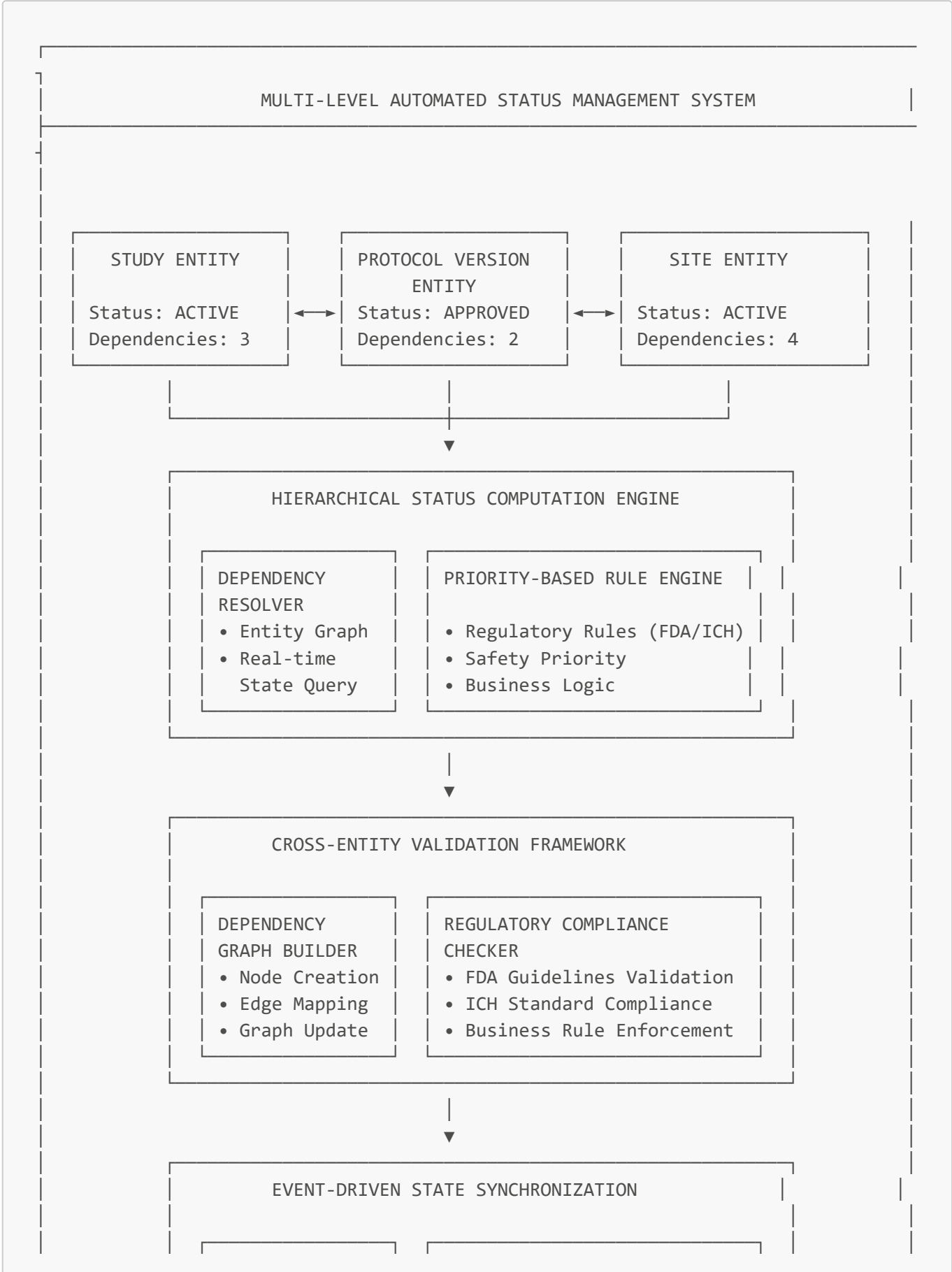
PATENT FIGURES AND ARCHITECTURE DIAGRAMS

FIG. 1: Overall System Architecture



```
│           │  │ EVENT DETECTOR  │  │ SYNCHRONIZATION ORCHESTRATOR │  │          │
│           │  │ • Status Change │  │ • Multi-Entity Updates       │  │          │
│           │  │   Monitoring    │  │ • Transaction Management     │  │          │
│           │  │ • Impact        │  │ • Rollback Capability       │  │          │
│           │  │   Analysis      │  │ • Audit Trail Generation    │  │          │
│           │  └─────────────────┘  └─────────────────────────────┘  │          │
│           └───────────────────────────────────────────────────────┘          │
│
│
└──────────────────────────────────────────────────────────────────────────────
┘
```

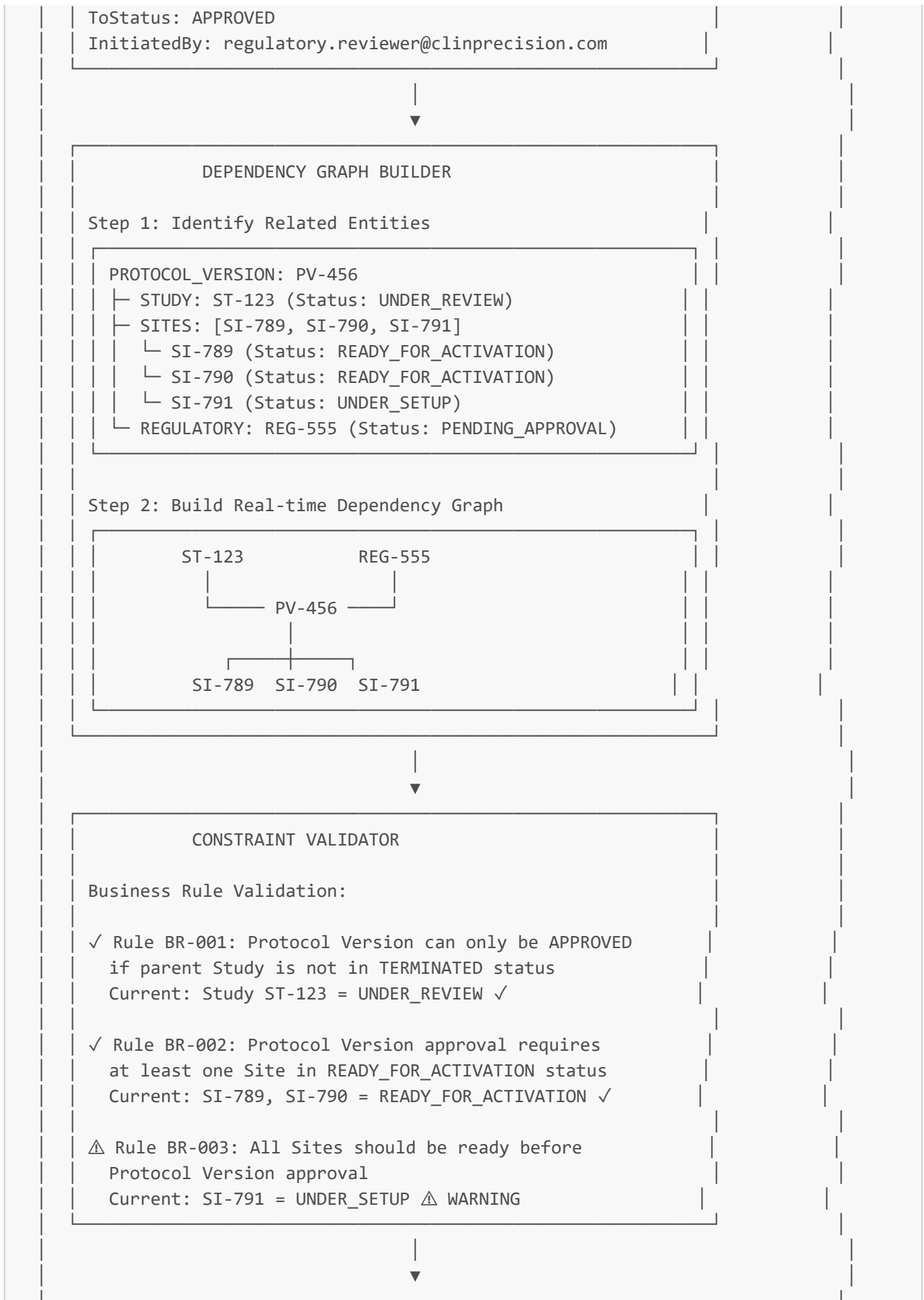
FIG. 2: Hierarchical Status Computation Engine Components

```
┌──────────────────────────────────────────────────────────────────────┐
│              HIERARCHICAL STATUS COMPUTATION ENGINE                  │
├──────────────────────────────────────────────────────────────────────┤
│                                                                      │
│  INPUT: Entity Status Computation Request                            │
│  ┌──────────────────────────────────────────────────────────┐       │
│  │ EntityType: STUDY                                        │       │
│  │ EntityId: 12345                                          │       │
│  │ RequestedStatus: ACTIVE                                  │       │
│  └──────────────────────────────────────────────────────────┘       │
│                              │                                       │
│                              ▼                                       │
│  ┌──────────────────────────────────────────────────────────┐       │
│  │              DEPENDENCY RESOLVER                         │       │
│  │                                                          │       │
│  │ Step 1: Query Database for Dependent Entities           │       │
│  │ • Protocol Versions for Study 12345                     │       │
│  │ • Sites associated with Study 12345                     │       │
│  │ • Regulatory approvals for Study 12345                  │       │
│  │                                                          │       │
│  │ Step 2: Build Dependency Context                         │       │
│  │ • Current States of All Dependencies                     │       │
│  │ • Relationship Types and Constraints                     │       │
│  │ • Business Rule Applicability                           │       │
│  └──────────────────────────────────────────────────────────┘       │
│                              │                                       │
│                              ▼                                       │
│  ┌──────────────────────────────────────────────────────────┐       │
│  │           PRIORITY-BASED RULE ENGINE                     │       │
│  │                                                          │       │
│  │ Priority Level 1: REGULATORY COMPLIANCE                  │       │
│  │ ├─ FDA Approval Status                                   │       │
│  │ ├─ ICH Guideline Compliance                              │       │
│  │ └─ Regulatory Submission Status                          │       │
│  │                                                          │       │
│  │ Priority Level 2: SAFETY CONSIDERATIONS                  │       │
│  │ ├─ Safety Review Status                                  │       │
```

```
│   │ ├─ Adverse Event Monitoring                              │     │
│   │ └─ Risk Assessment Completion                            │     │
│   │                                                          │     │
│   │ Priority Level 3: OPERATIONAL READINESS                  │     │
│   │ ├─ Site Activation Status                                │     │
│   │ ├─ Staff Training Completion                             │     │
│   │ └─ Equipment Qualification                               │     │
│   │                                                          │     │
│   │ Priority Level 4: ADMINISTRATIVE COMPLETENESS            │     │
│   │ ├─ Documentation Status                                  │     │
│   │ ├─ Contract Execution                                    │     │
│   │ └─ Budget Approval                                       │     │
│   └──────────────────────────────────────────────────────────┘     │
│                              │                                     │
│                              ▼                                     │
│   ┌──────────────────────────────────────────────────────────┐     │
│   │              STATUS CALCULATOR                           │     │
│   │                                                          │     │
│   │ Algorithm: Hierarchical Status Determination             │     │
│   │                                                          │     │
│   │ IF (All Priority 1 Rules Satisfied) THEN                │     │
│   │   IF (All Priority 2 Rules Satisfied) THEN              │     │
│   │     IF (All Priority 3 Rules Satisfied) THEN            │     │
│   │       Status = ACTIVE                                    │     │
│   │     ELSE Status = APPROVED                               │     │
│   │   ELSE Status = UNDER_REVIEW                             │     │
│   │ ELSE Status = DRAFT                                      │     │
│   └──────────────────────────────────────────────────────────┘     │
│                              │                                     │
│                              ▼                                     │
│  OUTPUT: Computed Entity Status with Justification                 │
│   ┌──────────────────────────────────────────────────────────┐     │
│   │ ComputedStatus: ACTIVE                                   │     │
│   │ Justification: All dependencies satisfied                │     │
│   │ DependencyDetails: [...detailed breakdown...]           │     │
│   │ NextReviewDate: 2025-10-28                              │     │
│   └──────────────────────────────────────────────────────────┘     │
│                                                                    │
└────────────────────────────────────────────────────────────────────┘
```

FIG. 3: Cross-Entity Validation Framework Workflow

```
┌──────────────────────────────────────────────────────────────────────────┐
│                CROSS-ENTITY VALIDATION FRAMEWORK                         │
├──────────────────────────────────────────────────────────────────────────┤
│                                                                          │
│  VALIDATION REQUEST                                                      │
│   ┌──────────────────────────────────────────────────────────────┐      │
│   │ EntityType: PROTOCOL_VERSION                                 │      │
│   │ EntityId: PV-456                                             │      │
│   │ FromStatus: UNDER_REVIEW                                     │      │
```


ToStatus: APPROVED
InitiatedBy: regulatory.reviewer@clinprecision.com
DEPENDENCY GRAPH BUILDER
Step 1: Identify Related Entities
PROTOCOL_VERSION: PV-456
├─ STUDY: ST-123 (Status: UNDER_REVIEW)
├─ SITES: [SI-789, SI-790, SI-791]
└─ SI-789 (Status: READY_FOR_ACTIVATION)
└─ SI-790 (Status: READY_FOR_ACTIVATION)
└─ SI-791 (Status: UNDER_SETUP)
└─ REGULATORY: REG-555 (Status: PENDING_APPROVAL)
Step 2: Build Real-time Dependency Graph
ST-123
REG-555
PV-456
SI-789 SI-790 SI-791
CONSTRAINT VALIDATOR
Business Rule Validation:
✓ Rule BR-001: Protocol Version can only be APPROVED
if parent Study is not in TERMINATED status
Current: Study ST-123 = UNDER_REVIEW ✓
✓ Rule BR-002: Protocol Version approval requires
at least one Site in READY_FOR_ACTIVATION status
Current: SI-789, SI-790 = READY_FOR_ACTIVATION ✓
⚠ Rule BR-003: All Sites should be ready before
Protocol Version approval
Current: SI-791 = UNDER_SETUP ⚠ WARNING
REGULATORY COMPLIANCE CHECKER
FDA Guidelines Validation:

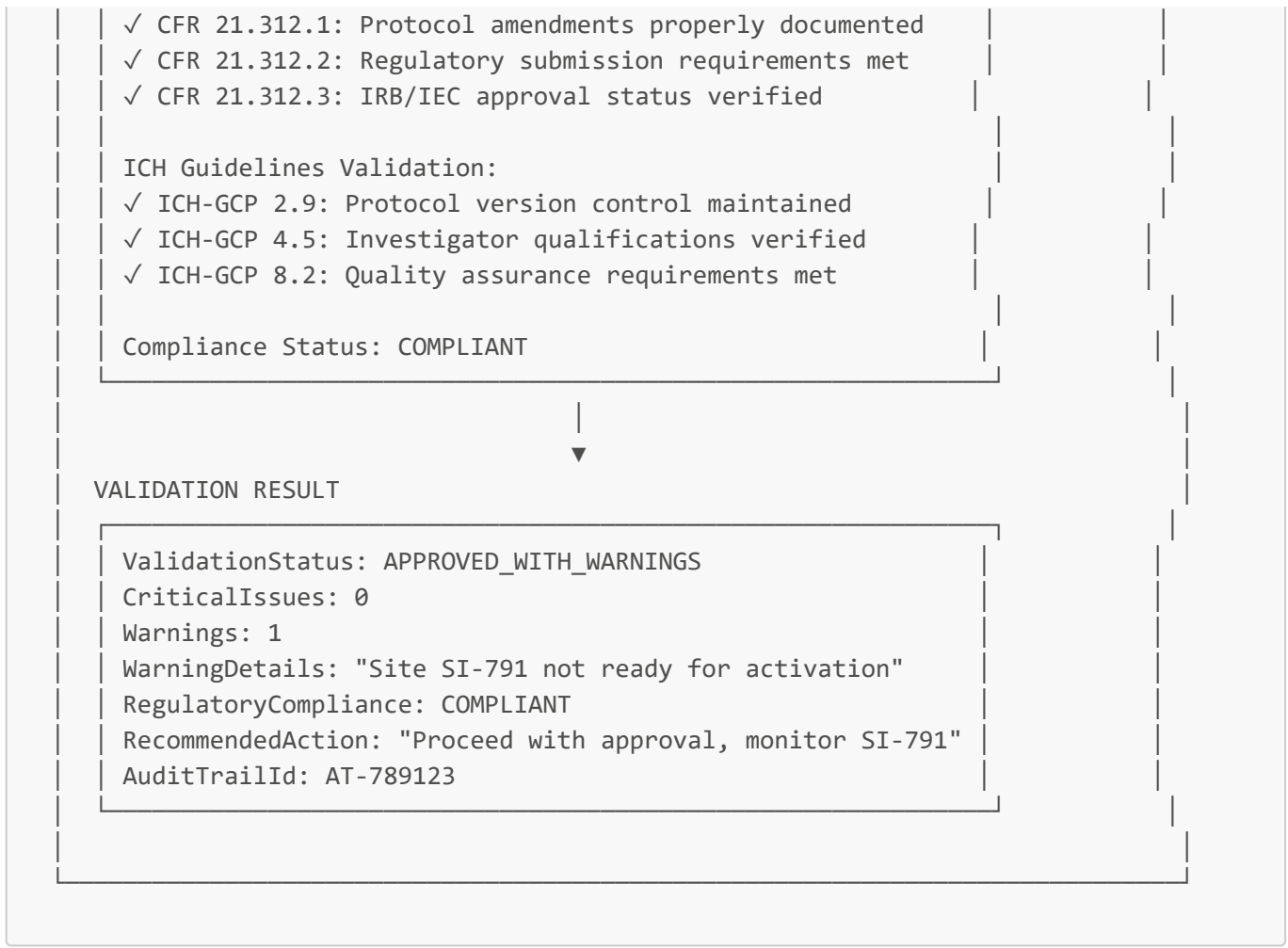
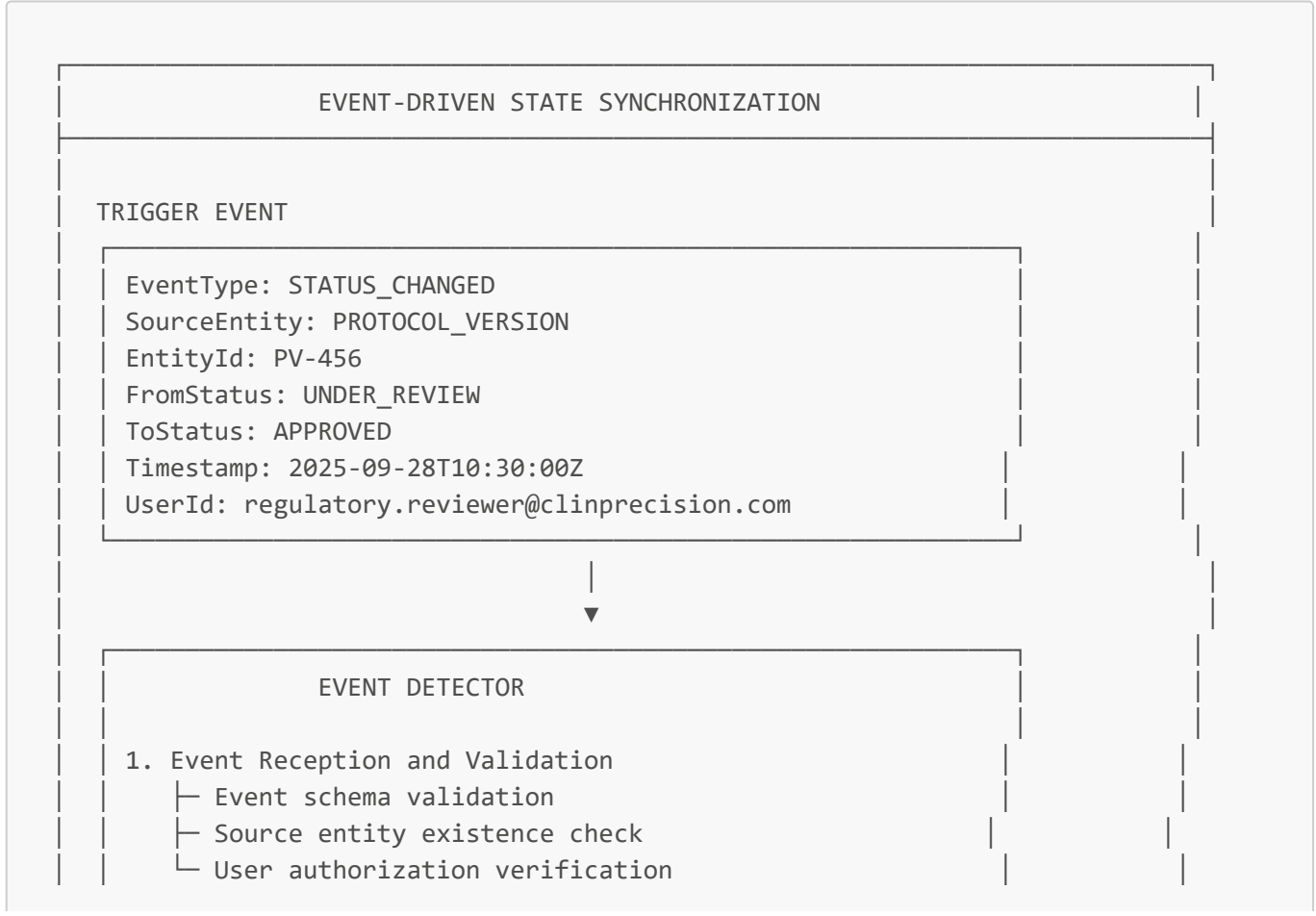
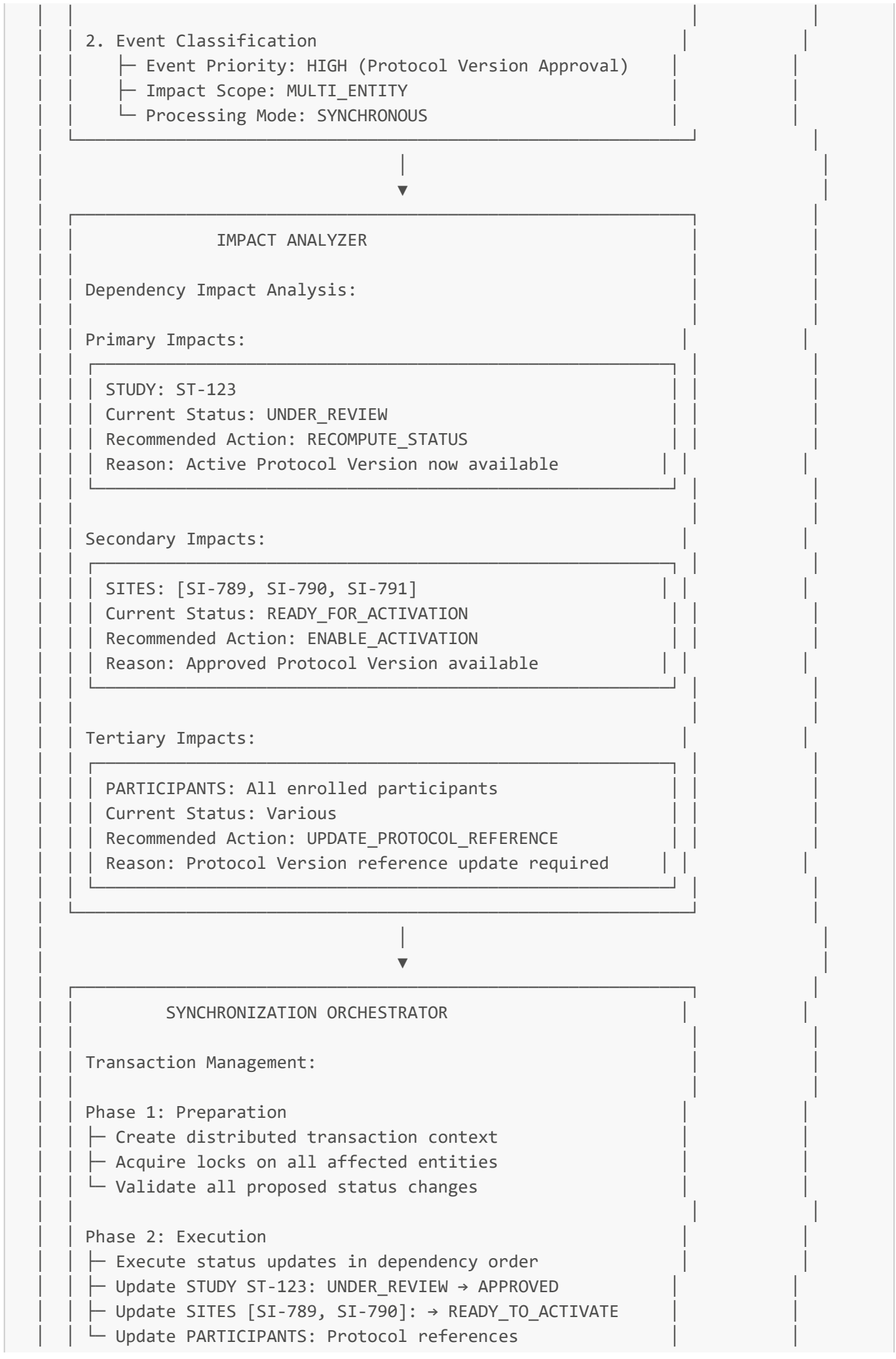


FIG. 4: Event-Driven State Synchronization Process




2. Event Classification
├─ Event Priority: HIGH (Protocol Version Approval)
├─ Impact Scope: MULTI_ENTITY
└─ Processing Mode: SYNCHRONOUS
IMPACT ANALYZER
Dependency Impact Analysis:
Primary Impacts:
STUDY: ST-123
Current Status: UNDER_REVIEW
Recommended Action: RECOMPUTE_STATUS
Reason: Active Protocol Version now available
Secondary Impacts:
SITES: [SI-789, SI-790, SI-791]
Current Status: READY_FOR_ACTIVATION
Recommended Action: ENABLE_ACTIVATION
Reason: Approved Protocol Version available
Tertiary Impacts:
PARTICIPANTS: All enrolled participants
Current Status: Various
Recommended Action: UPDATE_PROTOCOL_REFERENCE
Reason: Protocol Version reference update required
SYNCHRONIZATION ORCHESTRATOR
Transaction Management:
Phase 1: Preparation
├─ Create distributed transaction context
├─ Acquire locks on all affected entities
└─ Validate all proposed status changes
Phase 2: Execution
├─ Execute status updates in dependency order
├─ Update STUDY ST-123: UNDER_REVIEW → APPROVED
├─ Update SITES [SI-789, SI-790]: → READY_TO_ACTIVATE
└─ Update PARTICIPANTS: Protocol references

```
│  │                                                          │          │
│  │ Phase 3: Confirmation                                    │          │
│  │ ├─ Verify all updates completed successfully             │          │
│  │ ├─ Generate audit trail entries                         │          │
│  │ ├─ Release entity locks                                  │          │
│  │ └─ Commit distributed transaction                        │          │
│  │                                                          │          │
│  │ Rollback Capability:                                     │          │
│  │ ├─ Automatic rollback on any failure                     │          │
│  │ ├─ Entity state restoration to pre-event status         │          │
│  │ └─ Error notification and logging                        │          │
│  └──────────────────────────────────────────────────────────┘          │
│                                 │                                      │
│                                 ▼                                      │
│  SYNCHRONIZATION RESULT                                                │
│  ┌──────────────────────────────────────────────────────────┐          │
│  │ SynchronizationStatus: SUCCESS                           │          │
│  │ EntitiesUpdated: 4 (1 Study, 3 Sites)                   │          │
│  │ ParticipantsAffected: 25                                 │          │
│  │ TransactionId: TX-789456123                              │          │
│  │ ProcessingTime: 245ms                                    │          │
│  │ AuditTrailIds: [AT-789124, AT-789125, AT-789126]        │          │
│  │ NotificationsSent: 8                                     │          │
│  └──────────────────────────────────────────────────────────┘          │
│                                                                        │
└────────────────────────────────────────────────────────────────────────┘
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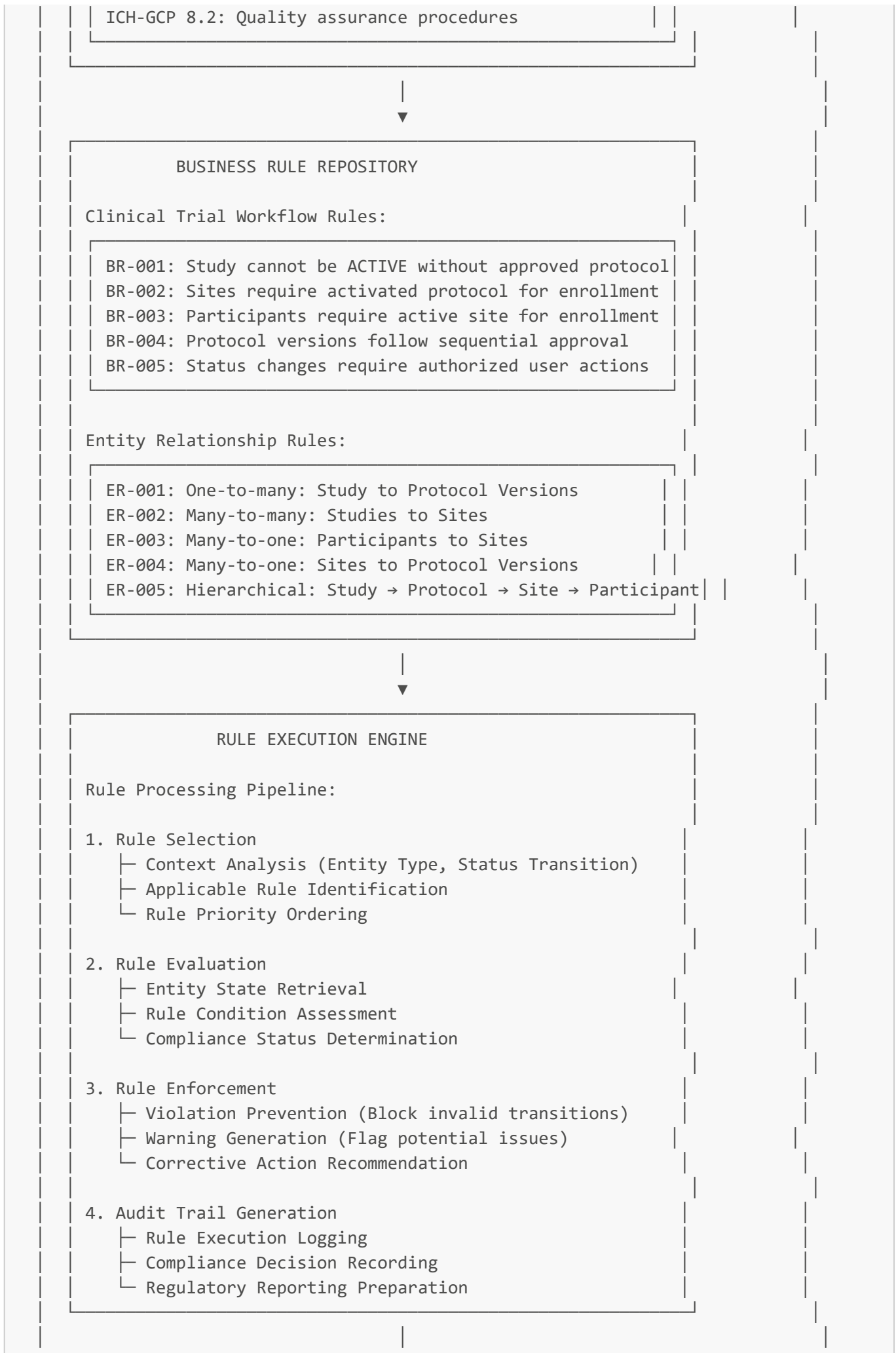
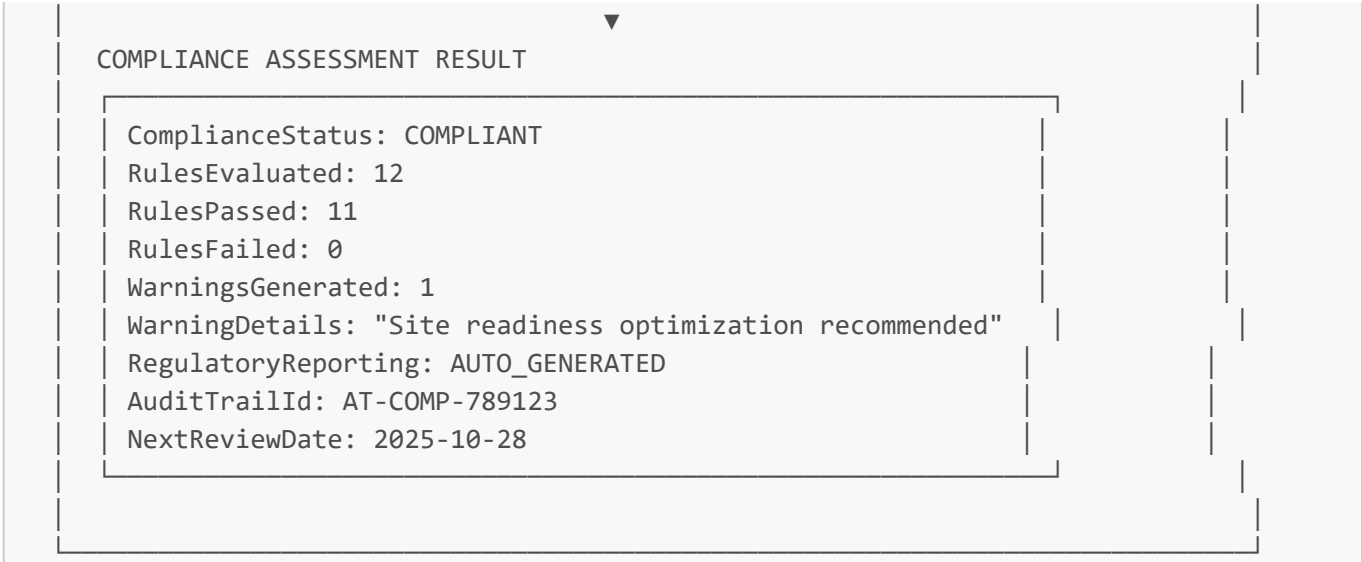
FIG. 5: Compliance Rule Engine Architecture

```
┌────────────────────────────────────────────────────────────────────────┐
│                   COMPLIANCE RULE ENGINE ARCHITECTURE                  │
├────────────────────────────────────────────────────────────────────────┤
│                                                                        │
│  ┌──────────────────────────────────────────────────────────┐          │
│  │            REGULATORY RULE REPOSITORY                    │          │
│  │                                                          │          │
│  │ FDA Rules (21 CFR):                                      │          │
│  │ ┌──────────────────────────────────────────────────────┐ │          │
│  │ │ CFR 312.60: General responsibilities of investigators │ │          │
│  │ │ CFR 312.62: Investigator record keeping requirements  │ │          │
│  │ │ CFR 312.64: Investigator reports                     │ │          │
│  │ │ CFR 312.66: Assurance of IRB review                  │ │          │
│  │ │ CFR 312.70: Sponsor responsibilities                 │ │          │
│  │ └──────────────────────────────────────────────────────┘ │          │
│  │                                                          │          │
│  │ ICH Guidelines:                                          │          │
│  │ ┌──────────────────────────────────────────────────────┐ │          │
│  │ │ ICH-GCP 1.1: Good Clinical Practice principles       │ │          │
│  │ │ ICH-GCP 2.9: Protocol compliance requirements        │ │          │
│  │ │ ICH-GCP 4.1: Investigator qualifications             │ │          │
│  │ │ ICH-GCP 4.5: Protocol deviations reporting           │ │          │
```


ICH-GCP 8.2: Quality assurance procedures
BUSINESS RULE REPOSITORY
Clinical Trial Workflow Rules:
BR-001: Study cannot be ACTIVE without approved protocol
BR-002: Sites require activated protocol for enrollment
BR-003: Participants require active site for enrollment
BR-004: Protocol versions follow sequential approval
BR-005: Status changes require authorized user actions
Entity Relationship Rules:
ER-001: One-to-many: Study to Protocol Versions
ER-002: Many-to-many: Studies to Sites
ER-003: Many-to-one: Participants to Sites
ER-004: Many-to-one: Sites to Protocol Versions
ER-005: Hierarchical: Study → Protocol → Site → Participant
RULE EXECUTION ENGINE
Rule Processing Pipeline:
1. Rule Selection
├─ Context Analysis (Entity Type, Status Transition)
├─ Applicable Rule Identification
└─ Rule Priority Ordering
2. Rule Evaluation
├─ Entity State Retrieval
├─ Rule Condition Assessment
└─ Compliance Status Determination
3. Rule Enforcement
├─ Violation Prevention (Block invalid transitions)
├─ Warning Generation (Flag potential issues)
└─ Corrective Action Recommendation
4. Audit Trail Generation
├─ Rule Execution Logging
├─ Compliance Decision Recording
└─ Regulatory Reporting Preparation


COMPLIANCE ASSESSMENT RESULT
ComplianceStatus: COMPLIANT
RulesEvaluated: 12
RulesPassed: 11
RulesFailed: 0
WarningsGenerated: 1
WarningDetails: "Site readiness optimization recommended"
RegulatoryReporting: AUTO_GENERATED
AuditTrailId: AT-COMP-789123
NextReviewDate: 2025-10-28