A Multicenter, Randomized, Blind Endpoint and Positive Drug Controlled Phase III Study of Recombinant Human Tissue-type Plasminogen Activator Derivative for Injection in the Treatment of Patients with Acute Ischemic Stroke

Independent Data Monitoring Board（IDMC）Statutes

Organization：	Beijing Tiantan Hospital of Capital Medical University
Principal Investigator of the Group Leader Unit：	Wang Congjun
Applicant：	China Resources Biopharmaceutical Co
Contact person/contact number of the sponsor：	Yongbiao Xu /19963540319
Program No.：	CRAD-001-03
Charter version number/version date：	1.0/January 20, 2022

Confidentiality statement

The ownership of all information contained in this program belongs to China Resources Biopharmaceutical Co. Therefore, it is only provided for review by the relevant healthcare organizations such as the trial sponsor, co-experimenters, ethics committees and supervisory and regulatory authorities. Without the written approval of the sponsor, it is strictly prohibited to communicate any information to third parties not related to this trial.

IDMC Charter Approval Page

This IDMC charter will be used to guide the IDMC operation and oversight of core safety for the clinical study "Multicenter, Randomized, Blind Endpoint and Positive Drug Controlled Phase III Study of Recombinant Human Tissue-Type Plasminogen Activator Derivative for Injection in the Treatment of Patients with Acute Ischemic Stroke" (Protocol No. CRAD-001-03), which was initiated by China Resources Ontario BioPharmaceuticals, Ltd. and will give advice on the trial's giving advice on issues such as whether to continue and/or whether protocol revisions are needed. Changes to any of the processes in the charter will require revision of this manual and re-approval.

As the sponsor's representative, I have reviewed this IDMC charter (v1.0/January 20, 2022) and have given my approval to.

Applicant：China Resources Biopharmaceutical Co

Signature of authorized representative：_____

Date：_____DD _____ MM _____YY

IDMC Membership declaration and signature page

This IDMC charter will be used to guide the IDMC operation and oversight of core safety for the clinical study "A Multicenter, Randomized, Blind Endpoint and Positive Drug Controlled Phase III Study of Recombinant Human Tissue-type Plasminogen Activator Derivative for Injection in the Treatment of Patients with Acute Ischemic Stroke" (Protocol No. CRAD-001-03), which was initiated by China Resources BioPharmaceuticals, Ltd. and will give advice on the trial's giving advice on issues such as whether to continue and/or whether protocol revisions are needed. Changes to any of the processes in the charter will require revision of this manual and re-approval.

As a member of the IDMC, I understand the responsibilities of my role and I have no conflict of interest with the study. I am committed to maintaining the confidentiality of information about subjects and related matters. I have been informed that I will be held liable for any resulting legal responsibility if I break my promise. I have reviewed this IDMC Charter (V1.0/2022/01/20) and given my approval.

IDMC Member's unit：_____

IDMC Name of member (in block letters)：_____

IDMC Signature of member：_____

Date：_____DD _____ MM _____YY

Note: Due to the different geographic locations of IDMC members, each IDMC member may sign this page individually.

Catalogues

Version number/version date: V1.0/2022 January 20

Abbreviations

Abridge	English Interpretation	Chinese Interpretation
AE	Adverse Event	不良事件
CSR	Clinical Study Report	临床研究报告
DM	Data Manager	数据管理经理
IDMC	Independent Data Monitoring Committee	独立数据监查委员会
IRC	Independent Review Committee	独立终点审核委员会
IB	Investigator’s Brochure	研究者手册
SAE	Serious Adverse Event	严重不良事件
SAP	Statistical Analysis Plan	统计分析计划
SAS	Statistical Analysis System	统计分析系统
SSG	Statistical Support Group	统计支持小组

1 Introduction to the charter of the Independent Data Monitoring Board

This document will provide the Independent Data Monitoring Plan for the multicenter, randomized, blinded, positive drug-controlled, phase III clinical study of recombinant human tissue-type Plasminogen activator derivative for injection in patients with acute ischemic stroke conducted by China Resources Biopharmaceutical Co. This charter will detail the purpose and responsibilities of the Independent Data Monitoring Committee (IDMC), and will define the membership and qualifications of the IDMC, and meeting times. This charter will also outline the IDMC's procedures for obtaining data, ensuring confidentiality, and the initial communication plan, IDMC minutes/reports, and statistical analysis plan to be provided to the IDMC for implementation.

2 Purpose and design of the study

2.1 research purpose

2.1.1 primary purpose

Evaluation of the Efficacy of Injectable Recombinant Human Tissue-Type Plasminogen Activator Derivative Versus Alteplase in the Treatment of Acute Ischemic Stroke Within 4.5 Hours of Attack.

2.1.2 secondary purpose

To evaluate the safety of injectable recombinant human tissue-type plasminogen activator derivative versus alteplase in the treatment of acute ischemic stroke within 4.5 hours of onset.

2.2 main design of the study

This study is a multicenter, randomized, blinded, outcome-assessed, positive drug-parallel controlled, phase III study of recombinant human tissue-type plasminogen activator derivative for injection (hereinafter referred to as "Ritonril") compared with alteplase for the treatment of acute ischemic stroke (AIS) within 4.5 h of onset of symptoms. The primary objective of this phase III study is to evaluate the efficacy of the trial drug based on the mRS scale at 90 days post-treatment.

The study was planned to enroll 1412 patients with AIS within 4.5 h of seizure, and the screened subjects were randomly assigned to the test drug and control drug alteplase groups in a 1:1 ratio. After receiving thrombolytic drug treatment, the subjects were required to undergo a series of safety and efficacy checks. mRS score and Barthel Index score visits were conducted 90 days (±7 days) after thrombolysis, and the subjects could be discharged from the group at the end of the visits.

In this study, independent blinded endpoint evaluators were set up in each study center to assess the mRS scale and Barthel Index score at 30 and 90 days after thrombolysis in a blinded manner.

3 IDMC purpose

An Independent Data Monitoring Committee (IDMC) will be set up for this study, and the IDMC will be responsible for the safety assessment of the cumulative data from the ongoing clinical trial to ensure the safety of the subjects.

During the course of the trial, IDMC meetings will be held when no more than 18 symptomatic intracranial hemorrhages (ECASS III criteria) occur in no more than 600 subjects, for a total of 42 symptomatic intracranial hemorrhages (ECASS III criteria)).

4 Membership and Duties

4.1 IDMC membership and duties

4.1.1 IDMC composition

The IDMC will be composed of experts in the field of stroke thrombolysis research, including 2 clinicians, 1 biostatistician with medical experience in thrombolytic therapy for acute ischemic stroke or experience in the statistical analysis of clinical trial data, and IDMC members, including the chairperson and the members of the IDMC, see the IDMC Related Personnel List document for more specific information (Attachment 1).

All members are prohibited from serving on or acting as consultants to the project team for this clinical study and will maintain only necessary contact with the sponsor.The IDMC, as the expert advisory panel for this clinical study, is responsible for determining its own operating procedures, including reviewing and approving the IDMC charter, and will conduct itself in accordance with the IDMC charter as approved by it.

The IDMC may request that experts from other specialties attend IDMC meetings as consultants to obtain information about unanticipated events or problems. To avoid possible conflicts of interest, these expert consultants must sign a confidentiality agreement and cannot have a conflict of interest situation as mentioned in 4.1.3. Consultants are not members of the IDMC and do not have voting rights in IDMC meetings.

IDMC membership will routinely continue until the end of the study, with the sponsor arranging for replacements in the event of early departure.

4.1.2 main responsibilities of IDMC

1）Member of the Independent Data Monitoring Board

Each member is responsible for maintaining the strict confidentiality of the study data.IDMC members will not share any of the study information with any individual outside of the IDMC.IDMC members may contact the SSG (Statistical Support Group) statistician directly for operational details related to the analysis and summarization of the data.All correspondence between IDMC members and the SSG statistician should be cc'd to the IDMC Chair.

Each member is required to confirm that he/she has no intellectual property or financial conflicts of interest with the study prior to confirming membership in the IDMC and to notify the IDMC Chair if changes occur during the course of the trial. In such cases, IDMC minutes must document the disclosure of the potential conflict of interest and the outcome of the discussion, e.g., making an IDMC member substitution.

IDMC members will perform the following key functions：

1) Agree and approve the IDMC Bylaws and any subsequent revisions.
2) IDMC members will review and provide recommendations regarding trial progress, demographic data and baseline characteristics, protocol violations, and safety data.
3) IDMC members shall review individual events deemed significant by the study

clinicians in a timely manner.

4) It is the responsibility of the IDMC member to alert the sponsor to any safety concerns. In addition, it is the responsibility of the IDMC to advise the sponsor regarding the conduct of the study.
5) IDMC members have the right to vote at IDMC meetings.
6) IDMC members will review meeting minutes and recommendations specific to the conduct of this clinical trial.

2）Chairman of the Independent Data Monitoring Board

In addition to the above IDMC member responsibilities, the IDMC Chairperson has the following responsibilities：

1) Develop meeting agendas with the SSG Statistician and/or other members of the SSG.
2) Leads and directs discussions at IDMC meetings.
3) Informs IDMC members of the completion of their responsibilities.
4) Collects feedback from IDMC members.
5) Seek consensus from IDMC members.
6) Ensure that the SSG statistician provides the information needed by the IDMC members.
7) Act as a liaison between the IDMC and the sponsor and report safety issues and recommendations to the sponsor.
8) Sign IDMC minutes and IDMC meeting reports summarizing the conclusions and recommendations of each IDMC meeting.
9) Ensure that IDMC recommendations are provided to the sponsor within 7 business days of each meeting.
10) Notify the sponsor of the need for additional IDMC meetings and set meeting schedules, recommend meeting times and data review specifications.

4.1.3 Financial disclosure and conflicts of interest

IDMC members shall disclose financial participation in products under development and DMC services for identical, related or competing products. Each IDMC member shall evaluate its own potential conflicts of interest. Any change in an IDMC member's interest or consultant relationship with a similar product pharmaceutical company, biotechnology company, or contract research organization should be reported to the IDMC Chair and sponsor.

IDMC meeting minutes should document potential conflicts of interest and the outcome of discussions (e.g., removal of member voting rights, recusal from discussions, etc.). Inquire at the beginning of each IDMC meeting if there has been a change in IDMC member interests Any potential conflict of interest involving an IDMC member after the IDMC has become officially operational should be immediately disclosed to the IDMC and the sponsor so that appropriate action can be taken, including withdrawal, replacement, and co-option of IDMC members, etc.

4.2 Membership and responsibilities of the Statistical Support Group (SSG)

4.2.1 SSG composition

A Statistical Support Group (SSG), independent of the sponsor, will support the IDMC. an

SSG usually consists of at least one statistician (SSG statistician) and one or more programmers. specific information on SSG members can be found in the document on the list of persons involved in the IDMC (annex 1).

4.2.2 SSG responsibility

Responsibilities of the Statistical Support Group：

1) Write the IDMC Statistical Analysis Plan (IDMC SAP) and ensure that the DMC SAP is reviewed and agreed upon by the research team and IDMC members.
2) Provide statistical analysis results to IDMC for review.
3) Ensure that appropriate documentation/data packages are prepared and sent to IDMC members according to the established schedule and obtain confirmation of receipt of documentation/data packages by IDMC members.
4) Review and validate documents obtained from IDMC (e.g. meeting minutes).
5) File data packets, meeting minutes, and needs assessment information required for IDMC execution in secure files. According to the sponsor's specifications, this archived document must be sent to the study team after the database for the Clinical Summary Report (CSR) is locked. Before sending the document to the study team, ensure that the electronic document is readable/usable. Upon receipt of the archived document, the study team must confirm that all appropriate documents have been returned and that all electronic documents are readable/usable.
6) Serve as a liaison between IDMC members and sponsors when additional information is required.
7) Other additional administrative responsibilities (if required).

4.3 Contact Person and Sponsor Responsibilities

4.3.1 Contact Person

PM Shimadi will act as a liaison between IDMC and the bidder. See the IDMC List of Relevant Persons document (Annex 1) for specific information. Responsibilities of the Contact Person for the Sponsor：

1) Send the IDMC proposal and related meeting information to the sponsor.

2) Delivering or communicating information to IDMC from sponsors.

3) Coordinate IDMC's work schedule with the Data Management and Statistical Analysis Departments.

4.3.2 Responsibilities of sponsors

The sponsor communicates IDMC recommendations internally and determines appropriate actions based on IDMC recommendations. In addition, the sponsor is responsible for：

1) Selection & Appointment of DMC Chair and Members

2) Agree to and approve the IDMC Bylaws.

3) Provide the IDMC with the resources necessary to fulfill assigned functions.

4) Communicate IDMC recommendations to researchers or interested persons and notify regulatory authorities as well as other agencies as necessary.

5) Cover IDMC member lodging, travel, and meeting expenses.

5 Organization chart

IDMCRelationships with other committees and functional organizations involved in the experiment are detailed in the figure below.：

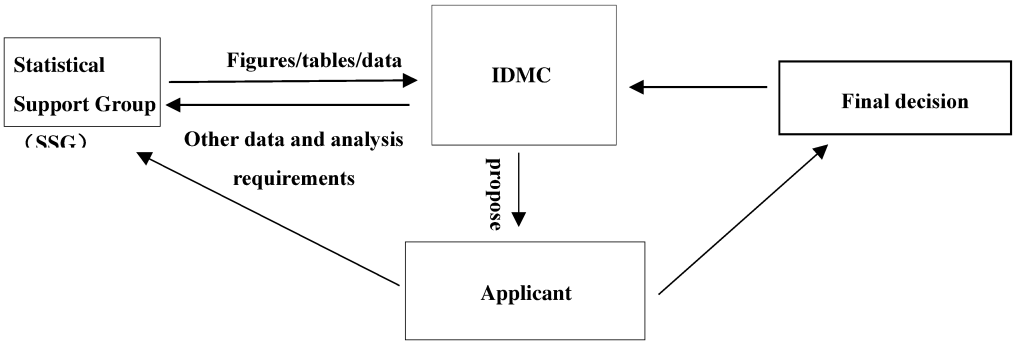

图 1 Organizational chart of IDMC with other committees and functions

6 IDMC meetings

IDMC meetings can be face-to-face meetings or teleconferences. Members of the sponsor's research team can provide internal data from ongoing research to IDMC members at the meeting and can also provide relevant external data. Participants may include researchers and other interested parties if desired, in addition to sponsor representatives, IDMC and independent statistical team members. Meetings are generally chaired by the sponsor, but may also be chaired by the IDMC.

IDMC meetings require that all IDMC members (including 2 clinicians and 1 biostatistician) attend and vote. If the IDMC is unable to reach consensus, the IDMC will report the lack of consensus to the sponsor and will be clearly documented in the IDMC meeting minutes.

6.1 Kick-off meeting

All IDMC members will be asked to attend a kickoff meeting. The purpose of the meeting is as follows：

1) Understand the study drug and familiarize with the study protocol.
2) Review the study protocol.
3) Review and finalize the IDMC Charter, including tasks and responsibilities and communication plan.
4) Review the IDMC statistical analysis plan, including tables/graphs/tables.
5) Determine meetings to be held by the IDMC and schedule discussion of issues related to the operation of IDMC meetings, including, but not limited to, frequency/timing and format of meetings, point in time and format for receipt of data and analyses, and management of meeting documents.
6) Other routine clerical duties.

The clinical study protocol, IB, IDMC charter and IDMC SAP shall be provided to IDMC

members at least 5 business days prior to the kick-off meeting.

6.2 Planned meetings

Data review meetings will be conducted via face-to-face or teleconference after IDMC members have reviewed the data packet. The Study Group will schedule these scheduled meetings, which will be attended by all IDMC members, SSG statisticians, and other SSG representatives. The purpose of the scheduled meetings is to discuss the data and make recommendations to the sponsor.

Scheduled meetings are planned when no more than 18 symptomatic intracranial hemorrhages (ECASS III criteria) occur in no more than 600 subjects and 42 symptomatic intracranial hemorrhages (ECASS III criteria) occur in total. If both of these conditions were not met, no further scheduled sessions were conducted.

6.3 Unplanned meetings

If the study may present safety issues or other relevant new information emerges, the IDMC will need to increase the number of meetings to ensure the safe conduct of the trial.The IDMC chair works with the sponsor to schedule unscheduled meetings as needed.The IDMC may request data reports from the sponsor as needed.

7 Data review and communication procedures

In order to improve the integrity and credibility of the clinical trial, as well as to ensure that proper communication is achieved between the IDMC and the trial investigators and sponsors, and to achieve different communication objectives, both open and closed meetings will be used. Provide opportunities for the IDMC to interact with others who have review input on trial-related issues.

All IDMC materials, discussions, and communication procedures are completely confidential.IDMC members and other participants in IDMC meetings are expected to maintain confidentiality and not to disclose information that would compromise the integrity of the data review to any other party, except in the interest of protecting the safety of the subjects.

7.1 Open meeting

In order for the IDMC to be fully informed of information provided by trial investigators or sponsors, IDMC meetings are conducted as joint meetings between IDMC members and non-IDMC members. Discussions focus on subject recruitment, data quality, adherence, drug safety, and other issues that may affect trial operations and results. The focus of the review was on assessing drug safety. Participants may include investigators and other interested parties if desired, in addition to sponsor representatives, IDMC and independent statistical team members, and may attend face-to-face meetings of the IDMC or participate by means of communication such as telephone. Meetings are generally chaired by the sponsor, but may also be chaired by members of the IDMC.

Prior to each IDMC meeting, the SSG will provide the results of the statistical analysis (see Section 9 for an overview of the results of the statistical analysis). The results of the open statistical analyses, including data on subject recruitment and baseline characteristics, protocol deviation information, and summary data on safety, will be reported by the SSG to everyone attending the IDMC meeting.

The results of the statistical analyses should provide accurate information and the data specifications are subject to the sponsor's agreement. Provide to IDMC members and sponsors at least 5 business days prior to the meeting date.

7.2 Closed meeting

Closed meetings are defined as meetings involving only members of the IDMC and relevant members from the independent statistical team to discuss confidential data from clinical trials. During these meetings, the IDMC will reach consensus on its list of recommendations, including whether to continue the trial, terminate the trial, or other recommendations.

7.3 Report of the Meeting

At each IDMC meeting, the CRO Medical Monitor will report the results of the open statistical analyses and the SSG will provide the results of the closed statistical analyses (see Section 9 for an overview of the content of these reports).

The results of the open statistical analyses, which are available to everyone attending the IDMC meeting, will include data on subject enrollment and baseline characteristics, protocol deviation information, and summary data on compliance.

Results of statistical analyses should provide accurate information and follow-up should be completed within approximately one month of the IDMC meeting date. The report shall be made available to IDMC members at least five business days prior to the meeting date.

7.4 Summary of proceedings

Minutes shall be provided and approved by the full IDMC membership for each IDMC meeting. Minutes and reports are typically prepared by the IDMC Chair and IDMC members designated by the Chair. Draft minutes will be sent to the IDMC Chair and/or sponsor for review within 7 business days of the meeting (Open Meeting Minutes only).

1) Open Meeting Minutes:

Minutes of open meetings will be written by the Study's Clinical Operations Team and sent to attendees for review and finalization upon completion of the first draft. Minutes of open meetings may be released to all attendees, and it is up to the sponsor to decide whether to pass on information about the meeting's relevant discussions to relevant parties such as ethics committees, investigators, and regulatory agencies;

2) Minutes of closed meetings: minutes of closed meetings are restricted to distribution to IDMC members only.

The minutes of the closed meeting will be written by the study SSG statistician and will be sent to the participants for review and finalization after the first draft is completed. At the end of the study, IDMC will send a complete set of open and closed meeting minutes to the sponsor for archiving.

7.5 Data review

1) Type and Frequency of Data Review:

Scheduled meetings to review data will be conducted when no more than 18 symptomatic intracranial hemorrhages (ECASS III criteria) occur in no more than 600 subjects, for a total of 42 symptomatic intracranial hemorrhages (ECASS III criteria). Other meetings or data reviews may be scheduled at the discretion of the IDMC or arranged by the sponsor.

2) Data Processing:

Four weeks prior to the scheduled IDMC meeting, the DM exports and transmits the relevant datasets from the completed cleanup to the Statistician.

3) Distribution of Data Packets:

Data packets will be sent by SSG to IDMC members and sponsors via email at least 5 business days prior to the scheduled data review meeting.

7.6 Document storage and archiving

Minutes and reports of open-door meetings shall be kept by the operations team of this study; minutes and reports of closed-door meetings shall be maintained and kept confidential by the IDMC SSG until the completion of the study, at which time all files shall be transferred to the sponsor.

8 IDMC Statistical Analysis Program

SSG will draft an IDMC SAP that describes the methods of statistical analysis of the safety data involved and how decisions about the subsequent continuation of enrollment in the trial will be made on the basis of the results of the statistical analyses, etc. The IDMC SAP must be agreed to by the IDMC members, the sponsors.

9 Content of statistical analysis results

9.1 Outline of the results of the open statistical analysis

- Subject screening information;
- Baseline subject characteristics;
- Prior treatment and other similar information;
- Number of days to start treatment;
- Summary of AE and SAE data;
- Analysis of overall safety data (including bleeding events by category, AE, SAE, SUSAR, and AESI)
- Study withdrawal or termination information;
- Protocol deviations.

9.2 Outline of the results of the analysis of closed-door statistics

- Repeat open statistical analysis information (add details by treatment group);
- Overall safety data analysis (by treatment group)。

10 IDMC recommendations

IDMC makes resolutions after carefully reviewing and discussing public reports. Voting is used and the number of participants must reach the number of valid votes specified in the IDMC bylaws. Voting is often based on the principle of majority rule.The IDMC Chair shall complete an IDMC Resolution (see Attachment 2 for a template) at the meeting, which needs to include the date of the meeting, the location of the meeting, the committee's recommended options and the specific content of the recommendation, as well as the Chair's signature and date. The IDMC recommendation approved by the Chair is sent to the sponsor within 7 business days of the meeting and provides the necessary data to the sponsor for decision making. Except for continuation as originally planned, the details or reasons for additional recommendations

should be clearly documented in the resolution letter.

IDMC recommendations may include as per but not limited to:

1) Continuing the study as currently scheduled until the next meeting is held as planned or on an ad hoc basis;

2) Continuing the study as currently planned, but calling the next meeting earlier, with a suggested date of ___DD___MM ___YY ____;

3) Continue the study as currently planned, but add an interim meeting;

4) Continue with the study, but with modifications to the protocol;

5) suspend enrollment until the following issues are resolved.

6) discontinue the study;

IDMC recommendations shall be clearly communicated to the sponsor's decision-making management through a written document signed by all IDMC members, which shall then be communicated by the sponsor's decision-making management to the sponsor's program research team in a predetermined manner.

Annex 1：

Table 1 IDMC Membership and Contact Information

Name	Position (Chairperson/Member)	Work unit	Specialized field	Contact number	Email
Dong Qiang	Chairperson	Huashan Hospital of Fudan University	neurology	13701747065	Qiang_dong163@163.com
Yan Chuanzhu	Member	Qingdao Hospital, Qilu Hospital, Shandong University	neurology	18561811888	chuanzhuyan@163.com
Chen Feng	Member	Nanjing Medical University	analytics	13813809333	Dr.chenfeng@163.com

Table 2 Members of the Statistical Support Group and contact details

Name	Work unit	Specialisation and division of labour	Contact number	Email
Cao Jinjin	Nanjing Baostar Pharmaceutical Technology Co.	Statisticians	182 6263 6057	jjcao@powerstat.cn
Zhu Tianyi	Nanjing Baostar Pharmaceutical Technology Co.	Programmer	183 5197 3953	zhutianyi@powerstat.cn

Table 3 Applicant contact information

Name	Work unit	Specialisation and division of labour	Contact number	Email
Zhao Huainan	China Resources Biopharmaceutical Co.	Clinical operation management	15104685123	zhaohuanan1@crbiopharm.com
Dai Shaogang	China Resources Biopharmaceutical Co.	Clinical operation management	15168957125	daishaogang@ crbiopharm.com

Liu Xinming	China Resources Biopharmaceutical Co.	Medical manager	13366518762	liuxinming16@ crbiopharm.com
Liu Yang	China Resources Biopharmaceutical Co.	Clinical operation management	18610755998	liuyang1466@ crbiopharm.com

Table 4 Contract Research Organisation contact information

Name	Work unit	Remit	Contact number	Email
Wen Pu	Ximedi Medical Technology Co., LTD	Senior medical Affairs Manager	15537591636	pu.wen@crmedicon.com
Zhang Tingting	Ximedi Medical Technology Co., LTD	Senior Manager of data management	18006736968	tingting.zhang@crmedicon.com
Sun Bing	Ximedi Medical Technology Co., LTD	Senior biostatistician	13771762561	bing.sun@crmedicon.com
Luo Qinghua	Ximedi Medical Technology Co., LTD	Clinical Program Director	13910843513	qinghua.luo@crmedicon.com
Ma Xingmiao	Ximedi Medical Technology Co., LTD	Clinical Project Manager	15905159129	xingmiao.ma@crmedicon.com

Resolution of the Independent Data Monitoring Committee (IDMC)

Date of meeting：

- **Venue of the meeting：**
- **Participant：**
- **Meeting format：**
  - □ meet and greet session
  - □ conference call
  - □ other

Reviewed at this meeting_____Project Safety Data，No._____，and the date of the meeting is_____；At the current meeting□conducted/□not conducted review of validity data；At the current meeting□conducted/□not conducted supervision of sample size re-estimation.

IDMC gives the following advice：

□ Continue the study according to the existing plan until the next meeting is convened as planned or on an ad hoc basis；

□ Continue the study as currently planned, but bring forward the next meeting to a suggested date of：____DD___MM___YY；

□ Continuation of the study as currently planned, with the addition of an interim meeting；
Describe the timing and content of the interim meeting：

□ Continued research, subject to programme modifications：
Describe the main elements of the modification：

□ Admission to the group is suspended until the following issues are resolved：
Describe the problem to be solved.

□ The study was discontinued for the following reasons：

□ Other comments and recommendations to the sponsors：

IDMC Signature of the Chairman and date：

_____