



**WHO International Standard
3rd International Standard For Prekallikrein Activator
NIBSC code: 16/364
Instructions for use
(Version 1.0, Dated 30/10/2019)**

1. INTENDED USE

Prekallikrein Activator (PKA), also known as activated FXII or activated Hageman Factor, is a contaminant in human albumin solutions and immunoglobulin solutions prepared from fractionated plasma. It is known that adverse events, including vasodilation and hypotension, may occur where albumin solutions are contaminated with significant levels of PKA and are infused into patients. This is of special concern since albumin may be administered as a plasma expander to counter hypovolemia and hence the treatment may exacerbate the existing problem. Limits are set on the maximum level of PKA allowed in plasma and assays for PKA are standardised using an International Standard (IS). The current 3rd IS for PKA replaces the 2nd IS (02/168). The 3rd IS is a freeze dried preparation of 20 % albumin containing a significant level of PKA.

2. CAUTION

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

The preparation contains material of human origin, and either the final product or the source materials, from which it is derived, have been tested and found negative for HBsAg, anti-HIV and HCV RNA. 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

30 IU of PKA per ampoule.

Each ampoule contains 30 IU/ml of PKA when reconstituted in 1 ml of distilled water.

Complete dissolution of the freeze dried plug may take up to 30 min and care should be taken to ensure that all solid material has been completely dissolved. Best results are obtained with gentle swirling. Vigorous mixing or vortexing should be avoided as this causes foaming leading to incomplete solubilisation of the ampoule contents.

Once reconstituted, the PKA solution should be stored on ice and used within 1 day. NIBSC does not guarantee a stable unitage over longer times and if the solution is to be aliquoted and stored users should determine the stability under their own conditions.

4. CONTENTS

Country of origin of biological material: United Kingdom.

Each ampoule contains the residue of 1 ml of freeze dried 20 % albumin solution manufactured for clinical use, from a commercial source, without any further additions. The mean filling weight was 1.0084 g (cv = 0.16 %). The residual moisture content after freeze drying was 0.20 % and no secondary desiccation was performed.

Uncertainty: the assigned unitage does not carry an uncertainty associated with its calibration. The uncertainty may therefore be considered to be the variance of the ampoule content and was determined to be +/- 0.16%.

5. STORAGE

Ampoules stored at -20 °C should be brought to room temperature before opening and reconstitution of the freeze dried contents.

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

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

The 3rd IS for PKA was calibrated in an international collaborative study where participants were asked to follow the European Pharmacopoeia method for the determination of PKA in human albumin solutions. The Standard is intended to be used as a primary reference calibrator for secondary working standards in a similar assay. The 3rd IS for PKA is in limited supply and large or repeat orders will not be shipped without prior approval.

Similar material is available in vials as Prekallikrein activator in albumin BRP batch 7 (Y 0000263), with a potency of 37 IU/vial from the EDQM in Strasbourg. This standard is available in larger quantities and may be suitable as a working standard. Information (product leaflet, safety data sheet) on the BRP and on purchase conditions can be found at <http://www.pheur.org>. Further enquiries and purchasing information may also be obtained by emailing CRS@pheur.org.

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.

All current indications suggest that the 3rd IS for PKA is very stable, as was the previous 2nd IS. Samples were held at -70, -20, 4, 20, 37, 45 and 56°C. Potencies were determined at NIBSC after 1 and 2 years storage to calculate loss of activity due to elevated temperature relative to the sample kept at -70 °C. Analysis of the raw data using the Arrhenius model has predicted a loss of activity of 0.005%/year at -20°C. The raw data showed excellent stability at ambient temperatures, allowing shipping of the IS without refrigeration. It is recommended that samples be stored at -20 °C for extended periods.

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

9. REFERENCES

10. ACKNOWLEDGEMENTS

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: Freeze dried powder	Corrosive: No
Stable: Yes	Oxidising: No
Hygroscopic: No	Irritant: No
Flammable: No	Handling: See caution, Section 2
Other (specify):	Contains material of human origin
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 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: 10mg
Toxicity Statement: Toxicity not assessed
Veterinary certificate or other statement if applicable.
Attached: 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 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.