**TITLE: Heparin Therapeutic Range**

**PRINCIPLE:**

The heparin-responsiveness of PTT reagents may change from lot to lot and among different reagents used on different instrument platforms. For this reason, it is necessary to establish the heparin therapeutic range for the PTT with each change of instrumentation and/or reagent type. The therapeutic range must be verified with each new lot of a given PTT reagent.

**Personnel:** Medical Technologists and Clinical Laboratory Scientists

**STEPWISE PROCEDURE:**

 **Initially to set up the Heparin Xa Curve:**

1. Collect 30-40 samples on patients receiving Unfractionated Heparin in 3.2% sodium citrate tubes.
2. Measure the PT/INR and PTT on all samples. If the INR is less than 1.3, the sample can be included in the heparin study.
3. Record the date, patient name, PTT result and the INR result on the log sheets in the department.
4. Separate the plasma into plastic tubes, place a label identifying them on the tube and place the samples in the Blood Bank freezer. There is a rack identified for the study.
5. These samples can be stored for 2 months, at which time we will begin the heparin therapeutic range study with the assistance of the vendor.
6. We also need 8-12 Normal patient samples frozen as well, to be used as pooled normal plasma. Label as Normal Plasma. Follow the same freezing protocol.

**Heparin Xa Calibration**

1. Reagents and Calibrators are reconstituted and set up on both analyzers by the vendor Clinical Analyst Specialist.
2. Frozen samples are thawed and Heparin Xa levels are run on the available samples, on both analyzers.
3. The CAS crunches the data and and calculates the therapeutic range for our current lot of PTT reagent.

 **Annual Lot to Lot Comparison**

1. It is our goal to select a reagent that has the same or nearly the same heparin responsiveness as the lot currently in use. This is useful for the clinician, who then does not need to change the way of treating or thinking about heparin dosing.
2. Perform PTT’s on samples using the current lot and the new lot of reagent, a minimum of 20 samples.
3. Using the EP Evaluator, plot the current lot PTT results on the X axis and the new lot PTT results on the Y axis.
4. The data for each PTT reagent are summed and the means and the standard deviation are determined.
5. The difference between the means of the new lot and current lot of reagents are recorded for future reference.
6. After the comparisons are complete, use the Cumulative Summation of PTT Reagent Mean Differences log to check the acceptance of the new lot of PTT reagent. Example of the log sheet follows the procedure.
7. Record the mean of the current lot of PTT reagent
8. Record the mean of the new lot of PTT reagent
9. The difference between the 2 must be less than 7.0 seconds.
10. The Cum Sum (difference of this year’s new and current lot, and the Cum Sum from the previous year added together) must be less than 7.0 seconds to be acceptable.
11. Calculate, review whether it is acceptable or not, fill out the action column and date and initial. Store in the Heparin Xa binder in the Coagulation department.

**A Cumulative summation of differences:**

Each time there is a change in reagents or instruments, the above method is performed. In addition to recording the difference in the mean, the laboratory should prepare a cumulative summation of the differences that have occurred in the past. In doing so, the cumulative shift in the reagent performance in the presence of heparin can be determined.

A difference between reagent means or a cumulative change of more than seven seconds is reason for concern and necessitates action. Actions may include:

1. Evaluating a different reagent to find one with an acceptable level of variation.
2. Informing all clinicians using heparin of the change in the therapeutic interval, recommending that they change their thresholds.
3. Reverification of the PTT using comparisons with heparin concentration.



 It is of interest that the cumulative summation has remained within a range that

has not required informing clinicians of the need to change the therapeutic range

for the PTT. Using PTT reagents from a single manufacturer facilitates the

simplicity of the method. In addition, this method can be applied even if there is an

instrument change.

 The reagents tested in numbers 2 and 4(above) are examples of reagents that have unacceptable variability (reagent 2a has a cumulative summation that is above 7, which is too high despite the differences in the mean being less than 7 seconds; reagent 4a has a difference in the mean that is greater than 7 seconds). As noted in the Action column, both of these reagents were

rejected and in both cases different reagents (2b and 4b respectively) were tested

and the problem resolved.

**REFERENCES:**

Coagulation Resource Committee, CAP Participant Summary

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