

National Health Commission Capacity- Building and Continuing Education Center
Chronic Disease Management Research Project Application

Project Category: Research on Medication Application and Management

Project Code: 10042

Project Title: A Clinical Study of Liposomal Bupivacaine versus Ropivacaine Hydrochloride for
Analgesia Management after Hemorrhoidectomy

Applicant: Bai Yonggang

Applicant's Institution: Tongliao People's Hospital

Submission Date: April 4, 2026

Issued by National Health Commission Capacity- Building and Continuing Education Center
March 2026

Letter of Undertaking

I undertake to be responsible for the authenticity of all information filled in this application form and guarantee there exists no intellectual property dispute. If the project is approved for initiation, I undertake to treat this application form as a legally- binding project initiation agreement. I will abide by relevant regulations of the National Health Commission Capacity- Building and Continuing Education Center, conduct research strictly in accordance with the plan and achieve expected research outcomes. The National Health Commission Capacity- Building and Continuing Education Center shall have the right to use all data and materials contained in this application form. Should any false information be submitted or relevant regulations be violated, I shall bear full corresponding liabilities.

Project Principal (Signature): _____

April 4, 2026

Completion Instructions

1. The Chronic Disease Management Research Project Application Form (hereinafter referred to as the Application Form) shall be completed item- by- item with truthful information. All codes shall follow the Chronic Disease Management Research Project Application Guidelines (hereinafter referred to as the Application Guidelines) issued by the Center.
2. For "Project Category", fill in the application categories specified in the Application Guidelines (e.g. "Research on Comprehensive Chronic Disease Management"). "Project Code" shall be combined by the category and sub- category codes defined in the Application Guidelines. For example, if applying for "3 Research on the Whole- chain Standard System for Chronic Disease Management" under category "1001 Research on Comprehensive Chronic Disease Management", the project code shall be "10013". The "Project Title" shall be self- formulated subject to the Application Guidelines.

3. Inside bold-border boxes, fill in codes or letters; inside thin-border boxes, fill in Chinese characters or Arabic numerals. Where a bold-border box is followed by a thin-border box, both the code and corresponding Chinese name shall be filled: enter the code in the bold-border box and the Chinese name in the subsequent thin-border box. For multiple-choice items, directly input the selected code into the preceding bold-border box.

4. Instructions for selected fields:

1) Project Title: Accurately and concisely reflect research content; subtitles are generally not allowed, with a maximum length of 40 Chinese characters (including punctuation marks).

2) Keywords: Filled in according to research content, maximum of 3 keywords separated by spaces.

3) Work Unit: Full official name consistent with the institutional seal.

4) Affiliated System: Name of superior competent authority.

5) Mailing Address: Must include street name and house number; the institutional name cannot replace the mailing address. Postal code shall be provided.

6) Project Team Members: Only researchers who actually participate in this project. Exclude the project principal, scientific research management staff, financial staff, logistics service personnel and other non-research personnel.

7) Expected Outcomes: Forms of final deliverables; multiple selections allowed. For instance, fill in “A” for “Research Report”; fill in “B” and “C” for “Applied Outcomes” and “Invention Patent”. Word count shall be counted in thousands of Chinese characters.

8) Applied Funding: In ten-thousand-Yuan units, filled with Arabic numerals. The applied amount may refer to the Application Guidelines.

Item	Content
Project Title	A Clinical Study of Liposomal Bupivacaine versus Ropivacaine Hydrochloride for Analgesia Management after Hemorrhoidectomy
Keywords	Liposomal bupivacaine; hemorrhoidectomy; postoperative analgesia
Project Code	10042
Project Type	B (A: Startup Project; B: General Project; C: Key Project; D: Major Project)
Project Principal	Bai Yonggang
Gender:	Male
Ethnicity:	Mongolian
Date of Birth:	July 31, 1972
Administrative Position:	Administrative Position: Department Director
Professional Title:	Professional Title: Chief Physician
Research Specialty:	Post-operative analgesia research for surgical patients
Highest Education:	Bachelor's Degree
Highest Academic Degree:	Bachelor

Social Concurrent Positions:	<p>Standing Committee Member, Anesthesiology Branch of Inner Mongolia Physician Association</p> <p>Chairman, Anesthesiology Branch of Tongliao Medical Association</p> <p>Vice-Chairman, Anesthesiology Branch of Tongliao Physician Association</p> <p>Standing Committee Member, Anesthesiology Branch of Inner Mongolia Medical Association</p> <p>Standing Committee Member, Pain Medicine Branch of Inner Mongolia Medical Association</p> <p>Deputy Group Leader, Orthopedics Group, Anesthesiology Branch of Inner Mongolia Medical Association</p>
Province / Autonomous Region / Municipality	Inner Mongolia Autonomous Region
Affiliated System	Tongliao Municipal Health Commission
Work Unit	Tongliao People's Hospital
Contact Phone	13947528787
Mailing Address	No.668 Ke'erqin Street, Tongliao City, Inner Mongolia Autonomous Region
Postal Code	028000
Expected Outcomes	D (A. Research Report; B. Applied Outcomes; C. Invention Patent; D. Journal Publication; E. Others)
Word Count (thousand characters)	—
Applied Funding (10 000 CNY)	5
Planned Completion Time	1 year

Name	Date of Birth	Professional Title	Degree	Work Unit	Research Specialty	Signature
Sun Bo	Nov 1993	Attending Physician	Bachelor	Tongliao People's Hospital	Post-operative analgesia research for surgical patients	
Du Xueming	Dec 1974	Chief Physician	Master	Tongliao People's Hospital	Minimally invasive treatment of hemorrhoid diseases, surgical treatment of complex perianal	

					infectious diseases and outlet obstructive diseases	
Yang Muxi	Sep 1989	Attending Physician	Bachelor	Tongliao People's Hospital	Ultrasound- guided anesthesia	
Liu Zhiwei	Jul 1981	Chief Physician	Master	Tongliao People's Hospital	Post-operative analgesia research for surgical patients, cardiovascular anesthesia	
Zhang Xinyao	Jun 1992	Attending Physician	Bachelor	Tongliao People's Hospital	Treatment of perianal diseases	
Sun Liying	Jun 1975	Chief Nurse	—	Tongliao People's Hospital	Post- operative nursing for surgical patients	
Jia Xiyuan	Mar 1986	Associate Chief Nurse	—	Tongliao People's Hospital	Post- operative nursing for surgical patients	
Ma Tianjiao	Jul 1988	Supervisor Nurse	Master	Tongliao People's Hospital	Post- operative nursing for anorectal surgery patients	
Wang Xiaotian	Nov 1975	Chief Physician	Bachelor	Tongliao People's Hospital	Anesthetic agents and postoperative analgesia	
Jia Yanbing	Nov 1979	Associate Chief Physician	Master	Tongliao People's Hospital	Post- operative analgesia research for surgical patients, cardiovascular anesthesia	
Bao Mulan	Oct 1983	Associate Chief Physician	Bachelor	Tongliao People's Hospital	Post- operative analgesia research for surgical patients	
Li Mu	Jul 1987	Attending Physician	Bachelor	Tongliao People's Hospital	Post- operative analgesia research for surgical patients, cardiovascular	

					anesthesia	
Jiang Man	May 1990	Associate Chief Physician	Master	Tongliao People's Hospital	Anesthetic agents and postoperative analgesia	
Bai Miao	Sep 1993	Attending Physician	Bachelor	Tongliao People's Hospital	Anesthetic agents and postoperative analgesia	

Part II Project Design and Demonstration

1 Rationale for Project Selection

Local anesthetics (LA) feature relatively small molecular size, which enables easy absorption into blood and rapid clearance from the site of action. When performing peripheral nerve blocks, intermediate-acting local anesthetics such as bupivacaine and ropivacaine only provide 8-12 hours of analgesia. Therefore, prolonging the duration of action of local anesthetics has long been a key topic in regional anesthesia.

Epinephrine is the most commonly used adjuvant for short- and intermediate-acting local anesthetics¹. Several studies have shown that epinephrine can increase the duration of local anesthetic action by up to 200%. For instance, for lidocaine, epinephrine prolongs block duration from 1-2 hours to approximately 3-6 hours. Nevertheless, evidence supporting epinephrine's effect on prolonging local anesthetic action remains limited. Furthermore, via direct activation of α_1 -adrenergic receptors, epinephrine may induce cerebral vasoconstriction. Such neurotoxic risk is particularly prominent in patients with smoking history, hypertension or diabetes². Buprenorphine and dexamethasone are the two most potent adjuvants identified so far for prolonging block duration³. When combined with bupivacaine or ropivacaine, they extend peripheral nerve block duration to 18 hours and 22 hours respectively⁴.

Hemorrhoidectomy is a common anorectal surgical procedure associated with severe and prolonged postoperative pain, which seriously impairs patient rehabilitation and quality of life. Conventional analgesia mainly relies on opioids, accompanied by adverse effects including respiratory depression, nausea and vomiting⁵. Traditional local anesthetics such as ropivacaine hydrochloride have a short duration of action (approximately 8-12 hours), and cannot fully cover the whole postoperative pain period. Consequently, patients require rescue analgesia with opioids, bringing risks such as nausea, constipation and potential dependence. Long-acting analgesia may shorten hospital stay, reduce medical costs and improve patient satisfaction through faster functional recovery. Hence, it is of great clinical significance to explore safe long-acting local anesthetics that reduce opioid consumption.

Liposomal bupivacaine injection adopts the DepoFoam technology to sustain-release bupivacaine for up to 72 hours. It was approved by the FDA in 2011 for wound infiltration analgesia after hemorrhoidectomy⁶. Although liposomal bupivacaine has obtained marketing approval in China (2024), clinical data for its application in anorectal surgery remain scarce. Direct head-to-head evidence

comparing its efficacy, safety and recovery advantages versus ropivacaine in hemorrhoidectomy is still lacking. High-quality evidence needs to be generated to optimize analgesic regimens.

This study intends to observe the analgesic efficacy and postoperative adverse reactions of liposomal bupivacaine compared with ropivacaine hydrochloride in patients undergoing hemorrhoidectomy, so as to provide clinical evidence for the application of liposomal bupivacaine in anorectal surgery.

1.2 Benefit-Risk Assessment

1.2.1 Benefits

Subjects receive study medication for postoperative analgesia free of charge, with reduced risk of respiratory depression and lower incidence of adverse events such as nausea and vomiting.

1.2.2 Risks

Liposomal bupivacaine injection (trade name: Aihengping) used in this study is a marketed product approved by National Medical Products Administration. Relevant risks have been well-controlled and residual risks are acceptable. When administered following medication instructions, its safety profile is guaranteed. Overall, benefits outweigh risks.

2 Research Contents

2.1 Primary Objective

To investigate the postoperative analgesic effect of liposomal bupivacaine versus ropivacaine hydrochloride after hemorrhoidectomy.

2.1.2 Secondary Objectives

To observe the incidence of adverse events including nausea and vomiting, hemodynamic parameters such as heart rate, blood pressure and respiratory rate, NRS / VAS pain scores, rescue analgesia rate, total consumption of study drugs, QoR-15 score, patient satisfaction, time to first ambulation, time to first oral intake, time to first flatus and defecation, and length of hospital stay.

2.2 Study Endpoints / Evaluation Indicators

2.2.1 Primary Endpoint

Analgesic efficacy at 1 h, 2 h, 4 h, 6 h, 12 h, 24 h and 48 h after infiltration anesthesia.

Evaluation indicator: NRS pain scores at multiple time-points within 48 hours after infiltration anesthesia.

2.2.2 Secondary Endpoints

- 1) Incidence of adverse events including nausea and vomiting within 48 hours post-infiltration anesthesia;
- 2) Hemodynamic parameters including heart rate, blood pressure and respiratory rate within 48 hours post-infiltration anesthesia;

- 3) VAS pain scores within 48 hours post- infiltration anesthesia;
- 4) Rescue analgesia rate within 48 hours post- infiltration anesthesia;
- 5) Total opioid consumption within 48 hours post- infiltration anesthesia;
- 6) QoR- 15 score, patient satisfaction, time to first ambulation, time to first oral intake, time to first flatus and defecation, length of hospital stay, etc.

3 Study Population

Patients scheduled for hemorrhoidectomy in the department of anorectal surgery.

3.1 Inclusion Criteria

- 1) Age: 40-60 years old;
- 2) Scheduled to receive hemorrhoidectomy;
- 3) ASA physical status class I- III;
- 4) BMI: 18-30 kg/m².

3.2 Exclusion Criteria

- 1) Pre-existing acute or chronic pain before surgery;
- 2) Advanced malignant tumor with ascites or extensive metastasis, receiving systemic chemotherapy / radiotherapy, or requiring postoperative hyperthermic intraperitoneal perfusion;
- 3) Pregnancy, lactation or planned pregnancy;
- 4) Known allergy or contraindication to study anesthetics, adjuvant analgesics, rescue analgesics or anti- emetics, antibiotics;
- 5) Long- term opioid therapy, or any analgesic use within 48 hours before surgery;
- 6) Obstructive sleep apnea syndrome;
- 7) Psychiatric or neurological disorders, gastrointestinal obstruction, chronic obstructive pulmonary disease, cor pulmonale, cardiovascular diseases and other relevant comorbidities;
- 8) Systemic corticosteroids (oral, inhaled or parenteral) administered within 3 months prior to surgery.

3.3 Withdrawal Criteria

- 1) Insufficient postoperative consciousness, delirium or other conditions preventing subject cooperation with trial procedures;
- 2) Severe postoperative hemodynamic instability or respiratory insufficiency;
- 3) Other circumstances judged by investigators rendering continued trial participation inappropriate or impossible.

4 Treatment Allocation

Experimental group (Liposomal bupivacaine): For postoperative analgesia after hemorrhoidectomy. Dilute 266 mg (20 mL) liposomal bupivacaine with 10 mL normal saline to a total volume of 30 mL. Divide the solution equally into 6 portions, for infiltration injection at six evenly distributed wound sites clock-wise around the anal sphincter.

Control group (Ropivacaine hydrochloride): For postoperative analgesia after hemorrhoidectomy. Dilute 200 mg (20 mL) ropivacaine hydrochloride with 10 mL normal saline to a total volume of 30 mL. Divide the solution equally into 6 portions, for infiltration injection at six evenly distributed wound sites clock-wise around the anal sphincter.

5.1 Randomization

Random number table method: This clinical trial adopts random number table. Investigators assign subjects to corresponding groups according to random allocation results.

5.2 Blinding and Unblinding

5.2.1 Blinding

- 1) Study personnel not participating in drug administration or clinical observation dilute study drugs with normal saline and deliver prepared syringes to investigators for administration.
- 2) Liposomal bupivacaine appears opaque milky- white while ropivacaine solution is colourless. All syringes for infiltration injection are wrapped with aluminium foil to ensure identical visual appearance for both groups.
- 3) Subjects, administering clinicians and outcome assessors remain blinded to group assignment.

5.2.2 Emergency Unblinding

Emergency unblinding shall be performed in rescue scenarios such as serious adverse event (SAE) with unclear causality to study drug, or severe drug- drug interaction that compromises rescue decision- making. After unblinding, document exact time, reason and operator of emergency unblinding, and notify the monitor as soon as possible. Once unblinded in advance, the subject shall discontinue trial participation, and relevant data shall be excluded from efficacy analysis. Corresponding medical care and subject protection shall be implemented.

6 Study Procedures

6.1 Treatment Period

6.1.1 Screening

Screen subjects according to inclusion and exclusion criteria.

6.1.2 Informed Consent

Fully inform eligible subjects and obtain written informed consent.

6.1.3 Pre-operative Examination and Eligibility Confirmation

Confirm inclusion/exclusion criteria by preoperative tests and record baseline characteristics: age, gender, height, weight, BMI, ethnicity, allergy history, smoking history, ASA classification, vital signs, etc.

6.1.4 Anesthesia and Surgery

- 1) Connect monitoring devices before anesthesia. Spinal subarachnoid block is adopted (Turen disposable anesthesia puncture kit model AS- SII).
- 2) Spinal puncture is performed by an experienced anesthesiologist; ultrasound guidance may be applied as needed. Prior to lumbar puncture, 2-3 mL 2% lidocaine is used for local skin infiltration. Puncture site is L3-4. After cerebrospinal fluid reflux is confirmed and no blood is aspirated, inject 3 mL 0.5% ropivacaine hydrochloride.
- 3) Upon completion of surgery, subjects receive allocated study- drug infiltration administered by the same anesthesiologist using six 5- mL syringes according to random envelopes to maintain blinding.
- 4) Record immediate complications (intravascular injection, paresthesia, etc.). All patients receive non- general anesthesia. If patients still report pain upon surgical forceps clamping before skin incision, block failure is considered. Such patients will receive conversion to general anesthesia and will not be enrolled for data collection.

6.1.5 Enrollment

Assess postoperative pain intensity using NRS within 48 hours after surgery.

NRS grading standard:

0 point: no pain;

1-3 points: mild pain;

4-6 points: moderate pain;

7-10 points: severe pain.

Subjects are assigned via random envelopes and enter subsequent observation and data collection procedures.

6.1.6 Treatment and Observation

Subjects are monitored with ECG and respiratory monitors for cardiac and respiratory surveillance.

Administer study medication and conduct scheduled assessments according to group assignment.

Assessment time- points: 1 h, 2 h, 4 h, 6 h, 12 h, 24 h and 48 h after infiltration anesthesia.

6.1.7 Post- operative Care

Within 48 hours post- surgery, patients shall receive liquid or soft diet and avoid irritating food.

Dressings are changed regularly to maintain perianal wound clean and dry.

6.2 Investigational Products and Monitoring Equipment

Drugs: Liposomal bupivacaine injection; Ropivacaine hydrochloride injection.

Monitor: Mindray BeneView T5 patient monitor.

6.3 Drug Administration and Dose Adjustment

Experimental group: Dilute 266 mg liposomal bupivacaine (20 mL) with 10 mL normal saline to total volume 30 mL, divided equally for six- site perianal wound infiltration.

Control group: Dilute 200 mg ropivacaine hydrochloride (20 mL) with 10 mL normal saline to total volume 30 mL, divided equally for six- site perianal wound infiltration.

Rescue analgesia: When NRS score persists ≥ 4 despite study medication, parecoxib sodium can be administered intravenously 20-40 mg every 6-12 hours; maximum daily dose shall not exceed 80 mg within 24 hours.

6.4 Concomitant Therapy and Follow-up Visits

(Content as per original document, to be supplemented in actual implementation)

6.5 Subject Adherence and Drop-out

Definition of drop-out: Any subject who has signed informed consent, passed screening and been randomized, yet fails to complete the observation period specified in the protocol for any reason.

1) Investigator-initiated withdrawal

- ① Occurrence of adverse events judged by investigators to warrant trial discontinuation.
- ② New complications or special physiological changes during trial rendering continued study participation inappropriate.
- ③ Poor subject compliance.

2) Subject-initiated withdrawal

- ① Subject voluntarily requests trial termination for any reason.
- ② Loss to follow-up without explicit withdrawal request.

3) Management of drop-out cases

- ① Try best to contact drop-out subjects, document withdrawal reasons and the last study-drug administration time; complete feasible evaluation items.
- ② For drop-out due to adverse events, provide appropriate medical interventions.

7 Evaluation

7.1 Efficacy Evaluation

7.1.1 Post-operative analgesic efficacy within 48 hours after infiltration anesthesia

Evaluate analgesic effect at time-points: 1 h, 2 h, 4 h, 6 h, 12 h, 24 h, 48 h after infiltration anesthesia.

Indicator: NRS pain scores within 48 hours post-infiltration anesthesia.

7.2 Safety Evaluation

- 1) Incidence of respiratory depression (defined as respiratory rate ≤ 8 breaths/min or $SpO_2 < 90\%$), nausea, vomiting and other adverse events within 48 hours after infiltration anesthesia;
- 2) Hemodynamic parameters including heart rate and blood pressure within 48 hours after infiltration anesthesia;
- 3) Ramsay sedation scale within 48 hours after infiltration anesthesia;
- 4) Rescue analgesia rate within 48 hours after infiltration anesthesia;
- 5) Total consumption of parecoxib sodium within 48 hours after infiltration anesthesia;

6) QoR- 15 score, patient satisfaction, time to first ambulation, time to first oral intake, time to first flatus and defecation, length of hospital stay, etc.

7.2.1 Baseline Signs and Symptoms

NRS pain scores are recorded as baseline after surgery; post- dose signs and symptoms are compared against baseline.

7.2.2 Physical Examination and Vital Signs

Baseline vital signs and physical examination are obtained upon subject enrolment; post- treatment findings are compared versus baseline within 48 h post- surgery.

8 Adverse Event Reporting

8.1 Definition of Adverse Events

8.1.1 Definitions

1) Adverse Event (AE): Any untoward medical occurrence after study- drug administration, manifested as signs, symptoms, disease or laboratory abnormality, which is not necessarily causally related to investigational product.

2) Serious Adverse Event (SAE): Untoward medical occurrence resulting in death, life- threatening condition, persistent or significant disability / incapacity, requiring inpatient hospitalization or prolongation of existing hospitalization, or congenital anomaly / birth defect.

8.1.2 Severity Grading

- Mild: Tolerable by subject; no special intervention required; no impact on recovery.
- Moderate: Hard to tolerate; specific treatment required; direct influence on subject recovery.
- Severe: Life- threatening, fatal or disabling; immediate emergency intervention is mandatory.

8.2 AE Documentation and Reporting

All adverse events (including significant adverse events) shall be fully documented in source medical records: onset time, clinical manifestations, management, duration, outcome and causal relationship assessment. For abnormal laboratory findings, follow- up shall be performed until indexes return to baseline or causality to study drug is ruled out. For SAE, complete SAE report form and notify the clinical research center within 24 hours.

Adverse events to be collected include nausea, vomiting, abdominal distension, diarrhea, constipation, abdominal pain, fever, dizziness, headache, somnolence, pruritus, etc.

8.3 Risk Prevention and Management

Risk assessment confirms that risks associated with the dosage of liposomal bupivacaine adopted in this trial are well- controlled.

Emergency medicines, mechanical ventilation equipment and resuscitation devices shall be readily available on- site to cope with residual potential risks.

9 Statistical Analysis

9.1 Sample Size Estimation

Since there are limited published references, sample size is estimated based on preliminary pilot study results. Eighty subjects are planned for each group. Primary endpoint is treatment response rate at 1 h post-loading dose.

Type-I error $\alpha = 0.05$, statistical power $(1 - \beta) = 90\%$. Total sample size is calculated accordingly.

9.2 Analysis Sets

9.2.1 Full- Analysis Set (FAS)

Based on intention- to- treat principle: all randomized subjects receiving at least one dose of study drug are included in FAS. FAS serves as primary dataset for baseline description and efficacy analysis.

9.2.2 Per-Protocol Set (PPS)

Subjects from FAS without major protocol violations, with good compliance and complete primary endpoint data. PPS is another key dataset for efficacy evaluation.

9.2.3 Safety Set (SS)

All subjects receiving at least one dose of study medication. SS is used exclusively for safety analyses.

9.3 Efficacy Analysis and Statistical Methods

9.3.1 Primary Endpoint Analysis

NRS pain scores across multiple time- points within 48 hours post- loading dose are analysed for inter- group differences.

9.3.2 Secondary Endpoint Analysis

Analyze secondary indicators listed in section 2.2.2, including adverse- event incidence, hemodynamic parameters, Ramsay sedation score, rescue analgesia rate, total parecoxib consumption, QoR- 15 score, patient- reported outcomes and recovery- related time indicators.

9.4 Safety Analysis

Safety analyses are performed on Safety Set (SS). All adverse events for enrolled subjects shall be analysed without omission. Characterize each adverse event: manifestation, severity and causality assessment with investigational product. Calculate and compare AE incidence related to study drugs between groups.

9.5 Interim Analysis

No interim analysis will be performed. Statistical analyses will be executed only after data collection, data cleaning and database lock. No stopping rule for statistical efficacy will be applied.

9.6 Data Monitoring Committee

No interim analysis; no Data Monitoring Committee will be established.

10 Data Collection and Management

10.1 Case Report Form / Electronic Data Capture

Plans for outcome indicator collection, baseline and other trial data are strictly implemented to guarantee reliability and accuracy of data entry tools.

10.2 Data Management

10.2.1 Study Implementation and Monitoring

Monitors assigned by the project principal will conduct periodic on-site monitoring visits to ensure strict protocol adherence and correct documentation. Investigators shall fill in Case Report Forms (CRF) truthfully, completely and carefully. All trial observations shall be cross-verified against source documents to guarantee data reliability and traceability of conclusions. Corresponding data management measures will be applied throughout trial conduct and data processing.

10.2.2 Document Preservation

Investigators shall properly maintain trial documents: subject confirmation records, signed informed consent forms, all CRFs, investigational drug dispensing records, etc. Upon trial completion, all clinical research documents shall be archived by institutional clinical research office.

10.2.3 Data Entry and Revision

Dual independent data entry and cross-validation by two data managers are implemented to ensure accuracy. For queries identified from CRFs, data managers will issue data query forms. Monitors will communicate with investigators for clarification. Investigators shall reply promptly. Data managers will modify and confirm database records according to investigator responses, and re-issue queries if necessary.

10.2.4 Data Validation

Validation includes programmed edit checks and manual review. Discrepant data are resolved; discrepancy reports are submitted for investigator confirmation before data modification.

10.2.5 Database Lock

Upon trial completion, investigators, sponsor and data management team jointly review dataset. After confirmation of data integrity, database will be locked. Locked dataset will be exported for statistical analysis.

11 Ethical Considerations

11.1 Ethics Committee Review

The trial protocol, written informed consent form and other subject-related documents must obtain written approval from Institutional Review Board / Ethics Committee before study initiation. Investigators shall submit annual progress reports to ethics committee as applicable. Written notification shall be submitted upon study completion or early termination. All protocol amendments shall be reported to ethics committee and shall not be implemented before approval, except changes aiming to eliminate imminent direct risks to subjects, for which ethics committee shall be notified afterwards.

11.2 Informed Consent

Investigators shall provide ethics-approved, easy-to-understand informed consent documents to subjects or legal representatives. Sufficient time shall be granted for subject consideration. No subject can be enrolled prior to obtaining signed written informed consent. Updated versions of informed consent shall be provided for ongoing participants. Informed consent forms shall be archived as key trial documents.

12 Confidentiality

In adverse-event reports and other trial documents, subject identities will be de-identified. Subject medical record numbers serve as unique study identifiers to ensure data traceability.

Study results may be published in medical journals. Individual patient information will be kept confidential in compliance with legal requirements and will not be disclosed unless compelled by law. Authorized representatives from regulatory authorities and institutional ethics committees may access source records according to regulations.

13 References

1. Graf, B.M., Abraham, I., Eberbach, N., & Martin, E. (2002). Prolongation of lidocaine-induced epidural anesthesia by epinephrine: A dose-response study. *Anesthesia & Analgesia*, 95(3), 734- 738.
2. Williams, B.A., et al. (2019). Adjuncts to local anesthetics: Current concepts and controversies. *Regional Anesthesia & Pain Medicine*, 44(8), 778- 785.
3. Kumar, K., Singh, S.I., & Nehra, A. (2015). Comparative evaluation of buprenorphine and dexamethasone as adjuvants to ropivacaine in supraclavicular brachial plexus block. *Journal of Clinical Anesthesia*, 27(3), 237- 242.
4. Huynh, T.M., et al. (2020). Dexamethasone and buprenorphine as adjuvants to ropivacaine in prolonged peripheral nerve blocks: A randomized controlled trial. *Anesthesiology*, 133(5), 1022- 1033.
5. Joshi, G.P., & Schug, S.A. (2016). Pain management after ambulatory surgery—Where's the disconnect? *Canadian Journal of Anesthesia*, 63(6), 707- 713.
6. FDA. (2011). FDA approves Exparel (bupivacaine liposome injectable suspension) for postsurgical pain management. U.S. Food and Drug Administration.
7. Rui P. Sample size estimation for randomized controlled clinical trials. *Shanghai Pharmaceutical Journal*, 2023, 44(01):48- 52.

Part III Research Foundation and Condition Guarantee

1. Academic Resume of Project Principal

Bai Yonggang, Chief Physician, Director of Department of Anesthesiology, West Campus of Tongliao People's Hospital. He holds multiple academic positions: Standing Committee Member of Anesthesiology Branch of Inner Mongolia Physician Association; Chairman of Anesthesiology Branch of Tongliao Medical Association; Vice- Chairman of Anesthesiology Branch of Tongliao Physician Association; Standing Committee Member of Anesthesiology Branch of Inner Mongolia Medical Association; Standing Committee Member of Pain Medicine Branch of Inner Mongolia Medical Association; Deputy Group Leader of Orthopedics Group, Anesthesiology Branch of Inner Mongolia Medical Association. He won the Second-Class Prize of Tongliao Science and Technology Progress Award in 2016.

He graduated from Inner Mongolia Medical College (now Inner Mongolia Medical University) in 1994 and received further training in anesthesiology at Peking University Third Hospital.

He is expert in clinical anesthesia for diverse surgical procedures, critical-care resuscitation, peri-operative management, painless examinations and pain therapy. With 30-year clinical experience in anesthesiology and department administration, he has participated in numerous rescue missions for critically- ill patients and technical innovation work.

2. Research Foundation

(To be supplemented with preliminary research achievements relevant to this project; irrelevant publications shall not be included; list collaborators with author sequence.)

3. Previously Undertaken Projects

(To be supplemented)

4. Relationship with Ongoing Completed Projects

(To be supplemented)

5. Condition Guarantee

The Department of Anesthesiology, West Campus of Tongliao People's Hospital, founded in 2010, is a key clinical department integrating medical service, teaching and research, and is accredited as Tongliao Municipal Key Specialty. Annual surgical volume reaches approximately 7 000 cases, delivering standardized and specialized clinical services.

① Talent Team

The department has 33 medical and nursing staff, including 6 chief physicians, 7 associate chief physicians, 15 attending physicians and 3 masters of medicine, forming a well- structured talent echelon combining senior, middle- aged and young professionals. The discipline lead, Director Bai Yonggang, is a distinguished expert in anesthesiology with multiple provincial- level academic appointments mentioned above.

② Clinical Scope of Service

1. Clinical anesthesia: General anesthesia, spinal anesthesia, nerve block anesthesia, ultrasound- guided precise anesthesia, covering surgical needs of general surgery, orthopedics, obstetrics and gynecology, neurosurgery, anorectal surgery, hand- foot microsurgery, burn surgery, minimally invasive laparoscopic surgery and other disciplines.
2. Comfort care: Painless gastroscopy and colonoscopy, painless abortion, labor analgesia, painless joint rehabilitation and other patient- friendly services.
3. Emergency resuscitation: Participate in critical- patient rescue and peri- operative life- support for both West and North Campus.

③ Equipment and Technical Advantages

The department is equipped with state- of- the- art anesthesia machines, multi- parameter patient monitors, video laryngoscopes, flexible fiberoptic bronchoscopes, ultrasound scanners, target- controlled infusion pumps, nerve stimulators, cardiac output monitoring systems and other devices to guarantee anesthesia safety and quality.

Advanced technologies implemented include ultrasound- guided visualization anesthesia, hemodynamic monitoring (FloTrac, PICCO), BIS (bispectral index) monitoring for individualized anesthesia. Enhanced Recovery After Surgery (ERAS) protocols are jointly optimized with surgical departments to shorten rehabilitation cycle. Multimodal analgesia combining pharmacotherapy and nerve- block techniques is applied to alleviate postoperative pain and improve patient comfort. Ultrasound- guided anesthesia and comfort- oriented medical services have reached advanced provincial level.

Part IV Budget Estimation

Category	No.	Budget Item	Amount (10 000 CNY)
Direct Costs	1	Literature & Document Fee	1
	2	Data Collection Fee	0
	3	Conference & Travel Fee	1.5
	4	Equipment Purchase Fee	0
	5	Expert Consultation Fee	0
	6	Labor Service Fee	0
	7	Publication & Printing Fee	1
	8	Other Expenses	—
Indirect Costs		Indirect Cost	1.5

Total			5
Applied Funding			5
Self-raised Funding			—

—

Annual Budget Plan

Year Amount (10 000 CNY)

2026 5

2027 0

Part V Review Opinion of Applicant's Institution

The information filled in this application is true and accurate. The project principal and team members possess adequate professional competence to undertake this research project. Our institution can provide sufficient time, working conditions and supporting resources required for project completion. Our institution agrees to undertake project administration and reputation guarantee for this study. This research project has passed ethical review of institutional Ethics Committee.

Seal of Scientific Research Administration / Institutional Official Seal

June 2, 2026