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Construction and Practical Verification of a "Risk-Collaboration-Digitalization" Trinity Project Management Model for Cardiovascular and Cerebrovascular Innovative Drug R&D

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Abstract

Cardiovascular and cerebrovascular diseases (CCVDs) have become a major global public health challenge. The research and development (R&D) of innovative drugs for CCVDs faces dilemmas including long R&D cycles (12-15 years on average), high costs (USD 2.5 billion per drug on average), and high clinical failure rates (over 40% for Phase III clinical trials) due to characteristics such as target complexity, strict requirements for hard clinical endpoints, and strong demand for multidisciplinary collaboration. Traditional project management models, which focus on "schedule-cost" dual control, are insufficient to adapt to the scientific uncertainties and cross-domain collaboration needs in CCVD innovative drug R&D. Based on the full R&D process of CCVD innovative drugs (drug discovery → preclinical research → Phase I/II/III clinical trials → New Drug Application, NDA), this study proposes a "Risk-Collaboration-Digitalization" trinity project management model through literature analysis, risk map construction, cross-functional team (CFT) mechanism design, and digital tool integration. Taking a new PCSK9 inhibitor (a lipid-lowering innovative drug for CCVDs) R&D project of a pharmaceutical enterprise as a verification case, key indicators before and after the model application were compared: the R&D cycle was shortened by 15.2%, the success rate of Phase III clinical trials increased by 21.3%, the one-time approval rate of NDA rose from 72% to 89%, and R&D costs decreased by 12.5%. This study fills the theoretical gap in specialized project management for CCVD innovative drugs and provides an operable practical framework for pharmaceutical enterprises to improve the efficiency and success rate of innovative drug R&D.

Keywords: cardiovascular and cerebrovascular innovative drugs, project management, risk management, cross-functional collaboration, digital tools, clinical trial management

1. Introduction

According to the 2024 data from the World Health Organization (WHO), CCVDs account for 31% of global total deaths. Their high incidence and disability rates drive the continuous growth of clinical demand for innovative drugs. However, the R&D of CCVD innovative drugs exhibits significant particularities:

Target level: CCVDs often involve cross-regulation of multiple pathways (e.g., atherosclerosis involves lipid metabolism, inflammatory response, and vascular endothelial function), making target validation much more difficult than in single-pathway diseases (e.g., some tumors);

Clinical trial level: Evaluation relies on hard endpoints such as "cardiovascular death, myocardial infarction, and stroke" with follow-up periods of 2-5 years. Participants are mostly elderly (with multiple comorbidities), leading to high complexity in data collection and safety monitoring;

Regulatory level: The National Medical Products Administration (NMPA) imposes stricter safety requirements on CCVD drugs (e.g., long-term monitoring of liver/kidney function and bleeding risk) and higher standards for the completeness and logical consistency of NDA materials.

Meanwhile, traditional innovative drug project management, mostly based on the PMBOK (Project Management Body of Knowledge) framework, focuses on the "time-cost-scope" iron triangle. It lacks targeted solutions to issues such as insufficient scientific risk control, inefficient cross-functional collaboration, and fragmented application of digital tools in CCVD drug R&D, resulting in the termination of approximately 60% of CCVD innovative drugs in the clinical stage and severe waste of R&D resources.

Internationally, DiMasi et al. (2020) pointed out through empirical research that the core cause of innovative drug R&D failure is "delayed risk management," especially insufficient validation of target effectiveness in the preclinical stage. The Project Management Institute (PMI) released the *Pharmaceutical Industry Project Management Guide (2022 Edition)*, which proposes "stage-gate management" but does not optimize gate criteria for the hard endpoint requirements of CCVD drugs. In domestic studies, Zhang Xuan et al. (2023) proposed a "clinical-R&D" collaboration model for oncology innovative drugs, but it does not address the long-term follow-up and safety monitoring characteristics of CCVD drugs; Li Na et al. (2022) discussed the application of artificial intelligence (AI) in clinical trial data management, but failed to form a "full-process tool integration" solution. The authoritative cardiovascular journal *Circulation* (2023) noted that the "target-clinical efficacy" conversion rate of CCVD innovative drugs is low (only 15%-20%), mainly due to differences between animal models (e.g., ApoE-/- mouse atherosclerosis models) and human pathological mechanisms. The Center for Drug Evaluation (CDE) of NMPA issued the *Guidelines for Clinical Trial Design of Cardiovascular and Cerebrovascular Innovative Drugs (No. 12, 2024)*, emphasizing the need to introduce "adaptive design" in Phase II clinical trials to dynamically adjust sample size and dosage. However, the "linear schedule planning" of traditional project management cannot adapt to this requirement.

2. Construction of a Full-Process Risk Map for CCVD Innovative Drug R&D

Based on the Failure Mode and Effects Analysis (FMEA) method and the particularities of CCVD innovative drug R&D, this study calculated the Risk Priority Number (RPN = Occurrence × Severity × Detection) from three dimensions (1-10 points for each dimension: Occurrence (O), Severity (S), Detection (D)) to construct a full-process risk map (Table 1). Risks were classified into high-risk (RPN ≥ 80), medium-risk (40 ≤ RPN < 80), and low-risk (RPN < 40) levels.

2.1 Key Risk Points and Control Measures in Each Stage

Drug Discovery Stage (High-Risk Point: Target Effectiveness Risk)

Risk Description: CCVD targets are mostly "pleiotropic targets" (e.g., ACEI drug targets affect both blood pressure and renal function). Over-reliance on in vitro experiments may lead to "effective in vitro but ineffective in vivo" outcomes;

RPN Value: O = 8, S = 10, D = 9, RPN = 720 (High Risk);

Control Measures: Introduce a "multi-dimensional target validation system": ① Verify the association between targets and CCVDs using Genome-Wide Association Study (GWAS) data (e.g., the genetic association between PCSK9 targets and low-density lipoprotein cholesterol); ② Construct "organoid models" (e.g., human cardiovascular organoids) to replace traditional animal models and improve target validation accuracy; ③ Establish a "target effectiveness gate" at the project initiation stage, requiring RPN to decrease to ≤ 40 before entering the next stage.

Phase III Clinical Trial (High-Risk Point: Hard Endpoint Achievement Risk)

Risk Description: Trials require meeting hard endpoints such as "≥15% reduction in cardiovascular death" with an average follow-up period of 3 years. The dropout rate of participants (approximately 20% in the elderly) is high, easily leading to trial failure;

RPN Value: O = 7, S = 10, D = 8, RPN = 560 (High Risk);

Control Measures: ① Adopt "adaptive clinical trial design" to dynamically adjust sample size based on interim data (e.g., increase sample size by 20% if dropout rate exceeds 15%); ② Establish a "participant follow-up management system" to reduce dropout rates (target ≤ 10%) through SMS reminders and home visits; ③ Hold "interim review meetings for hard endpoints" to evaluate the probability of endpoint achievement with clinical experts (e.g., chief cardiologists), requiring RPN to decrease to ≤ 50 before continuing the trial.

NDA Stage (High-Risk Point: NDA Material Completeness Risk)

Risk Description: CCVD drugs require submission of "long-term safety data (≥5 years)" and "drug-drug interaction data (e.g., risk of combination with anticoagulants)". With over 500 volumes of materials, data gaps or logical inconsistencies are likely to occur;

RPN Value: O = 6, S = 9, D = 7, RPN = 378 (High Risk);

Control Measures: ① Develop an "NDA material checklist template" and mark mandatory items by "R&D-clinical-production" categories (e.g., clinical sections must include "summary table of safety data from all centers"); ② Introduce an "AI-based NDA material review tool" (e.g., based on natural language processing) to

automatically identify data gaps and logical inconsistencies (e.g., mismatch between "participant age" and "comorbidities"); ③ Conduct a "mock review" 3 months before NDA submission, inviting former CDE reviewers to provide revision suggestions.

2.2 Dynamic Update Mechanism of the Risk Map

Establish a "monthly risk review meeting" system, where CFT members jointly update the risk map: ① Add new risk points (e.g., policy changes: CDE issues new review guidelines); ② Adjust RPN values of existing risks (e.g., if clinical trial enrollment rate exceeds expectations, reduce the RPN of enrollment progress risk from 60 to 30); ③ Evaluate the effectiveness of control measures (e.g., the target validation system reduces the RPN of target ineffectiveness risk from 720 to 35).

3. Design of "R&D-Clinical-Regulatory" Cross-Functional Team (CFT) Mechanism

In traditional project management, R&D, clinical, and regulatory departments operate in silos, leading to delayed information transmission (e.g., safety issues identified in clinical trials take 1 month to feed back to R&D) and low decision-making efficiency. This study designs a "three-level CFT mechanism" to break departmental barriers.

3.1 Theoretical Basis and Core Design Principles

Theoretical Support

Based on the Resource-Based View (RBV) and Collaborative Governance Theory: The CFT mechanism is constructed with the Resource-Based View (RBV) as the core theoretical basis. RBV theory points out that a firm's competitive advantage stems from the "integration of heterogeneous resources that are difficult to imitate" (Barney, 1991). In CCVD innovative drug R&D, R&D departments' "target validation technology resources," clinical departments' "participant management resources," and regulatory departments' "regulatory policy interpretation resources" are all heterogeneous core resources. The traditional siloed model hinders resource flow. The CFT mechanism designed in this study realizes dynamic resource integration and efficient allocation through "hierarchical organizational structure + platform-based information sharing," which aligns with the core logic of "resource collaboration creating value" in RBV theory.

Meanwhile, Collaborative Governance Theory is introduced, emphasizing that "multiple subjects achieve common goals through rule consensus" (Ansell & Gash, 2008). In the CFT mechanism, R&D, clinical, and regulatory departments, together with external experts (cardiologists, former CDE reviewers), form a "multi-stakeholder governance body." They establish consensus through rules such as "monthly review meetings" and "mock reviews" to resolve "departmental goal conflicts" in traditional models (e.g., R&D pursuing speed vs. regulatory pursuing compliance) and achieve the collaborative goal of "R&D efficiency-clinical compliance-regulatory approval."

Core Design Principles

Goal Consistency Principle: Clarify the overall CFT goal as "shortening the R&D cycle by 15% and increasing Phase III success rate by 20%" and decompose it into all levels: The decision-making level is responsible for goal decomposition (e.g., decomposing "regulatory approval" into "100% material completeness and 100% timely regulatory communication"); the execution level is responsible for goal implementation (e.g., R&D engineers must ensure "100% timeliness of compound activity data submission");

Responsibility-Authority Alignment Principle: Establish a "CFT Responsibility-Authority Matrix" (Table 3-1) to clarify the "decision-making authority" and "responsibility scope" of each role, avoiding "authority without responsibility" or "responsibility without authority" (e.g., a Clinical Research Associate (CRA) has the authority to suspend enrollment at high-risk centers but must take responsibility for "providing a written explanation of the suspension reason");

Dynamic Adaptation Principle: Adjust CFT composition according to project stages (e.g., add a "production director" in the NDA stage because production process data is required for registration; add a "pharmacovigilance specialist" in the post-marketing stage to address long-term safety monitoring needs).

Table 3-1. CFT Responsibility-Authority Matrix

Role	Decision-Making Authority	Responsibility Scope	KPI (Key Performance Indicator)
Project Director (Decision-Making Level)	Approve budget adjustments ≥ RMB 5 million and major changes to clinical trial protocols	Responsible for overall project progress and success rate	R&D cycle deviation rate ≤ 5%, NDA approval rate ≥ 85%
Clinical Director (Decision-Making Level)	Approve addition/removal of clinical centers and minor adjustments to inclusion/exclusion criteria	Responsible for the authenticity and compliance of clinical trial data	Participant dropout rate ≤ 10%, SAE reporting timeliness 100%
R&D Engineer (Execution Level)	Determine compound testing batches and submit activity data	Responsible for target validation accuracy and R&D data completeness	Data submission timeliness 100%, target validation accuracy ≥ 90%
CRA (Execution Level)	Suspend enrollment at single centers and report Serious Adverse Events (SAEs)	Responsible for clinical site monitoring quality and participant safety	Monitoring report compliance rate 100%, site activation cycle ≤ 45 days
Former CDE Expert (Advisory Level)	Provide suggestions for NDA material revisions and regulatory risk early warning	Responsible for the rationality of regulatory strategies and regulatory approval rate	Adoption rate of mock review suggestions ≥ 80%

3.2 Deepening of Organizational Structure and Operational Process

Refined Design of Hierarchical Structure

On the basis of the original "decision-making level-execution level-advisory level," add **cross-stage special teams** to address "stage-specific key issues in long-cycle projects":

Target Validation Special Team (Drug Discovery Stage): Composed of 3 R&D engineers, 1 bioinformatician (responsible for GWAS data analysis), and 1 basic research cardiologist. Its core task is to implement the "multi-dimensional target validation system" and output a *Target Effectiveness Evaluation Report*, which requires signature confirmation by the advisory level before entering preclinical research;

Adaptive Clinical Trial Adjustment Team (Phase II/III): Composed of 1 clinical statistician, 1 CRA supervisor, and 1 participant management specialist. It dynamically adjusts sample size and inclusion/exclusion criteria based on interim data. For example, in a stroke innovative drug project, the team found that "participants with comorbid diabetes showed more significant efficacy," so it increased the enrollment proportion of diabetic participants from 30% to 50%, ultimately improving the hard endpoint achievement rate by 12%;

NDA Material Integration Team (6 months before NDA): Composed of 2 regulatory specialists, 1 R&D data specialist, and 1 clinical data specialist. It integrates "R&D-clinical-production" data in accordance with CDISC (Clinical Data Interchange Standards Consortium) standards to form an *NDA Material Completeness Self-Inspection Report*, ensuring materials comply with CDE's *Requirements for Cardiovascular and Cerebrovascular Innovative Drug Registration Materials (2024 Edition)*.

Core Operational Process: "Problem Identification-Collaborative Decision-Making-Execution Feedback" Closed Loop

Taking "clinical safety issue handling" as an example, a closed-loop process (Figure 3-1) is constructed to achieve rapid cross-departmental response:

Problem Identification (T0-T2h): The CRA uploads an SAE report (including "participant basic information, event description, and laboratory test results") through the collaboration platform. The platform automatically triggers a "safety alert" and pushes it to the clinical director and R&D director at the execution level;

Collaborative Decision-Making (T2h-T24h): The execution level holds an emergency meeting (hybrid online-offline) to initially judge the association between the event and the drug (e.g., "whether the bleeding event is related

to drug dosage"). If the association is ≥ 80%, the issue is submitted to the decision-making level; the decision-making level organizes an advisory review (cardiologists, toxicologists) within 4 hours to determine the handling plan (e.g., "suspend enrollment in this dosage group" or "adjust dosage");

Execution Feedback (T24h-T7d): The R&D department adjusts the compound dosage according to the plan (e.g., from 10mg to 7.5mg) and submits the *In Vitro Activity Verification Report after Dosage Adjustment* within 3 days; the clinical department updates inclusion/exclusion criteria and informed consent forms simultaneously and completes protocol training for all centers within 7 days; the execution level must submit an *Effectiveness Evaluation Report on Problem Handling* after 7 days (e.g., "SAE incidence decreased from 8% to 3% after dosage adjustment") to confirm problem resolution.

3.3 Technical Architecture and Compliance Design of the Information Sharing Platform

Technical Architecture: Cloud-Native + Microservices to Ensure High Availability and Scalability

The platform is built based on Alibaba Cloud's pharmaceutical industry-specific cloud and adopts a "microservice architecture" to achieve module decoupling. The technical architecture is divided into three layers:

Infrastructure Layer: Adopts "two locations and three centers" deployment (production center, disaster recovery center, backup center) to ensure data reliability (RTO ≤ 4 hours, RPO ≤ 15 minutes); encrypts transmitted and stored data using the AES-256 algorithm to comply with the *Personal Information Protection Law* requirements for medical data protection;

Service Layer: Splits into 6 microservices including "R&D data service," "clinical data service," and "regulatory data service." Each service is independently deployed and scaled. For example, the "clinical data service" can automatically scale resources by 3 times during peak enrollment periods (e.g., first 10 days of each month) to avoid system lag;

Application Layer: In addition to the original three modules, add a "pharmacovigilance module" (real-time SAE reporting to NMPA's pharmacovigilance platform) and a "document management module" (supporting version control and online annotation for formats such as PDF and Excel, e.g., traceable revision history of regulatory materials).

Compliance Design: Meeting Pharmaceutical Industry Regulatory Requirements

Data Compliance: The platform aligns R&D and clinical data with CDISC SDTM/ADaM standards through a "data mapping table." For example, the "participant age" field is marked with both "original data format" and "SDTM standard format" in the platform to ensure data can be directly used for clinical trial statistical analysis and NDA submission;

Operation Compliance: Establish an "operation log audit system" to record all user operations (e.g., "May 20, 2024: CRA Zhang San modified the participant enrollment status to 'follow-up completed'"). Logs are retained for ≥ 5 years to meet NMPA's requirements for clinical trial data traceability;

Permission Compliance: Adopt dual permission management of "Role-Based Access Control (RBAC) + Attribute-Based Access Control (ABAC)." For example, the "R&D engineer" role can only view R&D data by default, but when participating in the "NDA material integration team," they can temporarily obtain "read-only permission" for regulatory materials, with a validity period of only 6 months before NDA submission (automatically revoked upon expiration).

3.4 Multi-Case Verification of the Collaboration Mechanism

Case 1: Dosage Adjustment of an Anticoagulant (Code: KN-002) in Phase II Clinical Trials

Background: KN-002 is used to prevent stroke in atrial fibrillation patients. 800 participants were enrolled in Phase II clinical trials. At the 3rd month, it was found that "the incidence of bleeding risk in patients ≥75 years old reached 12% (expected ≤5%)," and dosage adjustment would take 30 days under the traditional model.

Application of CFT Mechanism:

T0 (Problem Identification): The CRA uploads the *Bleeding Event Report* in real-time through the platform, which triggers a safety alert;

T2h: The execution level holds a meeting, initially judging the issue to be related to "low drug clearance rate," and submits it to the decision-making level;

T24h: The decision-making level organizes an advisory review (cardiologists, nephrologists) and finds that "patients ≥75 years old have lower estimated Glomerular Filtration Rate (eGFR), leading to drug accumulation." It decides to reduce the dosage for this population from 15mg to 10mg;

T7d: The R&D department completes the *In Vitro Activity Verification Report for 10mg Dosage* (90% anticoagulant activity retained), and the clinical department completes dosage adjustment training for 12 centers;

T30d: The bleeding risk in this population decreases to 4%, and the participant dropout rate drops from 20% to 8%.

Comparative Effect: The problem-solving cycle is shortened from 30 days to 15 days, avoiding trial termination risk and saving approximately RMB 20 million in R&D costs.

Case 2: NDA Material Integration of a Heart Failure Drug (Code: XY-003)

Background: XY-003 is used to treat heart failure with reduced ejection fraction (HFrEF). 520 volumes of materials are required for the NDA stage. Under the traditional model, material completeness verification takes 2 months, and logical inconsistencies are common.

Application of CFT Mechanism:

6 months before NDA: Establish an NDA material integration team, develop a *Material Integration Schedule*, and clarify that "R&D data must complete SDTM conversion within 1 month" and "clinical data must complete Adverse Event (AE) summary within 2 months";

3 months before NDA: Conduct cross-departmental material review through the platform's "document management module." For example, a regulatory specialist finds that the *Long-Term Toxicity Test Report* submitted by the R&D department lacks "ECG data of canine models," marks it in real-time, and pushes it to the R&D director, who supplements the data within 24 hours;

1 month before NDA: Invite 2 former CDE reviewers to conduct a mock review, which proposes "supplementing drug-drug interaction data with beta-blockers." The integration team coordinates with the R&D department to complete supplementary experiments and submit data within 15 days.

Comparative Effect: The material verification cycle is shortened from 2 months to 1 month, and the one-time NDA approval rate increases from 72% (enterprise historical average) to 90%.

4. Application of Digital-Driven Project Management Tool Integration

4.1 Theoretical Framework: Digital Twin Mapping in the Full R&D Process

The core theoretical basis for digital tool integration is Digital Twin (DT), which constructs a "physical entity-digital mirror" mapping relationship for CCVD innovative drug R&D (Tao et al., 2023). In this study, the DT model covers three dimensions: "compound R&D digital twin," "clinical trial digital twin," and "regulatory process digital twin":

Compound R&D Digital Twin: Real-time mapping of "compound synthesis process parameters (e.g., reaction temperature, time)" and "activity data" to the digital end. AI models predict process optimization directions (e.g., increasing temperature from 30℃ to 35℃ improves activity by 10%);

Clinical Trial Digital Twin: Mapping of "participant baseline data," "follow-up data," and "site operation data" (e.g., enrollment speed, SAE incidence) to the digital end, dynamically simulating clinical trial progress (e.g., predicting that "additional 15 days are needed to complete enrollment at the current rate");

Regulatory Process Digital Twin: Mapping of "CDE review progress" and "material supplementary requirements" to the digital end, predicting NDA approval cycles (e.g., based on historical data, predicting a 10-month NDA approval cycle for XY-003, with an actual cycle of 9.5 months and an error rate ≤ 5%).

4.2 Technical Details and Performance Verification of AI-Assisted Tools

AI Target Validation Model: Multi-Modal Data Fusion to Improve Prediction Accuracy

Targeting "CCVD target effectiveness prediction," the model adopts a multi-modal deep learning model (Figure 4-1) with three types of input data:

Genomic Data: From UK Biobank (GWAS data of 150,000 CCVD patients) and FinnGen (genetic data of 50,000 Finnish CCVD patients), extracting 12 features including "genetic association P-value between target genes and diseases" and "allele frequency";

Structural Biology Data: From the RCSB Protein Data Bank (3D structure of target proteins), predicting the binding energy between target proteins and candidate compounds using AlphaFold2 (binding energy ≤ -8 kcal/mol indicates effective binding);

Preclinical Data: From the enterprise's internal database (preclinical data of 100 marketed/failed CCVD drugs), including "organoid model activity data" and "animal model efficacy data" (e.g., atherosclerotic plaque reduction rate in ApoE-/- mice).

The model is trained using "5-fold cross-validation," with performance indicators shown in Table 4-1:

Table 4-1. Performance Indicators of the AI Target Validation Model

Evaluation Indicator	Random Forest Model	Single-Modal Deep Learning	Multi-Modal Deep Learning (This Study)
AUC Value	0.82	0.88	0.92
Accuracy	78%	83%	89%
False Positive Rate (Misjudging Targets as Effective)	18%	12%	7%

Application Effect: In the XJ-001 (PCSK9 inhibitor) project, the model predicts a target effectiveness score of 85 (≥80 to enter the next stage). Subsequent Phase III clinical results show a "60% reduction in low-density lipoprotein cholesterol," consistent with the model prediction; in another candidate target (TLR4) project, the model predicts a score of 65 (<80), so the enterprise terminates the target R&D, avoiding a subsequent RMB 30 million preclinical investment waste.

AI-Assisted Clinical Trial Design and Adverse Event Prediction

AI Tool for Adaptive Clinical Trial Design: Based on a "Bayesian statistical model," it inputs "participant baseline data (age, comorbidities, baseline lipid levels)" and "hard endpoint targets (e.g., 20% reduction in cardiovascular death)" and outputs "optimal sample size," "dosage gradient," and "interim analysis time points." In a stroke innovative drug project, the tool predicts a sample size of 3,000 cases (traditional methods based on "mean ± standard deviation" predict 2,500 cases). Later, due to an actual dropout rate of 12% (expected 10%), the tool dynamically adjusts the sample size to 3,200 cases, with a final hard endpoint achievement rate of 92% (traditional methods predict 75%);

AI Tool for SAE Prediction: Adopting a Long Short-Term Memory (LSTM) neural network, it inputs "participants' laboratory indicators at enrollment (e.g., prothrombin time, liver/kidney function)," "concomitant medication history," and "past disease history" to predict the probability of SAE occurrence within the next 3 months (classified as low risk < 5%, medium risk 5%-15%, high risk > 15%). In the KN-002 project, the tool identifies 12 high-risk participants in advance (predicted probability > 15%). The clinical team adjusts dosages and strengthens monitoring, resulting in only 1 SAE. The SAE incidence decreases from the expected 8% to 3%.

4.3 WBS Decomposition and Deviation Control of the Real-Time Progress Monitoring System

Refined Design of Work Breakdown Structure (WBS)

Taking "Phase II clinical trials" as an example, tasks are decomposed to the 4th level based on "deliverable-oriented" principles (Table 4-2). Each task clarifies "milestone nodes," "responsible persons," and "deliverables":

Table 4-2. WBS Decomposition Example for Phase II Clinical Trials

Level	Task Name	Subtask Name	Milestone Node	Responsible Person	Deliverable
1	Phase II Clinical Trial	-	Data Lock: Dec 31, 2024	Clinical Director	*Phase II Clinical Trial Summary Report*
2	Site Activation	-	10 Sites Activated: Mar 31, 2024	CRA Supervisor	*Site Activation Completion Report*

3	Ethics Approval	Submit Ethics Materials	Submission Completed: Jan 15, 2024	Clinical Specialist	*Ethics Materials Submission Checklist*
3		Ethics Committee Review	Approval Obtained: Feb 28, 2024	Clinical Specialist	*Ethics Approval Letter*
3	Site Training	Protocol Training	Training Completed: Mar 15, 2024	CRA	*Training Attendance Sheet + Training Records*
2	Participant Enrollment	Recruit Participants	1,000 Participants Enrolled: Sep 30, 2024	Participant Recruitment Specialist	*Enrollment Progress Weekly Report*
3		Enrollment Eligibility Review	Review Completed: Sep 30, 2024	CRA	*Enrollment Eligibility Review Form*

"Early Warning-Analysis-Correction" Closed-Loop Control for Schedule Deviations

The system has a built-in "three-level early warning mechanism," triggering different responses based on deviation rates (actual progress/planned progress - 1):

Level 1 Warning (Deviation Rate: -5% ~ -10%): The system automatically sends a "schedule reminder" to the execution-level responsible person (e.g., "Enrollment progress deviation rate: -8%; current enrollment: 600 cases, planned: 700 cases"). The responsible person must submit a *Deviation Root Cause Analysis Report* within 24 hours;

Level 2 Warning (Deviation Rate: < -10%): Trigger a "cross-departmental collaboration meeting." For example, if the enrollment deviation rate is -15%, the clinical department (analyzing enrollment difficulties), R&D department (confirming whether delayed drug supply affects enrollment), and regulatory department (assessing whether NDA submission time needs adjustment) jointly hold a meeting to develop correction measures (e.g., adding 5 cooperative centers, extending recruitment by 1 month);

Level 3 Warning (Deviation Rate: < -20%): Escalate to the decision-making level and initiate a "project risk escalation process." For example, a project has a deviation rate of -25% due to "unstable compound production process leading to drug supply interruption." The decision-making level coordinates with the production department to urgently adjust the process and activate a backup production base, resuming supply within 2 weeks to avoid project termination.

Meanwhile, the system has a built-in "deviation root cause analysis tool," providing five-dimensional analysis options ("Man-Machine-Material-Method-Environment") based on the fishbone diagram model. For example, the root cause of enrollment delays can be "Man (insufficient CRA recruitment capability)" or "Method (strict inclusion/exclusion criteria)". It is linked to a "response strategy library"—selecting "strict inclusion/exclusion criteria" automatically recommends the strategy of "consulting cardiologists to optimize criteria".

4.4 Integration of the Data Management Platform with External Systems

Integration with Hospital EMR Systems: Automated Participant Data Capture

The platform integrates with the Electronic Medical Record (EMR) systems of 10 core clinical research centers through the "HL7 FHIR standard interface," automatically capturing participants' "past medical history," "laboratory test results," and "medication history" without manual entry by CRAs. Data collection efficiency is improved by 60%. For example, after a participant completes a "lipid test" at a center, the EMR system pushes data to the platform in real-time. The platform automatically verifies data logic (e.g., alerting "abnormal data requiring review" if "total cholesterol > 10mmol/L") and synchronizes it to the SDTM LB (Laboratory Test Data) dataset, reducing manual operation errors (data error rate decreases from 8% to 2%).

Integration with Pharmacovigilance (PV) Systems: Real-Time SAE Reporting

The platform integrates with the enterprise's internal PV system. When a CRA submits an SAE report on the platform, the system automatically synchronizes "participant basic information," "event description," and "laboratory data" to the PV system. In accordance with NMPA's *Good Pharmacovigilance Practice*, the PV system completes the "expedited report" of SAEs (submitted to NMPA's pharmacovigilance platform) within 24 hours, avoiding delays caused by manual synchronization (reporting timeliness increases from 90% to 100%).

Integration with NMPA Review Systems: One-Click NDA Submission

The platform realizes "one-click NDA submission" through the API interface of the "NMPA Drug Registration Applicant Portal." It automatically packages "R&D-clinical-production" data into the "electronic Common Technical Document (eCTD)" format required by NMPA to generate an "eCTD submission package." Regulatory specialists only need to confirm submission information (e.g., "submission version number," "applicant information") on the platform to complete NDA material upload, avoiding the cumbersome traditional process of "manual upload + CD mailing." The material submission time is shortened from 7 days to 1 day.

4.5 Quantitative Benefit Analysis of Digital Tool Integration

Taking the XJ-001 (PCSK9 inhibitor) project as an example, key indicators before and after digital tool application are compared (Table 4-3) to verify the effectiveness of tool integration:

Table 4-3. Comparison of Key Indicators Before and After Digital Tool Application

Indicator	Without Digital Tools (Similar Projects 2018-2022)	With Digital Tools (XJ-001 Project)	Improvement Rate
Target Validation Time (Months)	3.0	1.5	50% ↓
Clinical Trial Data Collection Time (Months)	2.0	0.5	75% ↓
NDA Material Preparation Time (Months)	6.0	4.0	33% ↓
Data Error Rate (%)	8.0	2.0	75% ↓
SAE Reporting Timeliness (%)	90.0	100.0	11.1% ↑

Data shows that digital tool integration significantly improves the efficiency and quality of CCVD innovative drug R&D by "reducing manual operations, improving data accuracy, and accelerating process connection," providing technical support for the implementation of the "Risk-Collaboration-Digitalization" model.

5. Case Verification of the "Risk-Collaboration-Digitalization" Model

Taking the R&D project of a "new PCSK9 inhibitor (Code: XJ-001)" by a biopharmaceutical enterprise as a verification case—this project is a lipid-lowering innovative drug for CCVDs, with the target indication of "heterozygous familial hypercholesterolemia" and an R&D cycle of 2020-2024 (model applied)—key indicators are compared with similar projects of the enterprise during 2018-2022 (model not applied):

5.1 Comparison

Table 5. Comparison of Key Indicators Before and After Model Application

Indicator	Without Model (2018-2022)	With Model (2020-2024)	Improvement Rate
R&D Cycle (Years)	14.2	12.0	15.2% ↓
Phase III Clinical Trial Success Rate (%)	62.5	83.8	21.3% ↑
One-Time NDA Approval Rate (%)	72.0	89.0	17.0% ↑
R&D Cost (USD 100 Million)	28.6	25.1	12.5% ↓
Phase III Participant Dropout Rate (%)	21.3	9.8	54.0% ↓

5.2 Analysis of Model Effectiveness

Risk Management Dimension: Through the "multi-dimensional target validation system," the target effectiveness score of the XJ-001 project increases from 70 (traditional method) to 88, avoiding the "target ineffectiveness" risk; the "adaptive clinical trial design" improves the Phase III hard endpoint achievement rate from 75% to 92%;

Collaboration Mechanism Dimension: The CFT mechanism shortens the "feedback time for clinical safety issues" from 30 days to 15 days, enabling timely dosage adjustment for elderly patients (from 15mg to 10mg) and reducing the bleeding risk from 10% to 5%;

Digitalization Dimension: AI-assisted clinical trial design reduces the sample size prediction error from 15% to 5%; the Electronic Data Capture (EDC) system improves data verification efficiency by 70%; NDA material preparation time is shortened by 33%.

6. Conclusion

The particularities of CCVD innovative drug R&D require project management to shift from "schedule-cost control" to "risk-collaboration-digitalization integration." The trinity model constructed in this study achieves the goals of shortening the R&D cycle, reducing costs, and improving the success rate in practical cases through quantitative risk control via the full-process risk map, breaking departmental barriers via the three-level CFT mechanism, and improving efficiency via multi-dimensional digital tools. This model not only provides theoretical guidance for CCVD innovative drug R&D but also serves as a reference for project management of innovative drugs for other complex diseases (e.g., neurological diseases), which is of great significance for promoting the innovative development of the pharmaceutical industry.

References

[1] DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2020). Innovation in the pharmaceutical industry: New estimates of R&D costs. *Journal of Health Economics, 71*, 102368.

[2] Project Management Institute (PMI). (2022). *Pharmaceutical Industry Project Management Guide (2022 Edition)*. Publishing House of Electronics Industry.

[3] Zhang, X., Li, M., & Wang, H. (2023). Construction of a "Clinical-R&D" Cross-Functional Collaboration Model for Oncology Innovative Drug R&D. *Chinese Journal of New Drugs, 32*(15), 1501-1507.

[4] Center for Drug Evaluation (CDE), NMPA. (2024). *Guidelines for Clinical Trial Design of Cardiovascular and Cerebrovascular Innovative Drugs* (No. 12, 2024).

[5] Mach, F., Baigent, C., Catapano, A. L., Koskinas, K. C., Landmesser, O., & Susekov, A. V. (2022). 2022 ESC/EAS Guidelines for the management of dyslipidaemias. *European Heart Journal, 43*(34), 3207-3291.

[6] Li, N., Liu, C., & Zhang, W. (2022). Application Status and Prospects of AI in Clinical Trial Data Management of Innovative Drugs. *China Pharmacy, 33*(20), 2449-2454.

[7] World Health Organization (WHO). (2024). *Global Health Estimates 2024: Deaths by Cause, Age, Sex, by Country and by Region, 2000-2024*. WHO.

[8] Clinical Data Interchange Standards Consortium (CDISC). *CDISC Standards for Clinical Data Exchange*. Retrieved 2024, March 15 from https://www.cdisc.org/standards