ABSTRACT

A closed-loop micro-dosing apparatus for bioprocess streams combines (i) a skid-mounted rack of independently driven positive-displacement micro-annular gear pumps, (ii) a sanitary injection ring having a plurality of radial ports, (iii) in-line process-analytical sensors assigned one-to-one to each pump, and (iv) an optional bank of single-use reagent cartridges positioned downstream of the ring. Each pump draws from an RFID-identified mini-tank or γ-sterile bag and delivers sub-microlitre shots into the ring; a controller executes a three-tier hierarchy in which Vital-Override (VO) safety responses pre-empt Quality-Critical (QC) and Yield-Optimiser (YO) adjustments. Sensor deviations are closed-looped to the corresponding pump, and every dose is stored in an electronic batch record as LINEAGE_ID = BatchID‖PumpID‖Reagent. The pump wet-ends, ring and steam-jumper loop withstand 100 % v/v ethanol and are steam-in-place for at least 30 minutes at 130 °C without disassembly. Where solid-phase chemistry or single-use sterility is required, disposable cartridges—such as virus-clarifiers, endotoxin-binding beds, or nuclease coils—are inserted without modification to the control logic. The system delivers ≤ 1 µL pulses with < 1 % coefficient of variation, achieves real-time viral/endotoxin removal or formulation adjustment, and reduces off-spec batches to < 0.2 % while eliminating polymer compatibility failures associated with prior radial cartridge banks.