



REPUBLIC OF KENYA
MINISTRY OF HEALTH



KENYA MEDICAL LABORATORY TECHNICIANS AND TECHNOLOGISTS BOARD

**MANDATORY MEDICAL LABORATORY ANALYSIS INVESTIGATIONS FOR HAEMOPHILIA A AND B
DIAGNOSIS AND MANAGEMENT IN KENYA**

*Pursuant to the Medical Laboratory Technicians and Technologists Act CAP 253 A Laws
of Kenya.*

KMLTTB QUALITY ASSURANCE SERVICES

	MANDATORY MEDICAL LABORATORY ANALYSIS INVESTIGATIONS FOR HAEMOPHILIA A AND B DIAGNOSIS AND MANAGEMENT IN KENYA		DOCUMENT CONTROL CODE: KMLTTB/LABS HAEMOPHILIA/INV/01 Version: 001
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INTRODUCTION

The Kenya Medical Laboratory Technicians and Technologists Board (KMLTTB) is a statutory body mandated to oversee the training, practice, business, and employment of medical laboratory technicians and technologists, as stipulated under Cap 253A of the Laws of Kenya. The Board also provides government advisories on related matters, including the validation of in vitro diagnostics through Legal Notice No. 113 of 2011.

The Act gives the Board the responsibility of ensuring that students undertaking medical laboratory sciences (MLS) training and practising professionals acquire the desired knowledge and skills that are necessary for the delivery of medical laboratory services.

These standards will ensure the development of a robust human resource for health necessary to meet national and international health obligations that include sustainable development goals and universal health coverage. The implementation of these standards will no doubt contribute to achievement of the right to the highest attainable standard of health as outlined in the constitution of Kenya 2010 as well as achievement of Vision 2030. This shall be the hallmark of quality Healthcare and patient safety.

VISION, MISSION AND CORE VALUES

Our Vision: “That the Health of every Kenyan will be fully protected through effective regulation of the practice of laboratory medicine.”

Our Mission: “To Exercise General Control and Supervision over training, business, employment and practice of Laboratory Medicine and Advise the Government on all related matters.”

Our Core Values: Integrity; Selfless service; Innovation and open-mindedness; Sense of belonging; Pride in what we do.

MANDATORY MEDICAL LABORATORY ANALYSIS INVESTIGATIONS FOR HAEMOPHILIA A AND B DIAGNOSIS AND MANAGEMENT IN KENYA

Aligned to MOH, Kenya Haemophilia Association, and WFH Guidelines for Management of Hemophilia 2023

This is the Minimum Mandatory Panel for diagnosis, treatment, monitoring and prevention. No Medical Laboratory facility Class C TO G should manage bleeding disorders without this framework. It is auditable by KMLTTB and should inform other institutions such as SHA to ensure Quality Health care and patient safety in the republic of Kenya.

1. LEGAL AND CLINICAL BASIS

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Under CAP 253A, KMLTTB regulates validation of coagulation testing, referral and EQA. Haemophilia A [FVIII deficiency] and B [FIX deficiency] prevalence in Kenya is underestimated due to lack of factor assays. MOH estimates >2,500 cases, <15% diagnosed. Untreated bleeds cause 70% disability and high mortality. Accurate Medical laboratory diagnosis is mandatory before any Blood product or factor is issued.

Core Principle: aPTT alone is NOT diagnosis. Prolonged aPTT MUST be followed by mixing studies and specific Factor VIII / IX assay. PT must be normal.

2. CLASSIFICATION OF MANDATORY INVESTIGATIONS.

A. PREVENTION and CARRIER / FAMILY SCREENING PANEL [Class C MEDICAL LABORATORY AND ABOVE]

PURPOSE	MANDATORY TESTS	METHOD PRESCRIBED	WHEN/ SPECIMEN
Family Cascade Screening	aPTT, PT, FVIII: C assay for A families or FIX: C assay for B families	One-stage clotting assay or chromogenic assay. Citrated plasma	All first-degree male relatives, 3.2% sodium citrate tube, tested within 4 hours or frozen platelet-poor plasma
Carrier Detection [Obligate and Potential Carriers]	FVIII:C, FIX:C, FVIII:Ag, VWF:Ag, VWF:RCo Plus Genetic counseling referral	Factor levels may be 30-70% in carriers. Ratio FVIII: C / VWF: Ag helpful. Confirmatory: Molecular analysis - F8 gene inversion 22 and 1, F9 gene sequencing	Female relatives of hemophiliacs pre-marriage, preconception, antenatal
Antenatal / Preconception Prevention	Maternal factor level in 3rd trimester, fetal sex determination, referral for CVS/amniocentesis for molecular	Requires specialized genetic lab Plus Ethics approval	High-risk pregnancies



	diagnosis if severe family history		
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All carriers must be reported with: Factor level %, Interpretation [e.g., Carrier range], Bleeding risk for pregnancy/delivery.

B. DIAGNOSTIC CONFIRMATION PANEL [Mandatory Class D to G Medical Laboratories that are compliant with ISO 15189:2022]

This is mandatory before issuing diagnosis of Haemophilia A or B. To be done in steady state, not during acute bleed or after transfusion within 48 hours.

STEP 1 - TRIAGE COAGULATION SCREEN:

1. Complete Blood Count plus Peripheral Blood Film: Exclude thrombocytopenia, platelet clumps. Platelets usually normal in Haemophilia
2. Bleeding Time / PFA-100 Should be normal - to exclude platelet disorder
3. **PT / INR:** MUST be normal. If prolonged, suggests combined defect / anticoagulant / liver disease
4. **aPTT:** Prolonged in Haemophilia. Corrects immediately in mixing study. Degree correlates poorly with severity but required
5. Mixing Study - Immediate and incubated [1 and 2 hours at 37C]: Mandatory to rule out inhibitor / lupus anticoagulant. Correction = factor deficiency. No correction = inhibitor present

STEP 2 - SPECIFIC FACTOR ASSAYS - GOLD STANDARD:

6. Factor VIII Coagulant Activity [FVIII: C] for Haemophilia A: One-stage assay based on aPTT. Severe <1%, Moderate 1-5%, Mild 5-40%. Chromogenic assay preferred for monitoring emicizumab patients and mild cases
7. Factor IX Coagulant Activity [FIX: C] for Haemophilia B: One-stage assay. Same severity classification
8. Von Willebrand Screen [MANDATORY to exclude VWD]: VWF: Antigen, VWF: Ristocetin Cofactor Activity, FVIII: C. VWD can mimic Haemophilia A with low FVIII



STEP 3 - DIFFERENTIAL AND SEVERITY:

9. Factor XI, XII assay if aPTT prolonged but FVIII/FIX normal to exclude other deficiencies
10. Lupus Anticoagulant [DRVVT] plus Anticardiolipin if mixing study shows non-correction

STEP 4 - MOLECULAR / GENETIC:

- a) F8 gene intron 22 inversion for severe Haemophilia A [>45% cases]
- b) F8/F9 gene sequencing for mild/moderate
- c) For prenatal diagnosis and pre-implantation counseling [Referral]

NB: Medical Laboratories must NOT diagnose Haemophilia on prolonged aPTT alone. FVIII and FIX assays are mandatory.

C. BASELINE ASSESSMENT AT DIAGNOSIS [WITHIN 2 WEEKS OF CONFIRMATION]

- a) Inhibitor Screen: Bethesda Assay [Nijmegen modification] baseline - mandatory even if asymptomatic. Report in Bethesda Units [BU]
- b) Blood Group ABO/Rh plus Extended Phenotype plus Antibody Screen: For future transfusions
- c) **Infectious Disease Panel:** HIV Ag/Ab, HBsAg, Anti-HCV, VDRL - baseline due to historical plasma exposure plus vaccination status for HBV, HAV
- d) **Renal and Hepatic:** U/E/Creatinine, ALT, AST, ALP, Bilirubin, GGT - before starting prophylaxis
- e) **Musculoskeletal Baseline:** Joint ultrasound score if available, orthopedic referral
- f) **Pharmacokinetic Baseline:** Baseline factor level trough and recovery, body weight, BMI



D. ROUTINE MONITORING FOR STABLE PATIENTS ON PROPHYLAXIS

Every 3 Months:

- a) Factor trough level [30 min pre-next dose for prophylaxis] - Target >1-3% for standard prophylaxis
- b) CBC
- c) Inhibitor Screen if poor response to treatment
- d) Every 6 Months [Mandatory KMLTTB Audit Item]:
- e) Factor VIII: C or FIX: C peak [30 min post-infusion] and trough
- f) Inhibitor Assay - Bethesda if clinical suspicion or annually for severe cases
- g) LFT, RFT
- h) Joint assessment score plus Physiotherapy review

Annually:

- a) Comprehensive inhibitor screen [Nijmegen Bethesda]
- b) HIV, HBV, HCV if exposed to blood products
- c) Orthopedic X-ray / MRI for target joints, Bone densitometry if repeated immobilization
- d) Adherence check, bleeding diary correlation, ABR [Annualized Bleed Rate]

E. TREATMENT-SPECIFIC MONITORING

1. Standard Half-Life Factor Replacement [Plasma-derived / Recombinant]:

- a) Pre-infusion factor level if breakthrough bleed
- b) Post-infusion recovery: $(\text{Observed rise} / \text{Expected rise}) \times 100$. Expected = Dose [IU]/kg $\times 2$ for FVIII, $\times 1$ for FIX. Low recovery suggests inhibitor
- c) Half-life monitoring: Levels at 0, 0.5h, 4h, 24h, 48h for pharmacokinetic-guided dosing
- d) Inhibitor surveillance: Every 5 exposure days until 50 EDs, then every 10 EDs or every 3 months for first 2 years

2. Extended Half-Life [EHL] Factors:

- a) Same as above but use chromogenic assay for certain products - lab must know reagent-product interaction. One-stage may over/under-estimate
- b) Trough at 72-96h

3. Non-Factor Therapy - Emicizumab for Haemophilia A with/without Inhibitors:



- a) aPTT is SHORTENED and invalid - DO NOT use aPTT to monitor
- b) For bleed assessment: Use Bovine-based chromogenic FVIII assay - human-based assays overestimate
- c) FIX, FXI assays unreliable while on Emicizumab - lab must flag
- d) Anti-drug antibody test if breakthrough bleeding on adequate therapy [Hemlibra]

4. Inhibitor Eradication [ITI - Immune Tolerance Induction]:

- a. Bethesda titer monthly, Factor recovery monthly, anamnestic response monitoring

5. Blood Products / Cryoprecipitate [If factor unavailable]:

- a. Fibrinogen level, Calcium, PT/aPTT before and after, Viral NAT where available

F. ACUTE BLEED / EMERGENCY / PRE-OPERATIVE PANEL [STAT]

Acute Bleed Unresponsive to Treatment:

- a. Immediate: CBC, PT/aPTT, FVIII: C / FIX: C level, Inhibitor screen STAT Bethesda, Group and Crossmatch, Fibrinogen, D-Dimer
- b. If head trauma / suspected ICH: CT referral plus PT/aPTT plus Factor level plus Platelets plus Crossmatch - DO NOT wait for results to treat

Pre-operative Mandatory:

- a. CBC, PT/aPTT, FVIII/FIX:C, Inhibitor screen within 2 weeks of surgery, Blood Group and Crossmatch x 4 units, LFT, RFT, Viral serology, Thrombin Time if heparin exposure, Factor level immediately pre-op and 30 min post bolus plus daily trough for 14 days
- b. For inhibitor patients: Bypass agent monitoring - APPT/ROTEM where available

ACQUIRED HAEMOPHILIA / POSTPARTUM BLEED DIFFERENTIAL:

- a. APTT plus Mixing study that shows time-dependent non-correction plus FVIII: C <10% plus Inhibitor high titer plus Age >50

G. QUALITY and REPORTING REQUIREMENTS BY KMLTTB



1. **Pre-analytical:** Strict 3.2% citrate 9:1 ratio, fill >90%, no heparinized lines, test within 4h or double-spin platelet-poor plasma $<10 \times 10^9$ platelets/L and freeze at -70C, transport on dry ice
2. **Internal QC:** Normal and abnormal aPTT controls daily, Factor deficient plasma controls at low/medium/high levels, chromogenic assay controls
3. **EQA:** Mandatory participation in KMLTTB approved coagulation EQA
4. **Turnaround:** Emergency aPTT/PT <1h, Factor assay <24h, Inhibitor Bethesda <72h
5. **Referral:** Medical Laboratory Class B-C only aPTT/PT plus referral. Level 4 must have mixing study plus factor assay. Medical Laboratory Class F-G must have **Bethesda plus chromogenic plus molecular referral link**
6. **Reporting:** Report must include: Method [one-stage vs chromogenic], Reagent, Factor % and IU/dL, Severity classification, Reference range, Inhibitor BU with interpretation, and statement: "Interpret with clinical bleeding score.
7. **Safety:** No IM injections for sampling, use 23G needle, prolonged pressure 5 min.

This framework ensures no Kenyan patient is labeled or treated as haemophiliac without factor-level proof, prevents fatal missed inhibitors, and enables safe surgery and prophylaxis under SHA.

KEY

1. **ALT (Alanine Aminotransferase):** Found mostly in the liver, making it a highly specific indicator of liver inflammation or injury.
2. **AST (Aspartate Aminotransferase):** Found in the liver, but also in muscles and the heart. Doctors evaluate it alongside ALT to determine the pattern of liver stress
3. **ALP (Alkaline Phosphatase):** An enzyme found in high amounts in the bile ducts and bones.
4. **aPTT (Activated Partial Thromboplastin Time):** This measures the **intrinsic pathway** of coagulation, which relies heavily on Factors VIII and IX. In families with a history of Hemophilia A or B, the **aPTT is typically prolonged (delayed)**.
5. **PT (Prothrombin Time):** This measures the **extrinsic pathway**. Because Hemophilia A and B only affect the intrinsic pathway, the **PT result should be normal**. If both the PT and aPTT are prolonged, it points to a different or more systemic clotting issue rather than isolated hemophilia
6. **Bilirubin:** A yellowish waste product created when old red blood cells are recycled. The liver processes bilirubin and excretes it via bile. If the liver is struggling or a bile



duct is blocked, bilirubin builds up in the blood, which can cause jaundice (yellowing of the eyes or skin).

7. **Bethesda plus chromogenic plus molecular referral link** includes a hybrid of **chromogenic** substrate processing alongside a Nijmegen-modified **Bethesda**
8. **Creatinine**: A steady waste product created by normal muscle breakdown. Your kidneys filter nearly all of it out. **Creatinine is the primary marker used to calculate overall kidney filtration rate.**
9. **Electrolytes (E)**: Essential minerals—typically Sodium (Na^+), Potassium (K^+), and Chloride (Cl^-). They keep your body's fluids balanced, control blood pressure, and keep your muscles and nerves firing correctly.
10. **GGT (Gamma-Glutamyl Transferase)**: An enzyme highly sensitive to liver and bile duct irritation. Doctors often look at GGT alongside ALP. If both are high, it confirms the issue is coming from the liver/bile ducts rather than a bone issue. GGT can also rise from alcohol use or fatty liver changes. .
11. **HEMLIBRA (emicizumab-kxwh)** is a prescription monoclonal antibody manufactured by Genentech (part of the Roche Group) used for routine preventative treatment (prophylaxis) to reduce the frequency of bleeding episodes in adults and children of all ages with hemophilia A, both with and without factor VIII inhibitor.
12. **Urea (U)**: A waste product formed in the liver when protein breaks down. The kidneys filter it out. High levels can suggest dehydration or reduced kidney function.

