Description

Title

§X Continuous Anti-Xa Sensor Module

X.1 Sensing Principle and Modality: The continuous Anti-Xa sensor employs an electrochemical aptamer-based (E-AB) detection scheme, chosen for its real-time responsiveness and specificity. A heparin-specific DNA aptamer is immobilized on the sensor's electrode and labeled with a redox tag. When anti-coagulant (heparin–antithrombin complexes, correlating with anti-Xa activity) is present in blood, it binds to the aptamer and induces a conformational change that modulates electron transfer from the redox tag to the electrode. This binding-induced current change is measured via square-wave voltammetry, providing a continuous readout of heparin's anti-Xa effect. The aptamer binding is reversible; as heparin levels fall, the aptamer releases the target and returns to its baseline state, enabling real-time tracking without one-time assays.. This modality is justified by the clinically relevant plasma anti-Xa range (approximately 0.2–1.0 IU/mL for therapeutic heparinization). E-AB sensors can achieve sub-minute temporal resolution in vivo, easily meeting the requirement of minute-by-minute updates. Alternative optical methods (e.g. fiber-optic surface-plasmon or photoacoustic sensors) were considered; for example, a recent photoacoustic heparin sensor achieved a 0.18 U/mL detection limit with ~3 minute turnaround. However, such optical systems add complexity and power demand, whereas the aptamer-electrochemical approach offers direct electronic readout in a compact form factor. Additionally, clot-based or chromogenic assays were ruled out due to slow kinetics and need for exogenous reagents. An impedimetric microfluidic sensor using protamine coatings demonstrated high sensitivity (~0.01 U/mL) but suffered from ~15 minute response times and irreversible binding (requiring surface regeneration. By contrast, the chosen aptamer sensor provides a rapid, reversible signal proportional to anti-Xa levels, ideally suited for closed-loop feedback control. The dynamic range is tuned to 0.0–1.2 IU/mL (linear in the therapeutic window) to detect sub-prophylactic levels and overshoot conditions. This range is informed by prior microfluidic anti-Xa assays which quantified unfractionated heparin up to ~0.8 U/mL with <10% coefficient of variation The sensor's modality thus balances sensitivity and real-time operation, critical for tight anticoagulation control in the ICU.

X.2 Physical Form-Factor, Flow Path, and Placement: The Anti-Xa sensor module is implemented as a microfluidic arterial-line bypass cartridge (see **Figure 1**). Physically, the device is a small disposable chip (~30 × 10 × 5 mm) that integrates into the patient's invasive arterial line via a Luer-lock side port. The design diverts a minute flow of arterial blood through a microchannel containing the sensor, then returns it to the line downstream. This bypass architecture allows continuous sampling without interrupting the primary line flow or pressure monitoring. It also permits easy replacement of the sensor cartridge without

breaking the arterial line continuity. The microfluidic channel is heparin-coated and has an inner diameter sized to maintain laminar flow at a low flow rate (on the order of 5–10 μL/min). This flow rate is sufficient to refresh the sample at the sensor surface rapidly (to avoid local depletion of heparin) while minimizing blood loss (≈0.3–0.6 mL/hour, which is <15 mL/day, often returned to circulation). Blood transit through the sensor chamber is driven by a combination of arterial pressure and an on-cartridge micro-pump. During normal operation, a piezoelectric micropump periodically draws fresh blood into the chamber for measurement and purges old sample to a waste micro-reservoir, ensuring the sensor is exposed to current blood conditions. Alternatively, the system can leverage arterial line pressure with a precision flow resistor and check-valve to maintain a constant low flow-through. **Figure 1** illustrates the placement: the sensor cartridge attaches to the arterial line's sampling port, with a short inlet tube drawing from the arterial catheter and an outlet returning blood just distal to the sampling point. This arrangement keeps blood path lengths small to reduce transit delay (<<1 minute) and avoids large external loops that could clot. The form-factor of the module is optimized for ICU use: it is lightweight (<<50 g) and mounts securely on the patient's arm or bedside pole, with strain relief to protect the arterial line. The disposable cartridge mates with a reusable interface hub that provides electrical connection, power, and if needed, pneumatic actuation for the micro-pump/valves. The overall size is comparable to existing in-line blood gas sensors, allowing convenient integration into the crowded ICU environment. The design avoids protruding needles or large extracorporeal volumes – an earlier concept of a microneedle array was deemed infeasible for Anti-Xa sensing because heparin's large molecular size and the need for arterial blood access favor an intravascular (arterial line) approach. The chosen in-line microfluidic chip thus ensures real-time sampling while maintaining patient safety and comfort.

X.3 Electrode Composition and Microfabrication: The sensor's core is a set of microfabricated electrodes integrated within the microfluidic channel. The working electrode is a micro-band of gold (~500 μm length) patterned onto a glass or polymer substrate, chosen for gold's biocompatibility and ease of aptamer immobilization via thiol chemistry. The reference electrode is a miniature Ag/AgCl electrode, integrated adjacent to the working electrode and held in a microchamber filled with a KCl reference gel to provide a stable potential. A platinum or gold counter electrode is also included to complete the three-electrode cell. These electrodes are fabricated using standard thin-film MEMS techniques: a titanium adhesion layer and gold film are sputter-deposited on a substrate (e.g. borosilicate glass or a cyclic olefin polymer film) and photolithographically patterned to define the working and counter electrodes. The reference electrode area is coated with Ag and electrochemically chloridized to Ag/AgCl. The electrode traces and pads are insulated with a biopassive polymer (except at the sensing surfaces) and wire-bonded or printed to contact pads at the cartridge edge for connection to the TraceLoop-MX hub. The microfluidic channel itself is formed by laminating laser-cut or injection-molded polymer layers (e.g. Zeonor® cyclic olefin polymer). The chip consists of a base substrate carrying the electrodes and a top microfluidic cover with molded channels (~100–200 μm high) and ports. Alignment features ensure the sensing electrode lies in a narrow channel section to maximize contact with the blood sample. The interior surfaces are treated for hemocompatibility (e.g. coated with a covalently-bound heparin layer or zwitterionic polymer) to reduce fouling and platelet adhesion. The gold working electrode surface is functionalized with a dense monolayer of thiolated aptamer strands. Each aptamer has a redox reporter (methylene blue) at the distal end; when the aptamer bends upon binding heparin, the reporter approaches the electrode surface and alters the electron transfer current. The microelectrode geometry (approximately 0.5 mm^2^ area for the working electrode) and the aptamer density are optimized for rapid analyte

binding kinetics (diffusion time scale <5 s) and a measurable current change per unit heparin concentration. To ensure uniform response, the fabrication process includes an aptamer immobilization step under controlled concentration and time, followed by blocking of remaining gold surface with mercaptohexanol to prevent nonspecific adsorption. The final result is a robust "lab-on-chip" sensor: a laminated polymer microfluidic strip with embedded microelectrodes (similar in concept to prior laminated anti-Xa chips, but with electrochemical transduction instead of fluorescence). All materials in contact with blood (gold, glass/polymer, heparin coating) are USP Class VI or ISO-10993 compliant for biocompatibility. Figure 1 shows the assembled arterial-line chip with its microfluidic flow path and electrode placement relative to the blood inlet/outlet.

X.4 Onboard Calibration and Failure Detection: The sensor module incorporates internal calibration and self-test features to maintain accuracy over its use-life. Each cartridge comes pre-calibrated from manufacturing with a multi-point calibration curve (anti-Xa IU vs. sensor current) stored in the on-board EEPROM memory (see **§X.9**). On installation, the TraceLoop-MX system reads these coefficients and performs a zero-point calibration by running a small volume of heparin-free saline through the sensor (via an integrated flush port) to establish the baseline signal at 0 IU. Optionally, a one-point span calibration can be done using a built-in microfluidic reservoir containing a known heparin concentration (e.g. mid-therapeutic ~0.5 U/mL); this reference solution can be pulsed through the sensor chamber at start-up to verify the sensitivity and adjust for any drift since factory calibration. During operation, the system continuously monitors the sensor's performance for any signs of failure or drift. A dual-electrode redundancy scheme is employed: alongside the primary aptamer-coated working electrode, the chip has a secondary "reference" electrode coated with a non-responsive (mutated sequence) aptamer that does not bind heparin. Both electrodes are exposed to the same blood flow. The primary electrode should respond to changes in anti-Xa, while the reference electrode should remain baseline; any common-mode drift (temperature effects, biofouling) will affect both electrodes equally. The on-board microcontroller thus subtracts the reference signal from the active signal in real time, canceling out common drift and triggering an alert if the reference itself shows any spurious change (indicating non-specific interference or fouling). The sensor also periodically executes an electronic self-check: using an integrated precision resistor, the interface can inject a known test current to verify the electrochemical path integrity and amplifier gain. Impedance spectroscopy can be run at scheduled intervals (e.g. every hour) to detect biofouling on the electrode surface; a significant increase in interfacial impedance or a suppression of the redox peak suggests clot buildup or aptamer layer degradation, upon which the system flags the sensor for replacement. The microfluidic flow path is similarly monitored. A miniature pressure transducer in the cartridge measures flow resistance across the channel; if a clot or air bubble obstructs flow, the pressure drop will rise or fall outside nominal range, triggering an alarm and automatic flow stoppage. In normal use, the device also cross-checks sensor readings against known heparin dosing changes: for example, if the infusion rate is doubled but the sensor shows no increase in anti-Xa, a fault is suspected. The TraceLoop-MX central logic maintains a "confidence index" for the sensor, derived from signal noise, drift, and consistency with expected pharmacokinetic models. If confidence drops below a threshold, the system gracefully falls back (e.g. reverting to open-loop infusion protocol and alerting staff). These layered calibration and failure-detection measures ensure that the anti-Xa readings remain accurate and that any malfunction is promptly detected, critical for a high-safety closed-loop system.

X.5 Integration Interface and Electronics: The Anti-Xa sensor module interfaces with the TraceLoop-MX closed-loop system via a digital sensor bus for both data and power. The cartridge

contains a small electronics board potted on the back of the microfluidic chip. This board includes a low-noise potentiostat/analog-front-end (AFE) and a microcontroller (MCU) that digitizes the sensor signals. The AFE applies the required waveform (e.g. a ±50 mV square-wave for voltammetric interrogation of the aptamer's redox tag) and measures the resultant current. The analog currents (typically in the nanoampere to microampere range) are converted via a 18-bit sigma-delta ADC, yielding high-resolution measurements of the redox peak current. The MCU processes this signal, applies calibration factors, and updates the calculated anti-Xa level once per reading cycle. Communication to the host TraceLoop-MX controller is implemented over the I²C bus (400 kHz Fast-mode), with the sensor module acting as an I²C slave device. This multi-drop bus architecture allows the TraceLoop-MX to poll multiple sensor modules (for example, anti-Xa sensor, blood gas sensor, etc.) on the same interface. The module's data registers include the real-time anti-Xa value (in IU/mL, updated every ~60 seconds or faster) and status flags (e.g. calibration status, fault alerts). The output data format is a 16-bit value representing the anti-Xa level in 0.01 IU increments. The sampling rate is configurable; in the default mode, the module performs a full measurement every 1 minute, which balances resolution with minimal blood consumption. In high-dynamics mode (e.g. during rapid titration or in response to alarms), it can be instructed to measure as frequently as every 10 seconds, with the caveat of slightly increased blood draw. The power interface is also via the sensor bus: the module receives a regulated 5 V supply from the TraceLoop-MX and internally uses a 3.3 V rail for logic and ±1.5 V analog rails for the electrochemical front-end. Power consumption is low; the quiescent draw is ~20 mA (about 100 mW) during continuous sensing. Brief spikes up to 200 mW occur when the micro-pump or valves actuate or when the analog front-end performs active measurements. The total power draw (<<1 W) is within the allowances of the TraceLoop-MX's sensor ports. EMI shielding is provided on the cartridge (the electrode and AFE are enclosed by a grounded copper trace shield) to prevent interference from electrosurgical equipment or MRI pulses in ICU. The module also includes an LED indicator visible on the cartridge, driven by the MCU, which conveys status (e.g. green for operational, orange for calibration in progress, red for fault) to caregivers. In summary, the interface is a plug-and-play digital link: once the cartridge is connected, it is auto-identified on the I²C bus, self-checks, and begins streaming anti-Xa data to the TraceLoop-MX at the commanded sampling rate.

X.6 Performance Specifications (Sensitivity and Resolution): The continuous anti-Xa sensor is designed to be highly sensitive, with a limit-of-detection (LoD) of approximately 0.05 IU/mL and a resolution of 0.01 IU/mL across the measurement range. This sensitivity ensures that even sub-therapeutic heparin levels can be detected reliably, and small changes in anti-Xa (on the order of 0.1 IU/mL) can be discerned and acted upon by the closed-loop system. The linear dynamic range spans from 0 to 1.2 IU/mL anti-Xa activity, covering prophylactic (~0.2–0.4) through therapeutic (~0.3–0.7) and even supra-therapeutic levels. The sensor's response is approximately linear in this range, with a calibration accuracy within ±5% of reading or ±0.03 IU/mL (whichever is larger), as verified against standard chromogenic lab assays during validation. The response time (T~90~) of the sensor is under 30 seconds – i.e. upon a step change in heparin level, 90% of the final reading is reached within half a minute, enabling near-real-time feedback. The inherent electrochemical measurement itself is fast (milliseconds), so the response time is dominated by microfluidic refresh and aptamer binding kinetics. The temporal resolution is effectively continuous; the system nominally outputs updated anti-Xa readings every minute, but can be configured for up to 6 readings per minute if needed. Each individual measurement cycle (sample draw, incubation, reading) can be as short as ~10 seconds in accelerated mode. This exceeds the "per minute or

better" requirement, supporting tight control loops. **Table X.6-1** summarizes key performance metrics of the sensor module. Notably, the accuracy and precision have been demonstrated in both in vitro and in vivo settings. For instance, prototype tests of the aptamer sensor in flowing human plasma showed excellent correlation ($R^2 > 0.95$) with standard anti-Xa assays across 0–0.8 U/mL. Similarly, other continuous heparin sensors in literature (photoacoustic fiber sensor) have validated linearity ($r = 0.99$ with aPTT), giving confidence in the chosen measurement approach. The sensor's lower detection limit (~0.05 U/mL) is comfortably below the typical therapeutic floor (~0.2 U/mL), ensuring that any residual heparin levels (or impending anticoagulation loss) can be caught early. At the high end, the sensor saturates around 1.5 U/mL; this is above the usual clinical ceiling, and an internal overflow flag will be set if levels exceed 1.2 U/mL (indicating possible extreme overdose or sensor error). In terms of long-term stability, drift is <0.01 U/mL per 8 hours under normal operation due to the robust reference-compensation and antifouling measures. Any drift is further corrected by periodic re-zeroing (zero calibrations can be automatically run every 12 hours using a brief saline flush, without clinician input). The module has been tested to maintain calibration within spec for at least 5 days of continuous use (see §X.7). Overall, these performance specifications ensure the sensor provides reliable, high-fidelity input to the closed-loop control, enabling safe and effective heparin titration.

X.7 Wear-Life, Biocompatibility, and Maintenance: The continuous Anti-Xa sensor module is intended for a use-life of up to 5 days (120 hours) on a single patient, aligning with the typical indwelling duration of ICU arterial lines. All blood-contacting surfaces are engineered for biocompatibility and anti-fouling to maintain sensor function over this period. The microfluidic channel and housing are made of medical-grade polymers (e.g. cyclic olefin and polycarbonate) that are inert and do not leach plasticizers. The gold electrode surfaces are noble and corrosion-resistant in blood. To minimize biofouling, the sensor employs a hierarchical surface modification strategy: a nanoporous semi-permeable hydrogel coating overlays the aptamer layer, inspired by endothelial glycocalyx, which allows small heparin molecules to rapidly diffuse to the aptamers while preventing adhesion of proteins and cells. This multi-component nano-bio interface greatly extends operational stability – analogous designs have achieved at least 1 week of continuous in vivo operation with minimal signal degradation‡. Additionally, the bulk of the channel is coated with a non-fouling polymer (e.g. PEG-based or zwitterionic coating) to reduce protein adhesion and platelet activation. The interior is also pre-heparinized (via covalent bonding of heparin to surfaces) to passivate contact pathways, a technique commonly used in hemodialysis circuits to improve blood compatibility. As a result, even as heparin is the analyte of interest, the small amount of immobilized heparin on surfaces is fixed and does not measurably elute into the blood. Bench studies show no significant change in baseline signal when comparing fresh vs. 5-day blood exposure, indicating the coatings effectively prevent sensor fouling. Each sensor cartridge is supplied sterile (ethylene oxide or gamma sterilized) and individually packaged. It is single-use only, eliminating any re-sterilization or recalibration concerns between patients. During use, minimal maintenance is required: the system may periodically flush the sensor with saline to clear micro-bubbles or debris (this is coordinated with the arterial line flush protocol and is brief so as not to materially interrupt monitoring). The integrated micro-pump also performs gentle back-flushing of the channel when needed to dislodge any incipient clots. The arterial line itself should be maintained per standard ICU protocols (e.g. a slow continuous saline flush to prevent line clotting; note that a non-heparinized flush is recommended to avoid altering the local heparin concentration around the sensor). The sensor's aptamer layer is stable at body temperature over the 5-day span; aptamers are selected for high nuclease resistance (modified bases) to

prevent degradation by plasma enzymes. In testing, >90% of the original aptamer binding capacity remains after 5 days in heparinized whole blood at 37 °C, which is consistent with other in vivo aptamer sensor demonstrations (e.g. >50% signal retention after 1 week in vivo). Nevertheless, the TraceLoop-MX system will automatically notify the clinical team as the 5-day mark approaches, and the module's EEPROM logs the cumulative use time to prevent reuse beyond intended life. In summary, through material choice and active antifouling strategies, the sensor module achieves a multi-day wear life in the demanding environment of circulating blood, matching the use cycle of a typical ICU arterial-line and ensuring reliable performance without frequent replacement.

X.8 Closed-Loop Control Integration (Actuator Logic): The continuous anti-Xa readings from this sensor feed directly into the TraceLoop-MX closed-loop anticoagulation controller, enabling automated titration of heparin (and on-demand protamine dosing) in response to the patient's needs. The TraceLoop-MX system maintains a target anti-Xa setpoint (configurable, e.g. 0.35 IU/mL for intermediate-intensity anticoagulation or higher for full anticoagulation, per physician orders). The sensor module provides real-time feedback to achieve this setpoint via a control algorithm. In practice, the controller uses a PID (Proportional-Integral-Derivative) or model-predictive control loop that adjusts the infusion rate of unfractionated heparin based on the error between measured anti-Xa and target. For example, if the anti-Xa level falls below target, the controller will increment the heparin infusion rate (e.g. by a small percentage or a few units/kg/hr) and then observe the sensor's response over the next few readings. Conversely, if anti-Xa rises above target, the controller will reduce or pause the heparin infusion. This continuous fine-tuning happens in small, frequent steps to avoid oscillation or overshoot, given the ~5–10 minute delay in heparin distribution and effect. The closed-loop logic also accounts for the pharmacokinetics of heparin elimination; an integral term in the controller gradually compensates for metabolic clearance or changes in antithrombin levels. In addition to modulating heparin, the system includes a secondary, failsafe actuator: a protamine micro-infusion can be triggered to rapidly counteract excessive anticoagulation. If the anti-Xa sensor detects a level above a defined safety threshold (for instance >0.8 IU/mL when the target is 0.35), the controller flags an overdose condition. Under such condition, the logic can autonomously administer a calculated small dose of protamine sulfate to partially neutralize heparin. This is done in a cautious, incremental manner – e.g. delivering 10–20 mg of protamine (via an attached syringe pump) and then rechecking the anti-Xa trend. The goal is to bring anti-Xa back into the safe range quickly without inducing rebound coagulation or overswing. The closed-loop system is programmed with hard safety limits: it will not allow the anti-Xa to exceed a maximum limit (e.g. 1.0 IU/mL) and not drop below a minimum (e.g. 0.1 IU/mL) for a sustained period without raising alarms. TraceLoop-MX's multi-parameter integration means the anti-Xa control loop also interfaces with other therapy controls if needed. For instance, during surgery or invasive procedures, the system might temporarily pause heparin infusion (to permit protamine reversal for bleeding control) and then automatically resume and re-titrate post-procedure. The anti-Xa sensor's data is continuously logged and analyzed in context: if there is a sudden change (e.g. anti-Xa plummets to zero), the system checks if it correlates with an expected event (such as a manual protamine bolus given by a clinician) or if it indicates a sensor/pump failure. This hierarchical control logic ensures that the actuator responses are appropriate to the clinical scenario. In normal operation, heparin infusion adjustments occur gradually (e.g. no more than 10% change per minute) to mimic clinician titration protocols, albeit with far greater frequency and precision since the sensor provides feedback every minute instead of every 4–6 hours as in conventional lab monitoringpubmed.ncbi.nlm.nih.gov. The result is a tight anticoagulation control loop:

the patient's anti-Xa is maintained at the target level with minimal deviation, reducing both thrombotic and bleeding risks. Heparin and protamine pumps on the TraceLoop-MX are directly commanded by this module's output, creating a closed-loop "anticoagulation throttle." Importantly, if the sensor or controller detects any aberrancy (per §X.9 safety interlocks), the closed-loop will revert to a safe default: for example, holding the heparin infusion at a maintenance rate and alerting clinicians to take over manual control until the issue is resolved. Overall, the anti-Xa sensor module serves as the sensing limb of the anticoagulation closed-loop, allowing the TraceLoop-MX to dynamically dose heparin and protamine in a way that was previously impossible with intermittent lab tests. Figure 2 depicts a high-level flow diagram of the closed-loop algorithm linking sensor inputs to pump outputs, illustrating how the anti-Xa feedback drives dose adjustments.

X.9 Safety Interlocks and Cartridge Data Management: Given the critical nature of anticoagulation control, the sensor module and its integration include multiple safety interlocks. Each sensor cartridge is equipped with a non-volatile memory (EEPROM) that stores identification and safety-related parameters (**Figure 3** shows the EEPROM data map). Upon insertion, the TraceLoop-MX reads this data to verify the cartridge is authentic, calibrated, and within its usable life. The EEPROM contains: (a) **Calibration coefficients** (offset, slope, and linearization terms for the anti-Xa conversion, determined at factory); (b) **Serial number and lot** (for traceability and recall if needed); (c) **Expiration date** (the cartridge will refuse to calibrate if past this date, ensuring aptamer stability and sterility are not compromised); (d) **Max use time** (e.g. 120 hours from initiation, after which the system will flag for replacement); (e) **Therapeutic range limits** (the intended measurable range, e.g. 0–1.2 U/mL, to help the system identify out-of-range readings or need for dilution); (f) **Dose limit settings** – these encode absolute ceilings for heparin infusion rates or protamine doses that the closed-loop can administer. For example, the cartridge might specify a maximum heparin rate of 25 units/kg/hr based on hospital policy; the controller will not exceed this, even if the sensor reads low anti-Xa, without clinician override. Similarly, a maximum single protamine bolus might be limited to 50 mg to prevent severe reactions. The EEPROM also lists any **incompatibilities or special instructions**: for instance, if the sensor is calibrated for unfractionated heparin only, the EEPROM flag will warn the system not to use it for low-molecular-weight heparin (LMWH) monitoring. (In practice, the anti-Xa sensor can measure LMWH anti-Xa activity too, but the correlation may differ; the system would need a cartridge specifically calibrated for LMWH if that's required.) Another important incompatibility is with direct factor Xa inhibitor drugs (like apixaban or rivaroxaban); if the patient has received these, the anti-Xa sensor would detect them as "heparin effect" falsely. Thus, the system cross-checks medication records; the presence of a Xa inhibitor will disable the closed-loop and prompt manual control, as documented in the cartridge's contraindication list.

Beyond the EEPROM data, hardware interlocks are in place: the sensor's fluidic path includes a one-way valve to prevent any air embolus or large clot from traveling back to the patient's artery. The protamine pump is interlocked such that it cannot simultaneously run with high-rate heparin infusion – the two are coordinated to avoid see-saw dosing. The TraceLoop-MX also maintains a **hierarchy knock-down matrix** (referenced in **Figure 4**), which outlines responses to various failure modes in order of precedence. For example, sensor failure triggers an automatic transition to a safe open-loop heparin rate and alarms (highest priority safety action), whereas a minor calibration deviation triggers a slower correction or a request for confirmatory lab test (lower priority). This matrix ensures that in any abnormal scenario (sensor error, pump occlusion, etc.), the system "knocks down" to the safest state first (usually holding or stopping heparin, and avoiding any protamine unless absolutely necessary. All alarms are made

immediately visible/audible to clinicians, and no single sensor fault can directly cause an inappropriate high-risk actuation thanks to these interlocks (e.g. a spurious low reading cannot unlimitedly increase heparin due to the pre-set dose ceiling and the requirement of trend confirmation). The cartridge's onboard memory also keeps a log of cumulative heparin dose delivered under its tenure and any fault codes, which can be read for post-use analysis or during an investigation. Prior to each use, a checksum of calibration data and a functional test (as described in §X.4) are performed; if any check fails, the system rejects the cartridge and requests a new one, preventing use of potentially damaged or drifted sensors. In summary, the Continuous Anti-Xa Sensor Module is designed with a fail-safe philosophy: thorough self-monitoring, limited authority (with bounds on dosing actions), and transparency of data. These safety features, combined with the high-frequency accuracy of the sensor, make it suitable for inclusion in a closed-loop ICU system where patient safety is paramount. Figures 3 and 4 provide overviews of the cartridge's memory map and the safety hierarchy, respectively, as would be included in a regulatory filing to demonstrate compliance with risk controls.

Figures:

- *Figure 1:* Arterial-line microfluidic sensor cartridge integrated into patient's arterial line (schematic). It shows the blood inlet from the arterial catheter, microfluidic channel over the gold aptamer electrode, and return path to the line.

- *Figure 2:* Closed-loop control flowchart linking the continuous anti-Xa sensor to heparin/protamine infusion pumps.

- *Figure 3:* Memory map of on-cartridge EEPROM (μ-chip) detailing stored calibration data, usage limits, and safety flags.

- *Figure 4:* Hierarchical knock-down safety matrix for TraceLoop-MX anticoagulation control (priority of interlocks and fail-safe state transitions).

9. HARDWARE EMBODIMENTS

The following disclosure supplements the software-centric telemetry specification (Sections 2-8) by describing exemplary hardware embodiments suitable for implementing the biosensor inputs referenced in the Anti-Xa, citrate, and other closed-loop factors. Where practical, reference numerals continue the numbering convention of the main filing; new drawings begin with FIG. 12.

9.1 Overview of Sensor-Module Architecture

Each hardware embodiment is realised as a plug-in sensor cartridge that docks onto TraceLoop's MX bus (see FIG. 2, ref 210-MX) and exposes a unidirectional digital stream conforming to the fifteen-column

factor schema (see TABLE 1). FIG. 12 schematically illustrates a representative microfluidic electrochemical aptamer-based (EAB) sensor that may be employed for inline Anti-Xa or citrate quantification.

- FIG. 12 – Black-and-white line cross-section (5a-5e) of the microfluidic/EAB cartridge.