



Direction de l'Evaluation des Dispositifs Médicaux
Département Surveillance du Marché
Unité Evaluation et Contrôle du Marché - DIV
Dossier suivi par Françoise Chevenne
Tel : +33 (0) 1 55.87.42.61
Fax : +33 (0) 1 55.87.42.62
Email : francoise.chevenne@afssaps.sante.fr

RECOMMENDATIONS ON EVALUATION OF TROPONIN I/T CARDIAC MARKER DEVICES

Version issue : October 3rd , 2006

**Document related to
the Guidelines
on Instruction for use for
Troponin I/T cardiac marker devices**

Purpose :

These recommendations are proposed exclusively **in association** with the guidelines on Instruction for use for Troponin I/T cardiac marker devices in order to lead the manufacturers in their studies which results must be mentioned in the instruction for use.

That's why this document is not an exhaustive list of the studies to be carried for the performance evaluation but only the studies required in the guidelines on instruction for use for Troponin I/T cardiac marker devices.

- **Preanalytical phase :**

Carry on a study in order to justify the use of recommended specimen and to exclude the forbidden proved type specimen .

This study shall enable the user to conclude about the necessity of using the same anticoagulant or not for the patient's follow-up.

- **Functional sensitivity :**

Determine the Tn values referring to a coefficient of variation of ten percent and referring to the detection threshold for a precision profile in low concentrations toward the analyte in an environment as close as a physiological environment ; the precision profile must take account of the concentrations and not the analytical signals (IFCC).

- **Analytical specificity :**

Test the cross-reactivity toward non cardiac isoforms of TnI and TnT, and cardiac TnC,

- **Diagnostic sensitivity :**

Determine the interpretation threshold of acute coronary syndrome : the 99th percentile of a reference population with % CV of 10 and lower and the lowest troponin concentration to allow a 10% CV.

- **Diagnostic specificity :**

Carry out a clinical trial dealing with Tn increases without cardiac injury, eg: muscular injury, rheumatoid arthritis etc ...

If necessary, carry out a sensitivity and clinical specificity study for several thresholds values with the assistance of the « Receiver Operator Characteristic » (ROC) curve.

- **Correlation study :**

Carry out a correlation study toward the method of comparison (describe the comparison technique used), for the whole measurement range and on a significant number of tested samples, by calculating the gradient and ordinate to the origin.

- **Repeatability and reproductibility :**

Carry out studies for 3 concentration levels, one must be close to the interpretation threshold (20 samples minimum).

- **Lower limit of detection :**

Evaluate the lower limit of detection using a troponin-free media, for example : zero calibrator or a matrix close to human serum.

- **Measurement range :**

Evaluate the modalities for the dilution in case of high Tn concentration, the linearity limit, the highest dilution and the suitable medium for dilution.

Evaluate the highest concentration hook-effect free.

- **Interferences and method limits :**

Evaluate the interferences with common drugs, haemoglobin, bilirubin, triglycerids, indicating the first interfering concentration.

Evaluate the immunological specificity to : rheumatoid factor, HAMA (heterophilic antibody mouse antigen).

- **Determination of the reference interval :**

Carry out a study on a significant number of apparently healthy subject (120 minimum) in order to determine the 99th percentile reference limit. The reference population must include males and 50 years old and more subjects. Define the gender ratio and age, inclusion and exclusion criteria.

ANNEXE :

References :

- Wu AH, Apple FS, Gibler WB, Jesse RL, Warshaw MM, Valdes R, Jr. National Academy of Clinical Biochemistry Standards of Laboratory Practice: recommendations for the use of cardiac markers in coronary artery diseases. Clin Chem 1999; 45: 1104-21.
- Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined--a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000; 36: 959-69. Validation of NACB and IFCC guidelines for the use of cardiac markers for early diagnosis and risk assessment in patients with acute coronary syndromes.
- Panteghini M, Gerhardt W, Apple FS, Dati F, Ravkilde J, Wu AH. Quality specifications for cardiac troponin assays. Clin Chem Lab Med 2001; 39: 175-9.
- Mockel M, Gerhardt W, Heller G Jr, Klefisch F, Danne O, Maske J, Muller C, Stork T, Frei U, Wu AH. Validation of NACB and IFCC guidelines for the use of cardiac markers for early diagnosis and risk assessment in patients with acute coronary syndromes. Clin Chim Acta ; 303 :167-79.
- Alpert JS, Thygesen K, Antman E, Bassand JP Myocardial infarction redefined-a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol. 2000 ;36:959-69.
- Special issue on reference values and reference intervals Petersen PH, Kazmierczak SC Clin Chem Lab Med 2004; 42 (7): 685-876.
- Groupe de travail mixte SFBC – CNBH « Troponines » (responsable : C. Morin). B. Capolaghi, B. Charbonnier, M. Dumontet, B. Hennache, J. Henninot, T. Laperche, A. Lavoinne, G. Lefèvre, C. Morin, D. Pateron, Recommandations sur la prescription, le dosage et l'interprétation des troponines cardiaques. Ann Biol Clin 2005; 63(3) :245-61.
- G. Lefèvre, C. Morin, pour le groupe de travail mixte SFBC-CNBH « Troponines », Utilisation des marqueurs cardiaques et de la troponine en France. Spectra Biologie 2005 ; 145 :35-48