Weybridge, Surrey, UK. With effect from 1st June 1998, the National Institute for Biological Standards and Control (NIBSC), Potters Bar, UK is the custodian and distributor of this material.

For details of this International Standard, please refer to the enclosed package insert from the Veterinary Laboratories Agency. The Distribution statement in the package insert is no longer valid.

The package insert from VLA is attached.

### 2. CAUTION

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

Contains material from chicken eggs treated with formalin, along with lactose and aluminium hydroxide. 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

The International Unit is defined as the unitage contained in 1mg of the International Standard. For practical purposes each ampoule it may be assumed that each ampoule contains 525 International Units.

### 4. CONTENTS

Country of origin of biological material: United Kingdom.

Each ampoule contains aluminium hydroxide adjuvanted allantoic fluid of embryonated hen's eggs containing formalin inactivated Newcastle Disease Virus.

See attached package insert from VLA.

### 5. STORAGE

Ampoules should be stored at -20°C.

**Please note: because of the inherent stability of lyophilized material, NIBSC may ship these materials at ambient temperature.**

### 6. DIRECTIONS FOR OPENING

Tap the ampoule gently to collect the material at the bottom (labelled) end. Ensure ampoule is scored all round at the narrow part of the neck, with a diamond or tungsten carbide tipped glass knife file or other suitable implement before attempting to open. Place the ampoule in the ampoule opener, positioning the score at position 'A'; shown in the diagram below. Surround the ampoule with cloth or layers of tissue paper. Grip the ampoule and holder in the hand and squeeze at point 'B'. The ampoule will snap open. Take care to avoid cuts and projectile glass fragments that enter eyes. Take care that no material is lost from the ampoule and that no glass falls into the ampoule.

### 7. USE OF MATERIAL

No attempt should be made to weigh out any portion of the freeze-dried material prior to reconstitution

Please refer to the enclosed package insert from the Veterinary Laboratories Agency (below).

### 8. STABILITY

Reference materials are held at NIBSC within assured, temperature-controlled storage facilities and they should be stored on receipt as indicated on the label. It is the policy of WHO not to assign an expiry date to their international reference materials. They remain valid with the assigned potency and status until withdrawn or amended.

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

Users who have data supporting any deterioration in the characteristics of any reference preparation are encouraged to contact NIBSC.

### 9. REFERENCES

Please refer to the enclosed package insert from the Veterinary Laboratories Agency.

### 10. ACKNOWLEDGEMENTS

Not applicable

### 11. FURTHER INFORMATION

Further information can be obtained as follows:

This material: [enquiries@nibsc.org](mailto: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](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](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](mailto: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

[http://www.who.int/bloodproducts/publications/TRS932Annex2\\_Inter\\_biol\\_efstandardsrev2004.pdf](http://www.who.int/bloodproducts/publications/TRS932Annex2_Inter_biol_efstandardsrev2004.pdf) (revised 2004). They are officially endorsed by the WHO Expert Committee on Biological Standardization (ECBS) based on the report of the international collaborative study which established their suitability for the intended use.

Physical and Chemical properties	
Physical appearance: Freeze dried powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify): Contains material from chicken eggs treated with formalin, with lactose and aluminium hydroxide	
Toxicological properties	
Effects of inhalation:	Not established, avoid inhalation
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 an appropriate disinfectant. Rinse area with an appropriate disinfectant followed by water. Absorbent materials used to treat spillage should be treated as biological 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](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

<b>Country of origin for customs purposes*:</b> 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.
<b>Net weight:</b> 500mg
<b>Toxicity Statement:</b> Non-toxic
<b>Veterinary certificate or other statement</b> if applicable. <b>Attached:</b> No

#### 17. CERTIFICATE OF ANALYSIS

NIBSC does not provide a Certificate of Analysis for WHO Biological Reference Materials because they are internationally recognised primary reference materials fully described in the instructions for use. The reference materials are established according to the WHO Recommendations for the preparation, characterization and establishment of international and other biological reference standards



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**INTERNATIONAL STANDARD FOR NEWCASTLE DISEASE VACCINE  
(INACTIVATED) (NYIA)**

**Description**

The International Standard for Newcastle Disease Vaccine (Inactivated) was established in 1963. It was prepared from the allantoic fluid of embryonated hens' eggs infected with nine European strains of Newcastle disease virus. The fluid was inactivated with formalin and mixed with an equal volume of an aluminium hydroxide suspension containing 2% Al (OH)<sub>3</sub>. The resulting preparation was mixed with an equal volume of a 10% aqueous lactose solution (as a protective agent during freeze-drying) immediately before being dispensed. The mixture was distributed into glass ampoules in 8ml. amounts and freeze-dried. The ampoules were sealed under vacuum.

The average weight of dry material per ampoule has been determined as 527.4mg. with a standard deviation of 2.1%.

It has been shown that the Standard can be used to assay the potency of both formalin and propiolactone inactivated vaccines.

**International Unit**

The International Unit is defined as the activity contained in 1.0mg. of the International Standard.

For practical purposes it may be assumed that each ampoule contains 525 International Units.

**Distribution**

The Standard is distributed by the International Laboratory for Biological Standards, Ministry of Agriculture, Fisheries and Food, Central Veterinary Laboratory, New Haw, Addlestone, Surrey, England on behalf of the World Health Organization. It is available free of charge in limited amounts. If a laboratory needs more than one ampoule every six months, it is expected to prepare its own standard and to calibrate it against the International Standard.

**Reconstitution of International Standard**

The Standard should be reconstituted immediately before it is to be used.

The material in each ampoule may be reconstituted in any convenient volume of a suitable diluent. Care should be taken to ensure that the entire contents of the ampoule are completely resuspended.

**National and Laboratory Standards**

National and laboratory standards should be prepared in a stable form. This may be achieved by freeze-drying aliquots of the reference preparation in neutral-glass ampoules and sealing them in an oxygen-free atmosphere by fusion of the glass. The ampoules should be stored in the dark at a low temperature, e.g. -20°C.

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Fisheries and Food*

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The potency of such a standard relative to that of the International Standard should be determined by performing a series of comparative assays.

The following method is suggested:

Chicks of the same age, within the age range of 2-6 weeks, drawn from an unvaccinated flock known to be free from Newcastle disease, are used. Serum from each bird is examined by the haemagglutination-inhibition test for antibodies to Newcastle disease virus; the batch of chicks is accepted only if all sera are negative in this test. The chicks are distributed into groups of 25 chicks each. A minimum of three groups is injected intramuscularly with the International Standard, each group receiving one of a series of doses equally spaced on a logarithmic scale. The same number of groups is injected with a similar series of doses of the preparation being calibrated. The doses are chosen to cover the range from 10% to 90% protection. This can usually be achieved somewhere within the range of 1 to 40 units per chick. If the appropriate range for the strain of birds and the technique being used is not known, a small-scale, preliminary trial should be carried out to determine this. A group of at least 10 unvaccinated chicks is kept as a control.

Fourteen days later each chick is injected intramuscularly with 200,00 chick embryo LD<sub>50</sub> of a virulent strain of Newcastle disease virus. The chicks are observed for ten to fourteen days and deaths are recorded. Any chicks which show signs of paralysis at the end of this time are counted as unprotected. At least 90% of the control chicks should die.

The potency of the new standard relative to that of the International Standard is calculated by the usual statistical methods and the result is expressed in International Units. This calculation should be based on a series of at least three assays.

It is suggested that the potency of a National or Laboratory Standard should be checked against that of a fresh sample of the International Standard about once a year.

The International Laboratory for Biological Standards at Weybridge is willing to advise and assist laboratories in providing national and laboratory standards.

#### **Assaying Routine Batches of Vaccine**

The method used can be similar to the one described in the preceding section, but the number of chicks can often be reduced.

When it has been demonstrated that the assay method gives satisfactory and consistent results with any particular vaccine, a four point assay may be used, i.e. an assay with two groups of chicks for the standard preparation and two for the vaccine being tested. If the slopes of the dose-response curves do not vary significantly from assay to assay a three point or a two point assay may be satisfactory (Prigge, 1939) (Tootill, 1969). However, if this is done, it is advisable to perform a four or six point assay from time to time to detect any changes in the assay conditions or qualitative changes in the products being tested.

#### **Potency Requirements**

Although there are at present no international requirements for inactivated Newcastle disease vaccine, it is suggested that vaccines should contain at least 200 International Units per dose.

#### **References**

Prigge, R. (1939). *Ergebn. Hyg. Bakt.* 22, 18.

Tootill, J.P.R., Hebert, C.N. and Adams, A.G. (1969) *Symp. Series immunobiol.*