Summary of the Invention

This filing encompasses two modular biologic manufacturing platforms:

1. **Immune Cell Therapy Platform** – A GMP-compliant, feedback-regulated system for the ex vivo expansion and activation of immune cells. Features include real-time cytokine sensing, AI-guided dose modulation, and tumor lysate education protocols.
2. **Plasma Protein Fractionation Platform** – A sensor-integrated, programmable system for the fractionation and purification of therapeutic plasma proteins, including IVIG, albumin, and clotting factors. Features include per-protein yield optimization, automated buffer delivery, cartridge authentication, and safety interlocks.

Each platform can be operated independently, or connected to a shared GMP cloud infrastructure. This allows batch-level tracking, AI retraining, SOP deployment, and audit compliance across facilities, but does not require co-dependence. These inventions are structured such that each may form the basis of a separate non-provisional utility patent, with shared priority from this filing.

Background of the Invention

Biologic drug manufacturing continues to suffer from rigid, low-resolution automation and high manual burden. Cell therapy and plasma protein production are traditionally siloed, despite overlapping regulatory, infrastructure, and quality requirements. There is a need for adaptive platforms that:

- Enable AI-driven parameter modulation;
- Use GMP-compliant tracking and deviation prevention;
- Support modular integration without requiring system coupling.

This invention meets those needs by disclosing: (a) A fully programmable immune cell therapy production unit, optimized for immune phenotype modulation and AI-adjusted cytokine dosing; and (b) A real-time, cartridge-controlled plasma fractionation unit that modulates buffer flow and temperature based on inline sensors and GMP logic.

These systems may share a cloud interface for SOP management and compliance tracking, but each platform retains complete standalone utility and commercial viability.

Detailed Description of the Invention

The invention comprises two distinct systems, each optimized for a different biologic manufacturing domain. These systems can be deployed individually or operated under a shared compliance infrastructure.

I. Immune Cell Manufacturing Platform

System Overview

The immune cell expansion component of the platform comprises:

- A single-use bioreactor chamber
- A sterile tubing architecture with cytokine delivery, sampling, and waste lines
- Cytokine infusion cartridges containing IL-2, IL-15, IL-21, IL-12, IL-7, and/or IFN-γ
- Biosensors for cytokines, immune phenotype markers (CD25, CD45RO, CD127, PD-1, etc.), and metabolic conditions (pH, glucose, lactate, ammonia, DO)
- A programmable controller interfaced with a cloud-based GMP execution system

The bioreactor is configured for closed-loop processing and deviation-locked batch release, compliant with 21 CFR Part 11 electronic recordkeeping requirements. Immune cells are cultured and monitored continuously or at defined intervals using real-time sensor inputs.

Sensor Integration and Data Interpretation

Inline cytokine sensors—calibrated against standardized cytokine-specific validation curves—are inserted into the recirculation loop via sterile ports. Flow cytometry-compatible side loops allow real-time assessment of immune phenotype markers using cytometers from vendors such as BD Biosciences or Cytek Biosciences. Metabolic data is captured using devices like Nova Biomedical's BioProfile FLEX analyzers or optical biosensors embedded in the culture vessel.

A decision tree algorithm within the programmable logic controller determines whether to initiate cytokine infusion, dilution, rest, or batch hold based on real-time data.

AI and Transcriptomic Integration

Patient- or donor-derived transcriptomic data is uploaded prior to culture start to predict immune dynamics and personalize cytokine scheduling. The AI engine (trained on historical donor batches) updates dosing decisions based on actual batch performance, enabling retraining of future dosing schedules.

Tumor Lysate Personalization

Lysates are prepared by processing tumor biopsy or cell line material using freeze-thaw cycles, detergent lysis, or autophagic vesicle harvesting. Proteomic profiling guides lysate composition. During culture, granzyme B, CD69, CD25, and IFN-γ expression levels are measured to confirm successful immune education. If antigenic potency is low, co-culture with autologous APCs or lysate adjustment is initiated.

II. Plasma Protein Fractionation Platform

A. Core System: Includes a programmable fractionation skid, integrated inline sensors, GMP buffer cartridges, and programmable logic controllers.

B. OEM Compliance Architecture:

- **RFID Cartridge Authentication**: An RFID reader at the buffer input port scans metadata (lot, expiry, protocol match) to validate compatibility.
- **Metadata Flow and Lockout Logic**: If cartridge data fails validation, the system logs the metadata and triggers a cartridge lockout (see diagram: *Cartridge Metadata Flow*).
- **Interface Module**: Enables communication with external OEM devices using CAN bus, RS-485, or USB protocols. Supports auto-configuration of dosing schedules based on connected device firmware.

C. AI Optimization Layer:

- An embedded machine learning engine reviews prior batch yields and purity to recommend updated fractionation parameters.
- Batch-to-batch retraining ensures that optimal ethanol gradient, pH range, and temperature ramp profiles are always enforced (under Claim A10).
- AI logic is bounded by predefined GMP thresholds to prevent unsafe deviation.

D. Cloud-Based Oversight (see: Cloud Logic Tree):

- The cloud engine deploys GMP protocol sets across facilities, ensuring standardization.
- Real-time deviation alerts are logged and shared with QA/QC personnel.
- Exportable GMP records are stored for compliance audits (supporting Claim A12).

E. Vendor-Specific Features:

- Single-use or stainless-steel cartridge support
- Encrypted firmware validation for third-party hardware
- Operator interface allows upload of OEM calibration files

II. Plasma Protein Fractionation Platform

System Layout

The fractionation system includes:

- A modular, closed-loop fractionation skid (stainless steel or single-use)
- Skid-integrated inline sensors (for temperature, pH, ethanol %, UV280, turbidity, conductivity, and zeta potential)

- Programmable logic controllers for feedback control
- Disposable GMP buffer and ethanol cartridges with RFID metadata
- A real-time cloud-connected dashboard for batch tracking and regulatory audit support

Process Description

Plasma enters the skid and undergoes sequential fractionation steps including:

- Cryoprecipitation or ethanol-based precipitation
- Depth filtration or centrifugation
- Viral inactivation via solvent/detergent or low-pH hold steps
- Buffer exchange, diafiltration, and chromatography (if applicable)

Ethanol concentration, pH, and process temperature are continuously monitored and adjusted based on protein-specific logic. For example:

- IVIG: target UV280 absorbance and ethanol % adjusted for purity
- Albumin: pH control and zeta potential modulated for optimal precipitation
- Factor IX: extended hold times and low ionic strength buffer conditions

Viral Inactivation and Batch Safety

If the system detects suboptimal viral inactivation conditions (e.g., temperature or pH drift during hold step), it will lock out the batch and require operator override with documented validation. Sensor readings are compared against validated GMP specifications for each protein class, ensuring process reliability and safety.

III. GMP Compliance & Cloud Integration

Both manufacturing modules interface with a central execution platform offering:

- Remote monitoring of all batch parameters
- 21 CFR Part 11–compliant audit logs and deviation reports
- Redundant batch release validation (automated + manual)
- Real-time alerts for deviation events
- Secure cloud storage of process records, accessible by QA/QC teams and regulators

EXPANDED CLAIM SET