

Project Outline (SSC FXIII & Fibrinogen Subcommittee)

Proposal for Value Assignment for FXIII B-subunit (total & free) to the WHO 1st IS Factor XIII Plasma (02/206)

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Background

The current WHO 1st International Standard (IS) for FXIII plasma (02/206) was established by the ECBS in November 2004.

As the half-life of FXIII A depends on the amount of available FXIII B, it is important to establish the level of total and free FXIII B in current WHO 1st IS for FXIII plasma (02/206). Free FXIII B may have so far unknown functions in binding and regulating FXIII and other plasma proteins. FXIII substitution therapy with rFXIII depends on FXIII B.

Proposal

Collaborative study to value assign the WHO 1st IS Factor XIII Plasma (02/206) for FXIII B-subunit (total & free).

Considerations for Assignment of Priorities (WHO/ECBS - TRS932)

Rationale:

- FXIII carrier/inhibitory B subunits are in excess in healthy individuals
- 50% of B subunits circulate in plasma in free non-complexed form
- Half-life of FXIII A depends on the level of FXIII B available
- Inherited FXIII deficiency is important but rare
- Important for new recombinant FXIII product(s) (A2 subunit)
- Demand for new tests for assessment of Total/Free FXIII B
- Increasing evidence for clinically relevant acquired FXIII deficiency states

Approval status of medicine or *in vitro* diagnostic method:

- Value assignment to the WHO 1st IS needed for diagnostic tests, current methods, new products. Local calibrants are not available leading to poor standardisation.

No. of products or methods:

- 2 products: Fibrogammin (CSL Behring) & rFXIII (Novo Nordisk)

Public health Importance:

- Major role for FXIII in various medical conditions
- Indications for FXIII substitution are increasing

Global Importance:

- Use of standard will be by manufacturer, clinicians and R& D groups
- Use of recombinant products is increasing

Global need from Regulatory & Scientific bodies:

- Substitution of FXIII must be based on correct FXIII measures
- FXIII diagnostic depends on standardised material
- Research into new functions of free B requires correct quantitation

Aims & Objectives

- To calibrate the current WHO 1st IS Factor XIII Plasma for FXIII B-subunit (total & free) using antigen assays.
- To carry out a collaborative study involving laboratories including manufacturers, clinical labs and Control labs.
- To compare potency values calculated against locally collected pooled normal plasma using currently available antibodies for ELISAs.
- To submit to Factor XIII & Fibrinogen SSC Subcommittee for endorsement/approval.
- To submit to WHO-ISTH/SSC Liaison Group for endorsement/approval.
- To submit to WHO/ECBS for value assignment in November 2014.