Algorithm for Laboratory Investigations in case of a Prolonged aPTT

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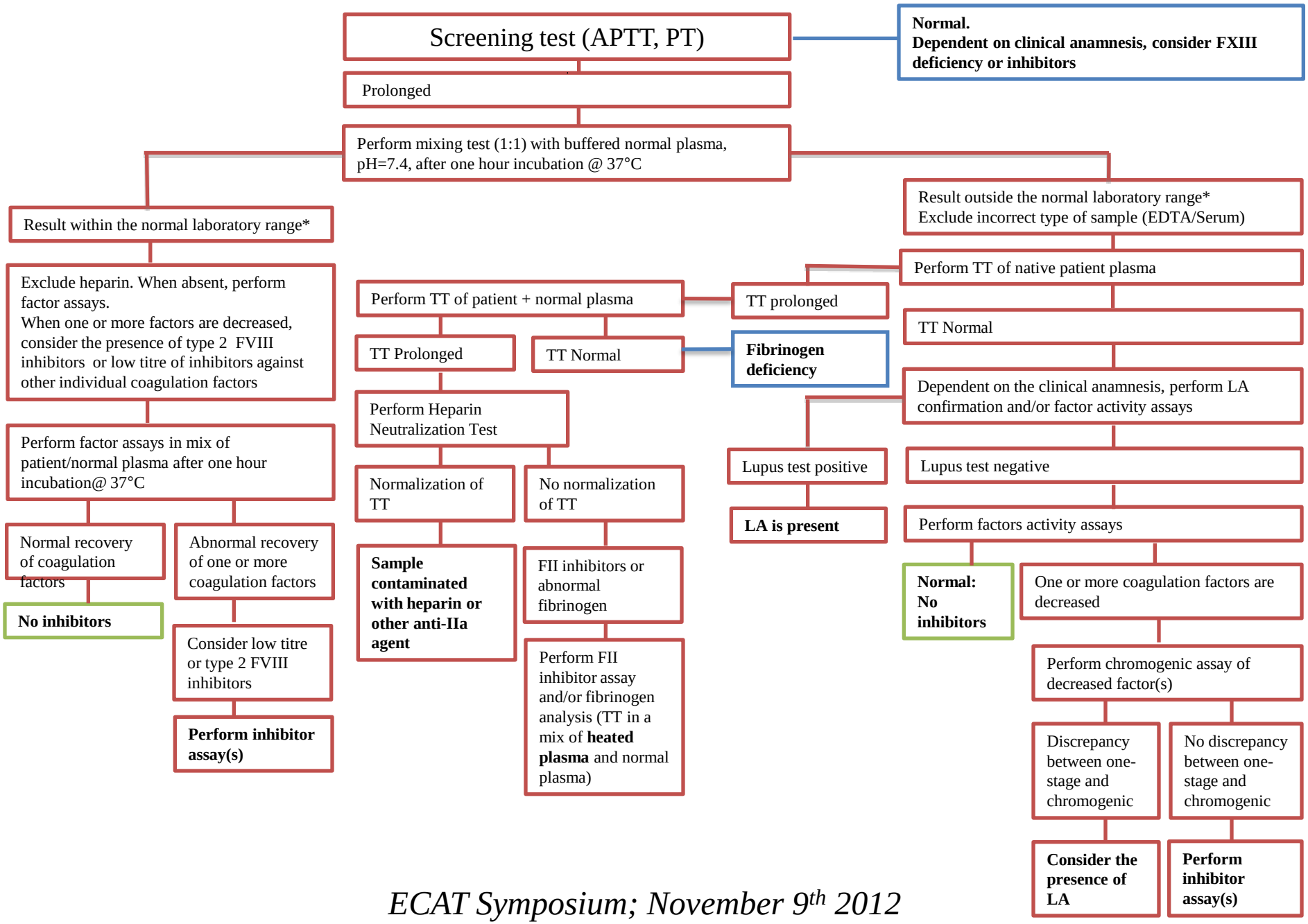
Detection of coagulation abnormalities

- Quick screening: TT, PT, aPTT
- Confirmation of inhibitors or Factors deficiencies
- Differential diagnosis

Why the need of an algorithm ?

- Variation between laboratories
- Lack of step by step procedure
- Costs and time efficiency

Diagnostic Algorithm for Acquired Coagulation Inhibitor Analysis



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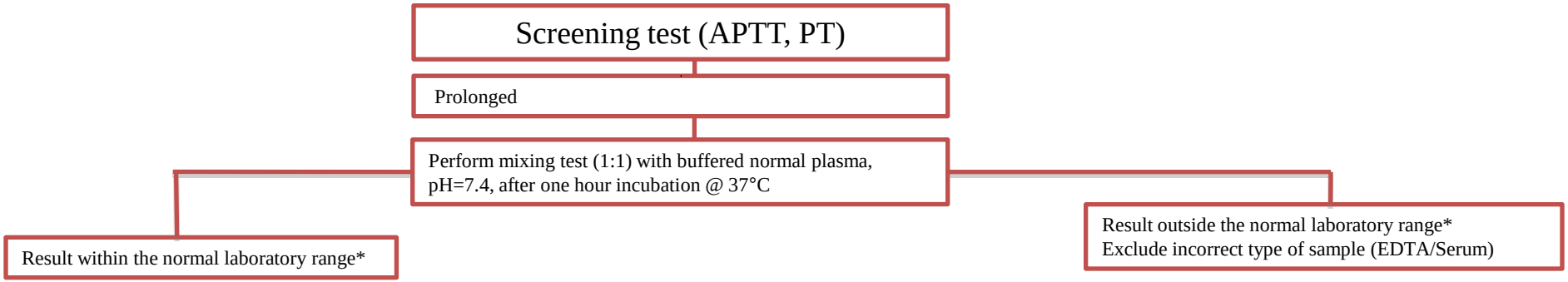
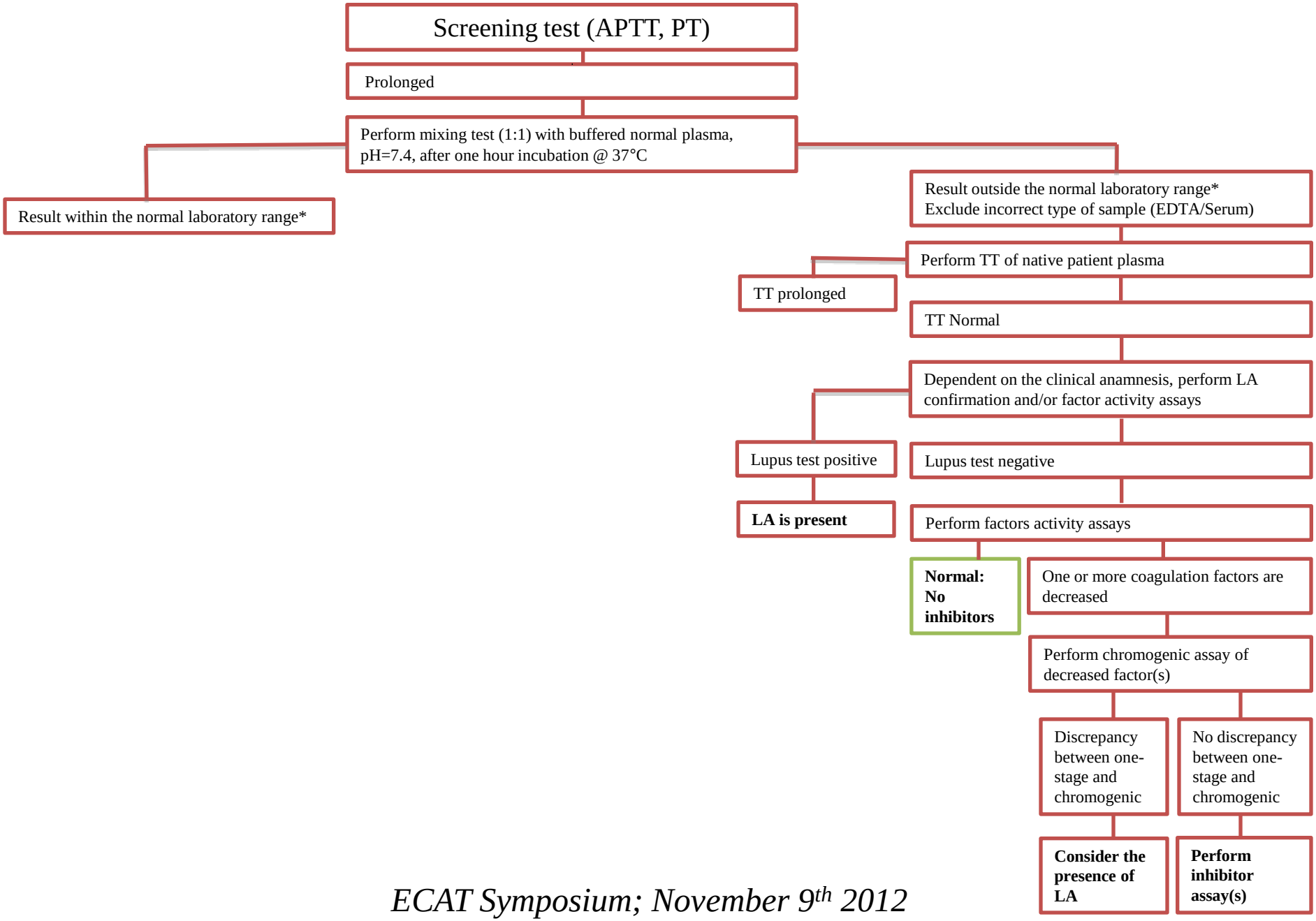
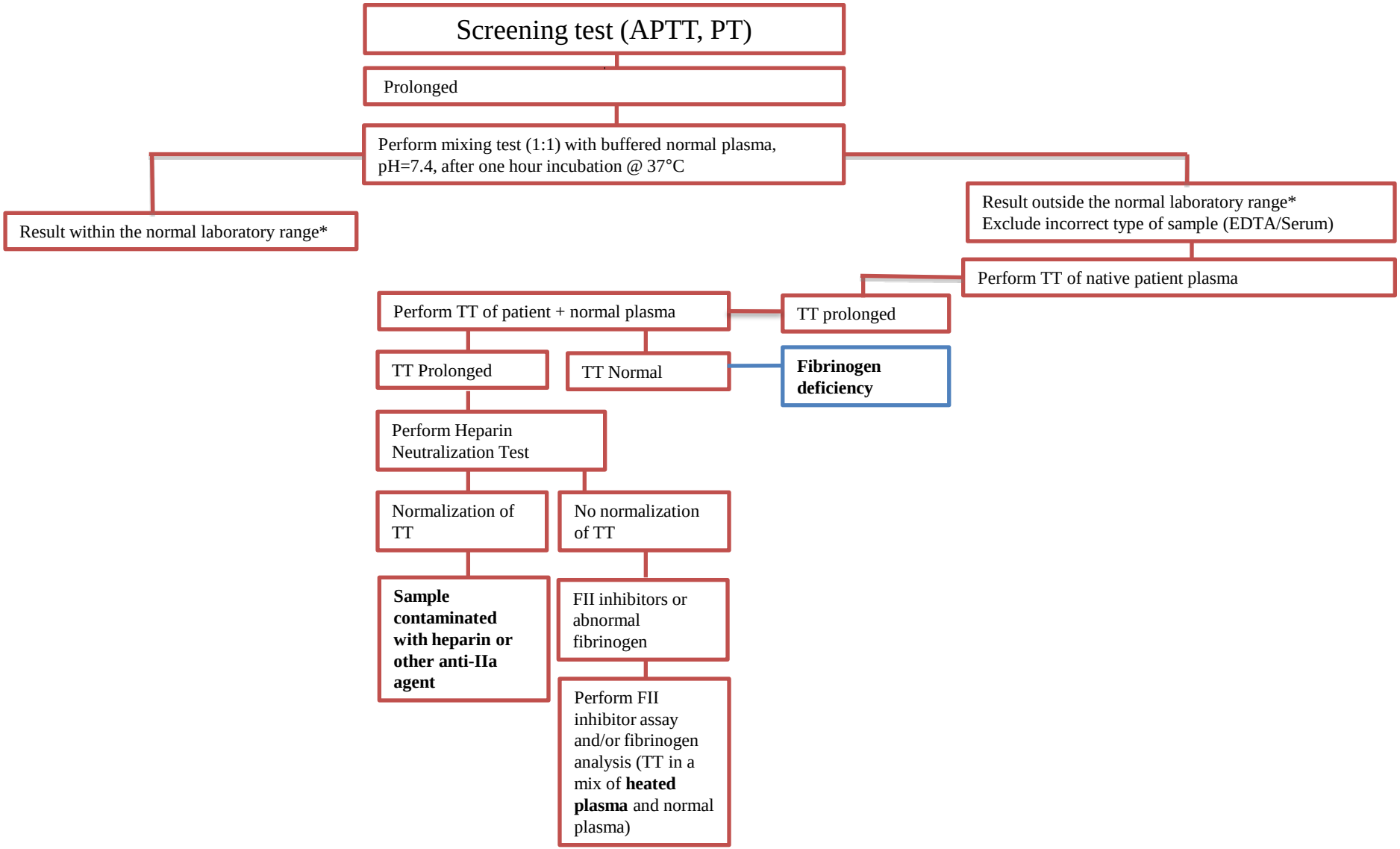
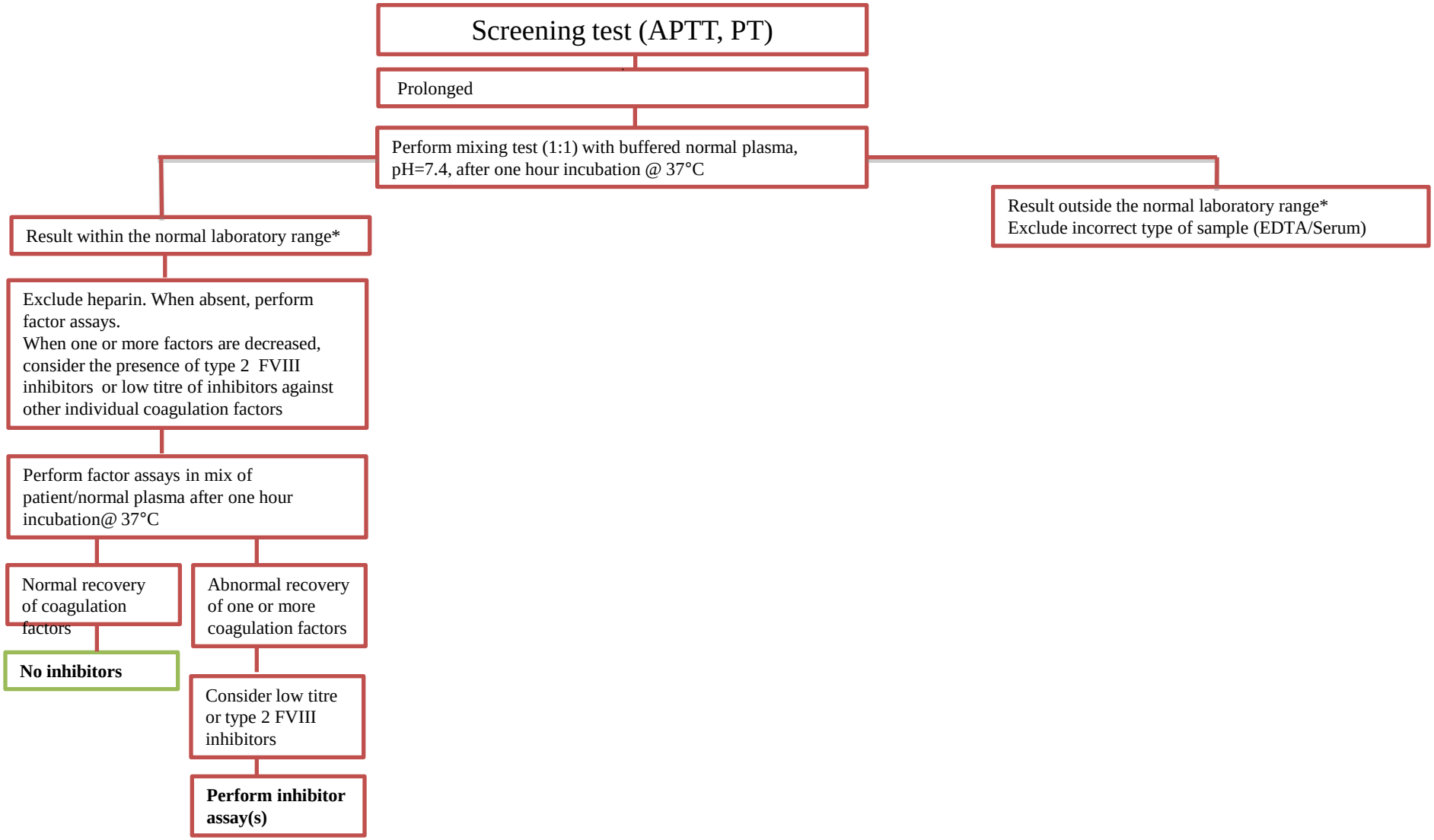
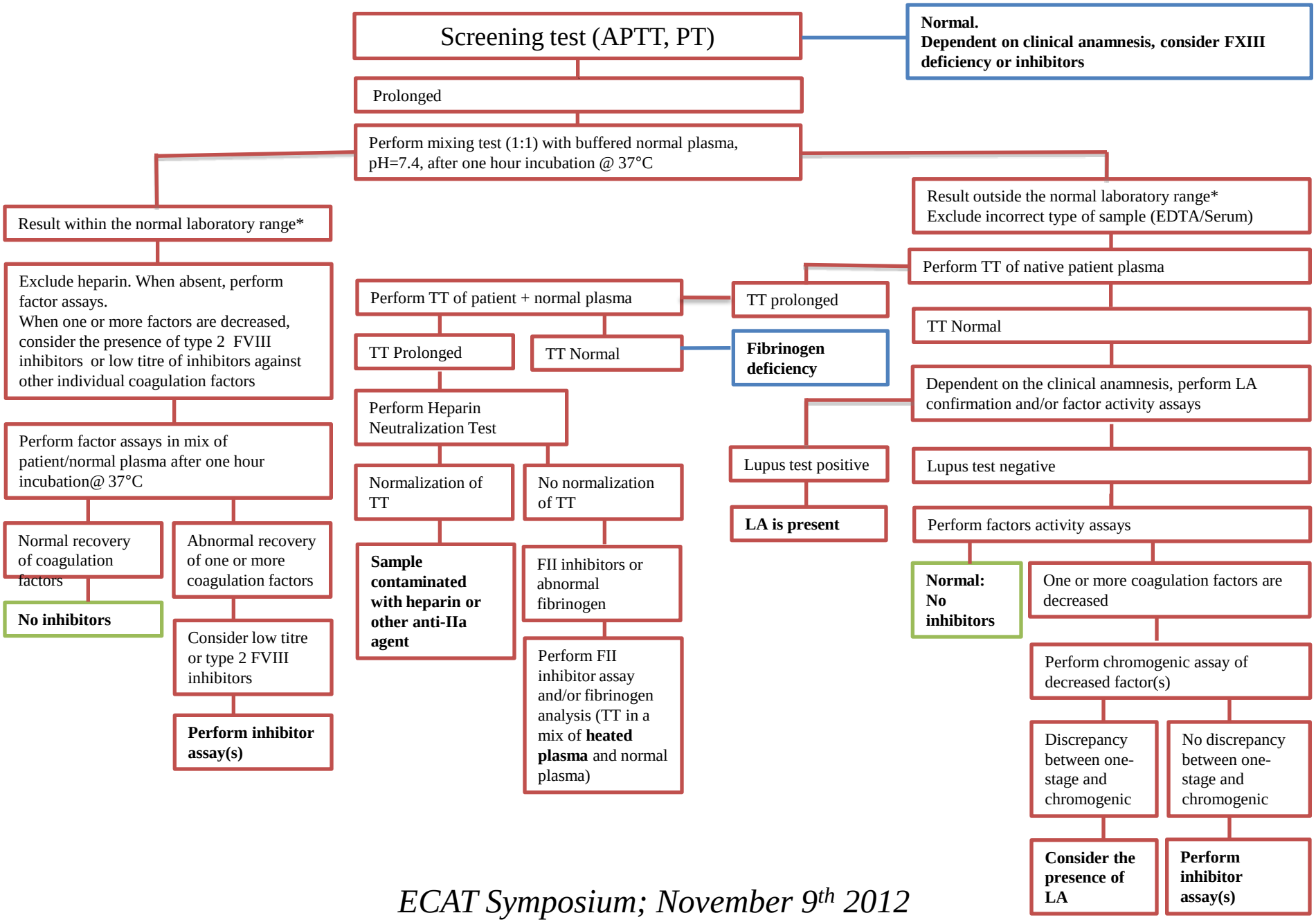

Screening test (APTT, PT)
Prolonged
Perform mixing test (1:1) with buffered normal plasma, pH=7.4, after one hour incubation @ 37°C
Result within the normal laboratory range*
Result outside the normal laboratory range*
Exclude incorrect type of sample (EDTA/Serum)


Screening test (APTT, PT)
Prolonged
Perform mixing test (1:1) with buffered normal plasma, pH=7.4, after one hour incubation @ 37°C
Result within the normal laboratory range*
Result outside the normal laboratory range*
Exclude incorrect type of sample (EDTA/Serum)
Perform TT of native patient plasma
TT prolonged
TT Normal
Dependent on the clinical anamnesis, perform LA confirmation and/or factor activity assays
Lupus test positive
Lupus test negative
LA is present
Perform factors activity assays
Normal: No inhibitors
One or more coagulation factors are decreased
Perform chromogenic assay of decreased factor(s)
Discrepancy between one-stage and chromogenic
No discrepancy between one-stage and chromogenic
Consider the presence of LA
Perform inhibitor assay(s)


Screening test (APTT, PT)
Prolonged
Perform mixing test (1:1) with buffered normal plasma, pH=7.4, after one hour incubation @ 37°C
Result within the normal laboratory range*
Result outside the normal laboratory range*
Exclude incorrect type of sample (EDTA/Serum)
Perform TT of native patient plasma
TT prolonged
Perform TT of patient + normal plasma
TT Prolonged
TT Normal
Fibrinogen deficiency
Perform Heparin Neutralization Test
Normalization of TT
No normalization of TT
Sample contaminated with heparin or other anti-IIa agent
FII inhibitors or abnormal fibrinogen
Perform FII inhibitor assay and/or fibrinogen analysis (TT in a mix of heated plasma and normal plasma)


Screening test (APTT, PT)
Prolonged
Perform mixing test (1:1) with buffered normal plasma, pH=7.4, after one hour incubation @ 37°C
Result outside the normal laboratory range*
Exclude incorrect type of sample (EDTA/Serum)
Result within the normal laboratory range*
Exclude heparin. When absent, perform factor assays.
When one or more factors are decreased, consider the presence of type 2 FVIII inhibitors or low titre of inhibitors against other individual coagulation factors
Perform factor assays in mix of patient/normal plasma after one hour incubation@ 37°C
Normal recovery of coagulation factors
Abnormal recovery of one or more coagulation factors
No inhibitors
Consider low titre or type 2 FVIII inhibitors
Perform inhibitor assay(s)

Diagnostic Algorithm for Acquired Coagulation Inhibitor Analysis



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Take home message

- The clinical anamnesis is guiding for the use of this algorithm

- Step by step procedure is necessary to exclude inaccurate diagnosis

- Always be aware of (pre) analytical mistakes.

(e.g. heparin contamination)

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