Taipei Medical University Hospital

Human Research Protection Program Policies & Procedures

February 17, 2021

Approved by Organization Official

Vice Superintendent in Research **Date**

Superintendent **Date**

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List of Abbreviations

ACHRP, Advisory Committee of Human Research Protection
BA/BE, Bioavailability/Bioequivalence
COI, Conflict of Interest
Co-PI, Co-Principal Investigator
CRC, Clinical Research Center
CHRP, Center of Human Research Protection
DMR, Department of Medical Research
DSMB, Data Safety and Monitoring Board
DSMP, Data Safety and Monitoring Plan
GC, General Convener
GCP, Good Clinical Practice
HRPP, Human Research Protection Program
IRB, Institutional Review Board
MOHW, Ministry of Health and Welfare
NC/UAP, Non-compliance/Unanticipated Problems
NHI, National Health Insurance
PI, Principal Investigator
PK, Pharmacokinetics
TFDA, Taiwan Food and Drug Administration
TMU, Taipei Medical University
TMU-COIMDC, TMU-Conflict of Interest Management and Deliberation Committee
TMU-DSMS, TMU-Data Safety Managing Section
TMU-ILC, TMU-Industrial Liaison Center
TMU-JCRC, TMU-Joint Clinical Research Center
TMU-JIRB, TMU-Joint Institutional Review Board
TMU-OHR, TMU-Office of Human Research
TMUH, Taipei Medical University Hospital
SHH, Shuang-Ho Hospital
SOPs, Standard Operation Procedures
WFH, Wan-Fang Hospital

TMUH Human Research Protection Program

1. Policy

Taipei Medical University Hospital (TMUH) is a regional healthcare provider and a teaching hospital in Taipei City of Taiwan. TMUH is one of the affiliated hospitals of Taipei Medical University (TMU). The other two affiliated hospitals of TMU- namely, the Wan-Fang Hospital and Shuang-Ho Hospital- are owned by Taipei City and the Ministry of Health and Welfare (MOHW) respectively. Previously, TMUH and Wan-Fang hospital had their own IRB separately. However, in order to reduce burden of duplication in reviewing and increase the cooperation between hospitals, the Board of Trustees of the university decided to merge the hospital's IRBs to a Joint-IRB (TMU-JIRB) in May 2009 to serve the ethics review for the university and three hospitals.

Base on the mission of TMUH –"To improve the health by incorporating life-respecting, innovation and excellence in teaching, research, and clinical care", TMUH fosters a research environment that promotes the respect for the rights and welfare of individuals recruited for, or participating in, research conducted by or under the auspices of TMUH. In the review and conduct of research, actions by TMUH will be guided by the principles (i.e., respect for persons, beneficence, and justice) set forth in the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (often referred to as the Belmont Report). The actions of TMUH will also conform to all applicable government laws and regulations. In order to fulfill this policy, TMUH has established a human research protections program (HRPP).

2. Mission

The mission of the HRPP is

- to safeguard and promote the health and welfare of human research participants by ensuring that their rights, safety, and well-being are protected,
- to provide timely and high quality review and monitoring of human research projects,
- to facilitate excellence in human research.

The HRPP includes mechanisms principles, policies and procedures of

- monitoring, evaluating, and continually improving the protection of human research participants.

- intervening appropriately in research to respond the concerns of research participants.
- educating investigators and research staff about their ethical and legal responsibilities to research participants and about the principles, policies, and procedures that ensure ethical human research.
- providing education for participants and potential participants in human research projects.
- coordinating the components involved in the HRPP and providing sufficient resources to carry out the above tasks.

3. Institutional Authority

The TMUH HRPP is approved in March 2013 and amended in February 2021. As stated in the section of "policy", the operating procedures in this document serve as the governing procedures for all human researches conducted under the auspices of TMUH. In addition to posted on the TMUH website, the policies as well as the operating procedures in this HRPP are introduced in regular meeting at TMUH and are made available to all investigators and research staffs.

4. Definition

Terms used in the HRPP are defined as follows:

- Human subject research: means any activity that meets the definition of “research” and involves ” human subjects” as defined by Taiwan Human Subjects Research Act, refers to research involving obtaining, investigating, analyzing, or using human specimens or an individual person’s biological behavior, physiological, psychological, genetic or medical information.
- Human trial: as defined by Taiwan Medical Care Act refer to experimental research of new medical technology, new medicament, new medical implement, or the bioavailability and bioequivalence of generic drugs conducted by medical care institutions on humans based on medical theory.
- Human specimens: refer to human (including a fetus and corpse) organs, tissues, cells, body fluids, or any derivative biomaterial arising from experimentation therewith.
- Research: a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalize knowledge.
- Human participants: individual about whom an investigator conducts research and obtains

either (1) data through intervention or interaction with the individual; or (2) identifiable private information. Or individual who is or becomes a participant in research or clinical trial, either as a recipient of the test article or as a control. A human participant includes an individual on whose specimen a medical device is used.

- Principal Investigator (PI). A PI is an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. When graduate students' research, the PI should be their advisor.
- Co-PI. A Co-PI is an individual who under the direction of the PI, is involving in some or all aspects of the research project, including the: design of the study, conduct of the study, analysis and interpretation of identifiable data, and writing of manuscripts resulting from the project.
- Research team: Research member in a study include PI, Co-PI(s), study coordinators and anyone who is involved in design of the study, conduct of the study, analysis and interpretation of identifiable data, and writing of manuscripts resulting from the project.
- Institutional Review Board (IRB). IRB is a board established in accordance with the "Human Research Act" and "Regulations for Organization and Operation of Human Research Ethics Review Board" for review and approval of human subject research.
- HRPP: The HRPP is a multi-tiered program which oversees the review and conduct of research involving human participants under the auspices of TMUH.

5. Ethical Principles

The TMUH is committed to conducting research with the highest regard for the welfare of human participants. It upholds and adheres to the principles of *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects in Research* by the National Commission for the Protection of Human Subjects in Biomedical and Behavioral Research (1979) and the Declaration of Helsinki (2013), including:

- Respect for Persons, which is ensured by obtaining informed consent, consideration of privacy, confidentiality, and additional protections for vulnerable populations.
- Beneficence, which is assured by ensuring that possible benefits are maximized and possible risks are minimized to all human participants.
- Justice, the equitable selection of participants.

To avoid the undue intervention in human participants during the research, the payment of

finder's fees and/or bonus payments for accelerating recruitment by sponsor or inventor is not permitted and conflict of interest (COI) should be claimed (details in Section 10).

6. Regulatory Compliance

The HRPP is responsible for ensuring compliance with Taiwan related laws, regulations, codes and guidance issued by Taiwan Central Government and the MOHW, such as Human Research Act, Human Research Ethics Policy Guidelines, the Medical Care Act, the Pharmaceutical Affairs Act, the Physicians Act, the Guidance on the Collection and Use of Tissue Samples for Research Uses, and the Taiwan GCP Code. The legal and regulatory requirements that apply to the use of investigational test articles: Prior to conducting a human trial involving drugs and devices, including in vitro diagnostic devices, an application must be submitted for review and approval of the proposed clinical trial by the MOHW. Upon the trial is completed or prematurely terminated, a complete and detailed clinical trial reports must be submitted as specified by the MOHW.

The TMUH commitment to the protection of human participants applies to all TMUH research, regardless of whether the research is funded by government, non-profit, industry sponsors or internal funds and regardless of the location of the research.

The PI remains responsible for the conduct of his or her human participant research protocol at TMUH. The PI must maintain overall responsibility for the oversight of the research study as well as all research staff and trainees involved. When appropriate, some research responsibilities and functions can be delegated but not the overall responsibility for the conduct of the research. All researchers and research staff must follow the requirements of the research protocol and adhere to the policies and procedures of the hospital and to the requirements or determinations of the TMU-JIRB.

According to Taiwan Medical Care Act article 70, medical records for human trials shall be retained indefinitely.

7. Research Covered by the HRPP

The HRPP is a multi-tiered program which oversees the review and conduct of research involving human participants under the auspices of TMUH.

All research involving human participants as defined by Taiwan Human Subjects Research Act or human trial as defined by Taiwan Medical Care Act and GCP Code are considered under the auspices of TMUH includes research conducted at the hospital, conducted by or

under the direction of any employee or agent of the hospital connection with his or her institutional responsibilities, conducted by or under the direction of any employee or agent of the hospital using any property or facility of the hospital, or involving the use of the hospital's non-public information to identify or contact human participants. The research may be externally funded, funded from internal resources, or conducted without direct funding.

In general, a research is overseen by the HRPP subject to Human Subjects Research Act, Medical Care Act and GCP Code and includes any of the following:

- Intervention for research purpose with any human subject of the research by performing invasive or noninvasive procedures.
- Intervention for research purpose with any human subject of the research by manipulating the environment.
- Interaction for research purposes with any human subject of the research.
- Obtaining the informed consent of human subjects for the research.
- Obtaining for research purposes identifiable private information or identifiable biological specimens from any source for the research. In general, obtaining identifiable private information or identifiable specimens includes, but not limited to:
  - ◘ Observing or recording private behavior;
  - ◘ Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens provided by another institution; and
  - ◘ Using, studying, or analyzing for research purposes identifiable private information or identifiable specimens already in the possession of the investigators.

But the research involving human subject, such as case report, surveillance activities, quality improvement program, or classroom, if had intention to publish, has to submit to TMU-JIRB for reviewing and covered by HRPP.

According to the official announcement by the MOHW, five categories of research activities not involving vulnerable populations that are exempt from TMU-JIRB review, but several conditions cannot exempt.

(1) Researches implemented by doing non-interactive and noninvasive activities without writing names in public occasions. The data collected is unable to link to certain individual.

◘ Implementing research in a ward, consulting room or waiting area is not in the extent of exempt.

◘ If identifying the reaction of any participant to the research might cause the danger of participant involving illegal activities in criminal/civil dimension, or cause his/her losses in economic condition, social status or reputation, the research is not in the extent of exempt.

(2) Using data already known by the public legally and the use of data accords with the purpose open to the public.

◘ National Health Insurance (NHI) database is not so-called open to the public legally, so it is not in the extent of exempt.

(3) The competent authorities entrust specialized institutions to implement the research of public policy evaluation or implement the research by themselves out of duty.

◘ If not having official letter specified the competent authorities are in need of implementation of the research of public policy evaluation out of duty, the research is not in the extent of exempt.

◘ If identifying the reaction of any participant to the research might cause the danger of participant involving illegal activities in criminal/civil dimension, or cause his/her losses in economic condition, social status or reputation, the research is not in the extent of exempt.

(4) Researches implemented in commonly accepted educational settings about an educational examination or test, teaching skills or effects evaluation.

◘ If involved with cases below, the research is not in the extent of exempt.

◘◘ New educational strategies.

◘◘ Randomized or purposive assignment for the educational groups division of students is not in the extent of exempt for it is not a general procedure of education.

◘◘ Physical education involved with extreme sports.

(5) Risks of research belong to the minimum level, and risks participants confront won't exceed the risks of people who don't participate in the research. The kind of research shall be approved and issued the certificate of exempt review by the board after the review. Minimum risks referring to the odds or level participants confront injury or disorders are not higher than injury or disorders in daily lives.

◘ Research simply about NHI database, not involving linking other official/non-official databases and/or databases of hospitals or systems of medical records, and also not involving any need of tracking nor intervention (consultation or blood sampling is not excluded or limited), and the result will not cause the doubt or risks of certain groups,

shall be evaluated by the board to be proved exempt.

TMU-JIRB retains ultimate authority to determine whether an activity is with the qualification of the exempt to JIRB for review. The Director of the CHRP has delegated to the General Convener (GC), Chair and Executive Secretary of JIRB the authority to make regulated/not regulated determinations in a manner consistent with their approved Standard Operation Procedures (SOPs).

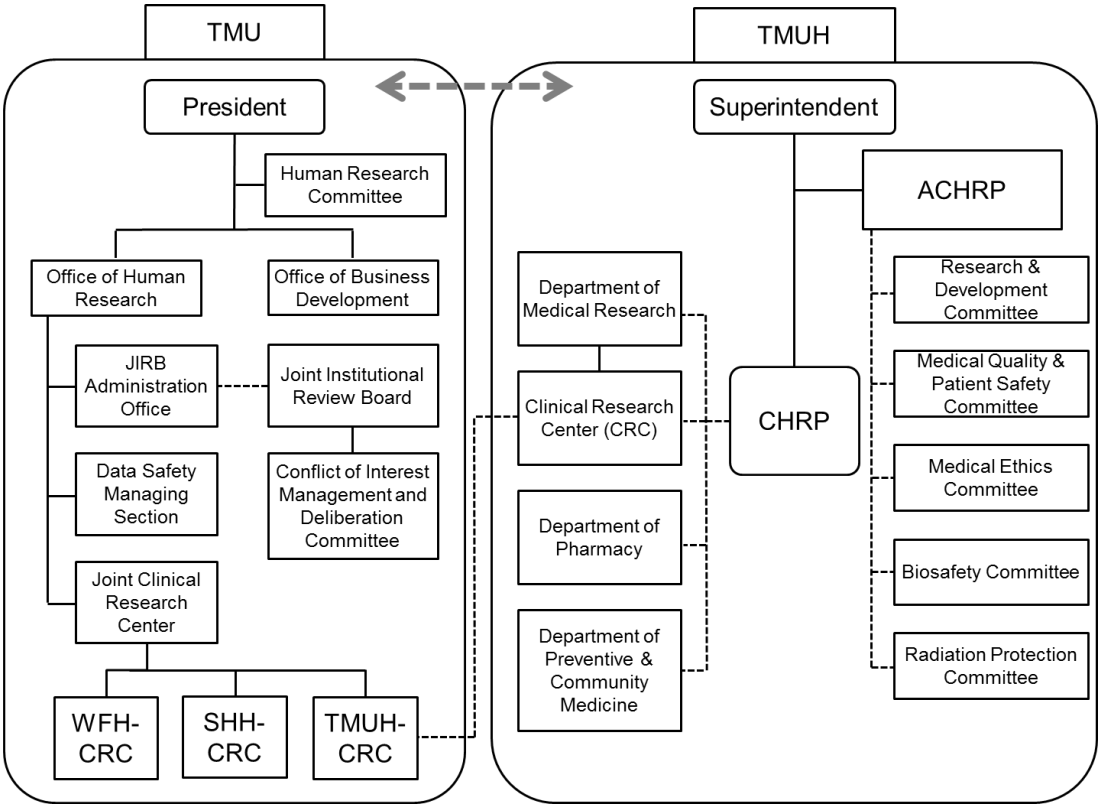
TMUH does not require investigators to seek a formal determination of "Not Regulated" from the TMU-JIRB when the activity falls outside Human Subjects Research Act or Taiwan Medical Care Act or GCP Code definitions of human subject research. Investigators may consult informally with TMU-JIRB staff or members to facilitate a self-determination. Investigators may alternatively request from a TMU-JIRB or TMU-JIRB staff member, explicit regulated/not regulated determinations in cases that do not fall clearly into the category of non-research activities, rather than making an assumption that may later be determined to be incorrect. Requests for an explicit determination will be made through the e-JIRB application.

8. Written Policies and Procedures

The HRPP policies and procedures are approved by the Institutional Official and maintained by the CHRP. The policies and procedures manual is intended to be flexible and readily adaptable to be reviewed and updated as needed, but no less than once a year by the CHRP Director and approved by the Institutional Official. The revised version is posted on the CHRP website with a disclaimer that it is the only official copy and that before using a printed copy, investigators should verify that it is the most current version by checking the document effective date on the website.

9. HRPP organization

The organization structure of HRPP.



The Center of Human Research Protection (CHRP), under the supervision of Advisory Committee of Human Research Protection (ACHRP), is responsible for ensuring the ethical and equitable treatment of all human participants in researches performed at TMUH under HRPP.

9.1. Advisory Committee of Human Research Protection (ACHRP)

The ACHRP comprises several internal and external experts and provides consultation, evaluation and guidance for the strategies and policies of HRPP. The committee also solves the controversial issues regarding implementation of the HRPP if necessary.

9.2. Center of Human Research Protection (CHRP)

CHRP oversees all HRPP functions in TMUH. TMUH delegates authority and primary responsibility to the Director of the CHRP to maintain and oversee the TMUH HRPP. The responsibilities for CHRP Director are:

- developing and maintaining the policies and procedures for the HRPP
- overseeing the performance of the HRPP.

- ensuring adequate resources to support the operations of the HRPP.
- responding to the reports of undue influence from TMU-JIRB members and staff.

The response of CHRP will be to identify the event, and depend on the severity and need to form a taskforce to make survey, then to call a meeting to deal with the finding. In the meantime, CHRP will protect the person been influenced and separate them to the related reviewing work.

- coordinating and facilitating the effective communication among the components of the HRPP and personnel involved in HRPP.
- resolving conflicts between applicable laws, regulations and ethical guidelines relevant to human research.
- resolving complains from human participants directly, or complains referred from TMU-JIRB.

9.3. Institutional Review Board (IRB)

TMU-JIRB is part of our human research protection program and is established to protect the rights and welfare of human research participants recruited to participate in research activities conducted under the auspices of participating institutions.

Research plan to conduct within TMU system should be reviewed and approved by TMU-JIRB to comply with HRPP policies and principles in human participant protection.

TMU-JIRB comprises of 4 review panels for biomedical and social/behavioral studies. Each TMU-JIRB panel consists of 15 standing members. The appointment of TMU-JIRB members is independent that the GC of TMU-JIRB appoints members in accordance Taiwan laws/regulations.

The TMU-Office of Human Research (TMU-OHR) will monitor the administrative compliance of TMU-JIRB and TMU-JIRB is continuously accredited and certificated by Taiwan MOHW, and Special Program for Research & Training in Tropical Disease WHO and The Association for the Accreditation of Human Research Protection Program (AAHRPP) to ensure the operation, review quality and laws/regulations compliance.

9.3.1. Authority of the TMU-JIRB

TMU-JIRB is empowered to act by the Board of Trustees and the President of TMU. TMU-JIRB has the authority to review, approve, require modifications in, or disapprove all research activities conducted under the auspices of the participating institutions.

In the review of research, actions by TMU-JIRB will be guided by the principles and policies (i.e., respect for persons, minimize risks/ maximize benefit, beneficence, and justice) set forth in the Nuremburg Code, the Declaration of Helsinki, the Belmont Report as well as Taiwan laws/regulations like the Medical Care Act, the Human Research Act, etc.

TMU-JIRB ensures that appropriate safeguards exist to protect the rights and welfare of research participants. In fulfilling these responsibilities, the panel reviews all the research documents and activities that relate directly on the rights and welfare of the participants of proposed research. The protocol, the consent/assent document(s), the investigator's brochure when applicable, tests, surveys, questionnaires and similar measures, and recruiting documents are examples of documents that each panel uses to conduct its review.

Before any human participant is involved in research in relationship to TMU system, TMU-JIRB will give proper consideration the following points:

- The PI’s qualification and expertise.
- Appropriate inclusion/exclusion criteria and population.
- The risks to the participants.
- The anticipated benefits to the participants and others.
- The importance of the knowledge that may reasonably be expected to result.
- The informed consent documents and process to be employed.

TMU-JIRB have the authority to suspend, restrict, or terminate approval of research activities that fall within its jurisdiction that are not being conducted in accordance with TMU-JIRB requirements or that have been associated with serious harm to participants. TMU-JIRB has the authority to observe the consent process and the trial/study if the panel determines it to be indicated.

Prior to conduct a human trial subject to Taiwan Medical Care Act #8, must obtain the approval from the central competent authority, or upon entrustment of the central competent authority. Thus those protocols have to obtain the approval from MOHW and TMU-JIRB. Those protocols could be submitted to TMU- JIRB and MOHW in parallel.

If TMU-JIRB approved first and MOHW had suggestions to change the protocol, the PI has to submit the revised version of the protocol to JIRB for amendment review; If MOHW approved first, the PI should attach the approval document from MOHW to the application for JIRB review.

According to Medical Care Act, article 80 “Medical care institutions shall submit trial report in accordance with notification by the central competent authority during human trial period. If the central competent authority feels there is concern for safety, the medical care institutions shall cease trial immediately. Medical care institutions shall submit trial report to the central competent authority at the completion of the human trial.” Once approved, clinical trial reports must be submitted as specified by the MOHW and TMU-JIRB.

9.3.2. Autonomy of the TMU-JIRB

TMU-JIRB is under the authority of the Board of Trustees and the president of TMU, but function independently. TMU-JIRB also functions in coordination with CHRP office and other committees. CHRP officials, investigators, employees and sponsors of research are prohibited from attempting to unduly influence or to interfere with the function or decision-making as established by accepted methods and regulatory requirements of the TMU-JIRB, any of its members or staff, or any member of the research team to obtain a particular result, decision or action. A decision by TMU-JIRB to un-approved research is final and should not be over-ruled.

Research that has been reviewed and approved by TMU-JIRB may be reviewed and disapproval by officials of the institution. However, those officials may NOT approve research if it has been disapproved by one of the TMU-JIRB panels.

9.3.3. Jurisdiction of the TMU-JIRB

TMU-JIRB have jurisdiction (as defined above) over all human participant trial/study conducted in TMU system and cooperate with institutions which their protocol reviewed and approved by TMU-JIRB to ensure the compliance and participants’ protection.

9.3.4. TMU-JIRB Relationships

The TMU-JIRB functions independently of, but in coordination with, other institutional regulatory committees. The panels, however, makes its independent determination whether to approve or disapprove a protocol based upon whether or not human participants are adequately protected. The panels have review jurisdiction over all trial/study involving human participants conducted, supported, or otherwise subject to regulation by any governmental department or agency that has adopted the human participants’ laws/regulations.

TMU-JIRB may choose, on a case-by-case basis, to provide human trial/study protection oversight for another institution. In order for the panel to provide this oversight, a formal

relationship (cooperative agreement) must be established between the TMU-JIRB and the other institution through any official documents. This relationship must be formalized before the TMU-JIRB will accept any human trial/study proposals from the other institution.

In the conduct of cooperative trial/study projects, TMU-JIRB acknowledges that each institution is responsible for safeguarding the rights and welfare of human participants and for complying with applicable laws/regulations. When a cooperative agreement exists, TMU-JIRB may enter into a joint review arrangement, rely on the review of another qualified IRB, or make similar arrangements for avoiding duplication of effort.

9.3.5. TMU-JIRB Offices

The TMU-JIRB Office (i.e. the Department of Administration) reports directly to the GC when anything about the review functions of TMU-JIRB and to the CHRP if anything not related to the review function of TMU-JIRB. The Chief of the TMU-JIRB Office has expert knowledge in regulatory issues regarding human participants and serve as the Executive Secretary of TMU-JIRB.

Each panel at TMU-JIRB has a support staff, panel coordinators, with administrative support. More detailed descriptions of the staffs are included in the written policies and procedures.

The TMU-JIRB Offices located outside the TMU campus and personnel are as outlined in the current organizational charts. The duties and responsibilities for all staff are found in their respective job descriptions, and their performance is evaluated on an annual basis.

The TMU-JIRB Offices provide the staff and space for the ethical review functions and serve as the initial point of contact for faculty, staff, students, and outside agencies. The TMU-JIRB Offices maintain communications by distributing newsletters, maintaining websites and distributing directed mailings as needed.

9.4. Other Related Components

9.4.1. Clinical Research Center (CRC)

9.4.1.1. Organization

TMUH CRC, a part of TMU-Joint CRC (TMU-JCRC), is authorized by TMUH to promote, facilitates and executes clinical trials at TMUH under the supervision of Department of Medical Research (DMR).

9.4.1.2. Service providing

TMUH CRC provides clinical trial-related services including:

- Protocol submission administration assistance
- Feasibility assistance
- Budget confirmation
- Project management: BA/BE/PK/Phase I-IV/device trial/other clinical research
- Trial conduct and management: BA/BE/PK/Phase I-IV/device trial/other clinical research
- GCP and regulation education
- Sample temporary storage

9.4.1.3. Facility and equipment:

- Central office
- Ward: regular beds, physiological monitor, 12-lead EKG, electronic manometer, electronic thermometer, defibrillator, electronic nurse and medical recording system, meeting room, auditing room, consultation room, living room, laundry room, transportation bed, central gas supply system, emergent medication car.
- Document archive room
- Sample storage and processing room: -70°C refrigerator -30°C refrigerator, 4°C refrigerator, room temperature centrifuge,4°C centrifuge, drug storage cabinet
- Central humidity and temperature monitor system
- Outpatient clinics
- Trial-product storage room in Department of Pharmacy

9.4.1.4. Staff

- Director
- Vice-director
- Project manager: BA/BE/PK, phase I, phase II-IV, device trial, other clinical research
- Study coordinator: BA/BE/PK, phase I, phase II-IV, device trial, other clinical research
- Medical consultant team
- Pharmacist
- Nursing consultant
- Administration assistant

9.4.2. Department of Medical Research (DMR)

The DMR is responsible for the promotion, oversight and management of research projects. DMR confirms TMU-JIRB approval, agreement, and the resources needed for participant protection before the conduction of the research. The DMR works with Data Safety Managing Section (DSMS) at TMU to implement periodical and non-periodical auditing for selected active protocols. All reports of auditing will submit to CHRP and/or ACHRP. In addition, the DMR oversees the published journal articles, and takes responsibility for consultation, auditing, correction, education and improvement for the research or researchers.

9.4.3. TMU-Office of Human Research (OHR)

TMU-OHR established JIRB Administration Section supports the administrative affairs of the TMU-JIRB; The DSMS of TMU-OHR leads or joint with the DMR of TMUH to conduct the routine audit for human researches, and assists the investigator to propose the Data Safety and Monitoring Plan (DSMP), or according to the need to set up the Data safety and Monitoring Board (DSMB) to monitor the data and related activities; The JCRC of TMU-OHR integrates the receiving of clinical trials and the resources of CRC of TMU 3 affiliated hospitals.

9.4.4. TMU-Office of Business Development (TMU-OBD)

The mission of TMU-OBD is to enhance TMU's research enterprise, including intellectual property's commercialization and sponsored research collaborations by establishing and maintaining multifaceted relationships with companies. TMUH set a policy of managing the grants and contracts and delegates the JCRC of TMU-OHR to take a responsibility for the contract engaging with the sponsors and the Industrial Liaison Center (ILC) of TMU-OBD taking the sign of affidavit from researcher for the PI-initiated studies. All protocols from the external sponsor or PI-initiated studies that involve human participants must be approved by TMU-JIRB, the DMR of TMUH, and by TFDA if needed. Then, the TMU-JCRC and TMU-ILC can process the contracting or taking the affidavit.

9.4.5. Department of Pharmacy

Investigational products should be sent to the Investigational Products Pharmacy of TMUH for management and dispensing. Regarding the handling of investigational or unlicensed medications, the Investigational Products Pharmacy follows the SOP "Work Instruction for Management of Investigational Products" to confirm that the handling of investigational or unlicensed products completely conforms to legal and regulatory

requirements.

9.4.6. Other Related Committees of TMUH

The other related committees, which participate in ACHRP, provide consultation, evaluation and guidance for controversial issues regarding implementation of HRPP.

9.5. Relationship between Components

The ACHRP provides consultation, evaluation and guidance for the strategies and policies of HRPP. CHRP oversees all human research protection functions in TMUH. TMU-JIRB maintains its independency and serving the ethics and scientific review for the Human Researches of TMU healthcare system.

Any study involving human participants must first undergo TMU-JIRB review and approval; thereafter, the study must be approved by the DMR to confirm what researchers determine that the resources necessary to protect participants are present before conducting the research.

The study execution has to follow the approved protocol in compliance with the guidelines in HRPP, the policies and procedures of the TMU-JIRB, CHRP and CRC. Compliance is a crucial element of the HRPP process because it is here that the collective effort of individual investigators ensures the integrity of TMUH as a research institution.

All personnel involved in human research protection closely to safeguard rights and welfare of participants. In order to ensure dialogue is maintained between the various compliance divisions, the Director of CHRP reviews the reports from all related units of HRPP monthly and meets every 3 months with the staffs of related components in HRPP.

The purpose of the meeting is to:

- Check and communicate with the mission/program progression
- Identify emerging research compliance risks;
- Exchange information and resources;
- Assess research compliance needs and opportunities; and
- Oversee and implement HRPP.

9.6. HRPP Resource

For evaluating the resources needed for the HRPP, the Director of CHRP reviews the reporting of data including legal counsel, conflict of interest, the efficiency of IRB reviewing, research review processes, quality improvement plan, community outreach, the complains and so on every year, and the summarized report will be presented at the meeting with the

CHRP and/or ACHRP.

Adequate human resources and financial support facilitate a well-functioning and effective HRPP. TMUH and TMU demonstrate a high level of institutional commitment to its HRPP in terms of human resources and financial support. The Director of CHRP is responsible for human resource management and the proposal of annual budget prediction based on:

- Adequate number of IRBs
- Adequate staffing
- Adequate office space, material and equipment
- Adequate technology support
- Adequate funds for educational opportunities for TMU-JIRB members, TMU-JIRB administrative staffs, HRPP relevant staffs
- Adequate direct financial support (salaries, supplies, equipment)

The adequacy of personnel and non-personnel resources of the HRPP is assessed on an annual basis by CHRP Director at TMUH as part of the annual TMU/TMUH budget review process. CHRP Director ensures that the HRPP funding allocation is conducted on a timely and appropriate basis.

10. Conflict of Interest (COI)

TMU/TMUH encourages and supports outside interactions of its faculty and employees with national and local governments, and with the business community and industry as important parts of their research, education and public service activities. Since outside interactions also carry with them an increased potential for conflict of interest and/or commitment, either actual of perceived, TMU-JIRB has developed procedures for identifying potential conflicts through annual disclosure, and ensure rigorous and consistent review of such disclosures.

10.1. General Conflict Management

To meet the above stated goals, TMU-JIRB set up the Conflict of Interest Management and Deliberation Committee (COIMDC) and is charged to review the annual disclosure forms submitted by researchers and their research team as well as related personnel accordance with TMU-JIRB SOPs and to make recommendations on how to manage, mitigate or eliminate individual and institutional COI. The committee exists to protect the integrity of all faculty

and investigators at TMU system, and maintain the public trust in TMU system. Because serious financial and other COI can harm the reputation of TMU system, as well as adversely affect its ability to fulfill its missions in education, patient care and research, these conflicts should be subject to the oversight and recommendations of duly-constituted and broadly representative committees. The committee carries out this charge in a manner that is intended to foster, not hinder, researches and other entrepreneurial faculty relationships.

TMU-JIRB requires all (covered individuals and institutions) to comply with the COI policies, disclosure process and management plans in TMU system. Covered individuals include faculty, individuals who are responsible for the design, conduct and reporting of basic or clinical trial/study, this includes anyone who obtains informed consent, those who determine eligibility, those who review data or conduct data analysis, TMU-JIRB GC, Chairs of panels, members, staff are also follow COI policies and signed TMU-JIRB COI Declaration when join TMU-JIRB. Disclosures are required on an annual basis and within 30 days of a change.

As part of its general financial disclosure, the TMU-JIRB COIMDC will review the COI issues of the PI when conduct trial/study involving human participants on an annual basis and when status changed. TMU-JIRB panels have the final say for the management plan in trial/study that involves human participants.

The TMU-JIRB panels will review the conflict management plan to determine if the conflict will adversely affect the protection of human participants and if the management plan is adequate. Based on the significance of the conflict and the potential adverse effects on the protection of subjects, conflict management plans can include：

- disclosure to subjects through the consent process；
- modifications in the research plan;
- monitoring by independent reviewers;
- divestiture of financial interests;
- appointment of a non-conflicted PI; or
- prohibition of the conduct of research at TMU system.

The TMU-JIRB panels can

- accept the management plan and recommend approval;
- recommend changes in the management plan; or
- refer the review to the Full Board if originally assigned for Expedited review.

All the review documents, decision documents, minutes will be kept on file in the TMU-JIRB Office along with the master file of each trial/study.

10.2. Protocol-Specific Conflict Management

The TMU-JIRB application asks protocol-specific questions regarding conflict of interest for investigators and key personnel.

As part of its review process, the TMU-JIRB panel will make a determination as to whether the conflict adversely affects the protection of human participants. If the answer is yes and an approved conflict management plan exists, the TMU-JIRB panels will review to determine if it adequately protects the human participants in that protocol.

If no approved COI management plan exists but needed, or discovered while reviewing, the TMU-JIRB panels will ask for adequate COI management plan and forward the review result and conflict information to the COIMDC for individual/institutional COI record and future review.

Review of conflict management plans are documented in the COIMDC minutes for the relevant panel to review and in the protocol file. If a conflict of interest exists, final TMU-JIRB approval cannot be given until an approved conflict management plan that adequately protects the human participants in the protocol is in place.

If the conflict of interest status of an investigator or key personnel changes during the course of a study, the individual is required to notify the TMU-JIRB Office and the COIMDC within 30 days of the change. The TMU-JIRB COIMDC will review the change and forward to related TMU-JIRB panels for a modification to the protocol.

10.3. Institutional Conflicts of Interest

Respect to Institutional Conflicts of Interest, the TMU-JIRB that parallels the policy and requirements for individual conflicts of interest. Where institutional conflicts may arise from royalties or intellectual property rights associated with a technology that is the subject of the research, TMU-JIRB manages these potential institutional COI as an extension of the individual conflict of interest on a protocol specific basis. TMU-JIRB has integrated the institutional conflict of interest management program with its existing program that has been described above.

11. Quality Assurance/Improvement Plan

TMUH maintains a quality assurance/improvement plan to measure and improve the HRPP effectiveness, quality, and compliance with organizational policies and procedures and applicable national and local laws.

11.1. Subject Chart Compliance Monitoring

Besides the reviewing of non-compliance/unanticipated problems (NC/UAP), progress report and final report by TMU-JIRB, DMR of TMUH and TMU-DSMS are responsible for periodical and non-periodical auditing for selected active researches. The summarized results from auditing will report to the CHRP and/or ACHRP. TMU-JIRB also reviews the NC/UAP report to determine whether which is a serious or continuous non-compliance. According to the determination, TMU-JIRB will take special actions of suspension or termination or develop a corrective action plan with the DMR and CHRP of TMUH.

The Director of DMR has a responsibility for implementing the corrective action plan, the completion of which will be evaluated by the TMU-JIRB/CHRP. Systemic issues will involve meeting with relevant individuals and deciding on a course of action.

11.2. HRPP Quality Assurance/Improvement

The HRPP is assessed by a variety of program assessments by both internal and external means. Some are regularly scheduled and others are conducted on a more casual basis.

- The MOHW performs the certification of the TMU-JIRB every 4 years. The most recent certification was a site-visit review in 2020. TMU-JIRB also earned AAHRPP accreditation in March 2014 and keeps renewing accreditation.
- Informal self-assessments are conducted by the CHRP to prepare for the internal and external assessments.
- The policies, procedures, forms and approach to community outreach in HRPP are constantly scrutinized to evaluate their effectiveness, efficiency and suitability and to ensure that they reflect current regulations, guidance and institutional requirements by the ACHRP.

HRPP quality assurance was reviewed once a year by the ACHRP, and the indicators of HRPP quality are:

- Assessment on the un-anticipated problem/adverse event reporting process by ensuring all reports have been completed and reported as appropriate;

- Evaluation of the continuing review process to ensure that no lapse has occurred since the previous TMU-JIRB approval;
- Protocol files review to assure appropriate documentation according to current policies and procedures;
- Other monitoring or auditing activities deemed appropriate by the CHRP components.

12. Education, Training and Outreach

As part of its commitment to human subject protection, TMU/TMUH has educational requirements for staff of the TMU-JIRB Office, TMU-JIRB members and for individuals engaged in the conduct of human participant research.

12.1. Initial and Continuing Education Requirement

12.1.1. Researcher

When a protocol submitting for IRB's review, TMU-JIRB requests all researchers and research staff listed in the protocol providing at least 6-hour training certificate within the past 1 year on human trials, human research, research ethics, regulations on medical research, or patient safety. For the research under the Regulation on Human Trials pursuant to Taiwan Medical Care Act, item #8, training record/certificate should be 30 hours on human trials and 9 hours on medical ethics within the past six years serve as the minimal criteria of qualified PI or Co-PI(s) for experimental research of new medical technology, new medicament, new medical implement, or the bioavailability and bioequivalence of generic drugs. If the trial involved somatic cells or gene therapy, 5 hours on relevant issues are required. If the researchers fail to fulfill the above requirements, the protocol submission will be rejected for ethical and scientific review.

12.1.2. TMU-JIRB Members and HRPP relevant administrative officer

When all the members (including IRB Chairs) joining TMU-JIRB, he or she will be provided a manuals and SOPs by administrative, and have basic educational training for 6 hours. The training covers SOPs, domestic and international regulation as well as the members within the scope of his trial/research related specification.

HRPP relevant administrative staffs should complete a 12-hour orientation training course covering the relevant SOPs, operational skills, basic concept of ethical review, GCP, ethical guidelines, etc. within 3 months after being employed.

The HRPP related administrative officers must have at least 6 hours training of concept of ethical review, GCP, ethical guidelines, community based participatory research, etc. every year as a sum, and provide supporting documents to related directors for record as well as appointment assessment and may not be appointed if not complete the continuous training on time.

12.1.3. Education Program for Human Research Protection

CHRP communicates with related subordinate units to plan the annual training program of HRP regarding the protection of the rights and welfare of research participants. Training program also includes any revision of regulations and SOPs content.

CHRP announces the related domestic or oversea training programs for related individuals to attend. The DMR of TMUH records and issues the certifications of the trainings, and to remind individuals to keep sufficient credit of education.

12.2. Outreach

The CHRP has a website for research participants entitled “Research Participant Information”. This website includes information about on-going human participant research, as well as resources such as questions to consider before deciding to participate and links to studies that are recruiting participant. CHRP also provides human protection program education program for the physicians of community clinics and for relevant community through the community activities conducted by the Department of Preventive and Community Medicine. CHRP implements periodical HRP perception survey for participants, prospective participants or community to evaluate and improve the outreach activities.

CHRP provides the "Human Subject Protection Handbook" for participants and researchers which describe the information about human participant research and involvement of community members, when appropriate, in the design and implementation of research and the dissemination of results. The researchers can recruit the participants to involve the research through the community outreach activities.

Additional considerations for reviewing research that involves community members in the research process, including the design and implementation of research and the dissemination of results, TMU-JIRB has various actions as following:

- Continuing education of TMU-JIRB members including community based participatory research.
- Inclusion of TMU-JIRB members with expertise in community based participatory

research.

- Inviting the representative from the community of the research to participate the TMU-JIRB meeting for consultation if needed.
- Inclusion of information on TMU-JIRB applications concerning community based research.
- TMU-JIRB experience with this type of research.
- Providing "Human Subject Protection Handbook" which including information on the concerns of community based research.

13. Reporting and Management of Concerns

Question, concerns, complains, allegations of undue influence, allegations or findings of non-compliance, or input regarding the HRPP may be reported orally or in writing.Employees are permitted to report concerns on an anonymous basis. Concerns may be reported to CHRP or TMU-JIRB, which have the designated person and SOPs providing a safe, confidential, and reliable channel for current, prospective, or past research participants or their designated representatives to express their questions, concerns and complains.

TMU-JIRB is responsible for reviewing and determining the property of UAP and each allegation of NC. Other than TMU-JIRB may take specific actions, including suspension or termination, to protect participants and ensure the study still fit criteria for approval or not, CHRP, TMU-JIRB and related departments in hospital work together to develop a corrective action and manage the process of non-compliance and unanticipated problems.

For the research with definitely against Medical Care Act, Physicians Act, Pharmaceutical Affairs Act, or Human Subjects Research Act, TMU-DSMS will report to the Director of CHRP of TMUH immediately for stopping the research and taking the essential actions according to the related Laws/Regulations in Taiwan.

If the input concern is submitted non-anonymously, the submitter will receive a direct response by phone number or e-mail. If the outcome of the review shows a need for ongoing monitoring or education, then the appropriate individuals (e.g., HRPP staff) are asked to contribute their expertise. TMU-JIRB also makes notification to the researcher or research staff with the Feedback Sheet and aggregates the frequent QAs that are put in the website for researchers to search the answers.

14. Sponsored Research

All study protocols from external sponsor that involve human participants must be

approved by the TMU-JIRB and DMR before conducting. TMU-JCRC review sponsored research agreements should include the following statements:

- The sponsor will pay for the medical expenses of reasonable and necessary medical treatment if a study subject is injured during a research study and the injury is a direct result of (1) the effects of the study drug or (2) the performance of study procedures pursuant to the protocol.
- For research monitored by the sponsor, the sponsor shall submit a written plan for reporting to TMUH findings that could affect the safety of participants or their willingness to continue participation, influence the conduct of the study, or alter the TMU-JIRB's approval to continue the study. The plan must address how such findings will be communicated to study participants.
- The sponsor must submit plans for disseminating findings from the research and defining the roles that the investigators and sponsors will play in publication or disclosure of results.
- The duties and functions transferred by the sponsor to the contract research organization are specified in the contract.