
PURPOSE

It is the policy of The University of Texas MD Anderson Cancer Center (MD Anderson) Institutional Review Board (IRB) to comply with Federal regulations governing human subject research.

POLICY STATEMENT

Patients participating in clinical trials at MD Anderson are almost exclusively cancer patients, and thus, as defined by the MD Anderson IRB are considered a vulnerable population. The MD Anderson IRB must be vigilant in protecting vulnerable populations from coercion or undue influence during their participation in a clinical protocol.

To assure appropriate enrollment of participants in research protocols, the IRB will consider the risk, harm and benefit to study participants when deciding whether or not to allow pharmacokinetic and/or pharmacodynamic procedures to be included in the protocol design.

This policy is adopted as a measure to assure the voluntary nature of human subject research participation and to ensure that decisions by patients to commit to research procedures in the clinical protocol are voluntary.

SCOPE

This policy applies to all human subjects research at (or conducted with) UTMDACC. Governmental or Industry sponsored studies may have additional requirements beyond what is stipulated in this policy.

DEFINITIONS

Pharmacokinetics (PK) -- The process by which a drug is absorbed, distributed, metabolized and eliminated by the body.

Pharmacodynamics (PD) -- The study of the action or effects of drugs on living organisms.

Minimally Invasive Procedure1 -- a blood draw or biopsy when the area to be biopsied is easily accessible and the risk of hospitalization from the procedure is relatively low (e.g., less than 1% chance of hospitalization)

PROCEDURE

Requirements for Inclusion of Pharmacokinetic and Pharmacodynamic Procedures in Clinical Protocols
Patients typically participate in clinical trials with an expectation or hope that they will obtain some benefit from their study participation. The inclusion of pharmacokinetic (PK) and pharmacodynamic (PD) procedures are important aspects of clinical protocols because the results may allow the investigator to determine if the study agents being used in the protocol are effective. The IRB will evaluate clinical protocols on an individual basis when considering whether PK/PD procedures will be permitted as components of the protocol research. The risk assessment for inclusion of PK/PD testing in the protocol will be part of the overall risk, benefit, burden assessment for the participant in the clinical protocol.

When making its determination, the IRB will consider the phase of the clinical protocol, the risk versus benefit to the participant, the participant population being studied, the types of procedures included in the PK/PD analysis and the potential scientific knowledge to be derived from the study results. The IRB recognizes that a clinical protocol in any phase could require that PK/PD procedures be performed, if necessary, to confirm participant eligibility and/or if the PK/PD procedures are included as a primary objective in the trial.

The IRB will consider the following issues when determining if PK/PD procedures may be mandated to be included in the protocol design:

1. What is the frequency and volume of any blood or bodily fluid specimens to be obtained both in the study and as required in supportive care?
2. Is the biopsy necessary for the participant’s care and/or management?
3. What are the costs and social implications for the participant?
4. What is the complexity of the invasive procedure (i.e., is the area difficult to biopsy or does the procedure require hospitalization)?
5. What is the scientific knowledge to be derived from the PK/PD study results?

The IRB will apply the following criteria when evaluating clinical protocols that contain a PK/PD component.

**Criteria for Including Minimally Invasive PK/PD Procedures in Clinical Protocols**:¹

For Phase 1 and 2 clinical protocols, PK/PD procedures will be permitted if the procedures are no more than minimally invasive and provide information regarding the study drug/agent. A minimally invasive procedure includes a blood draw or biopsy when the area to be biopsied is easily accessible and the risk of hospitalization from the procedure is relatively low (e.g., less than 1% chance of hospitalization).

For these studies, the PK/PD procedures may be included as a requirement for trial participation, even if not a part of the primary trial objectives.

The IRB will evaluate the inclusion of PK/PD involving minimally invasive procedures for Phase 3 clinical protocols on an individual study basis. For Phase III studies in which the PK/PD are not expected to provide direct benefit for the participant, the PK/PD studies will be optional at the discretion of the IRB. Consideration will be given to studies that are critical for future application of the drug and supported by sound hypotheses and rigorous statistical testing.

Examples of PK/PD involving minimally invasive procedures include:

- Lymph node aspiration
- Needle biopsy
Criteria for Including PK/PD Procedures that Represent a Higher Risk of Hospitalization in Clinical Protocols:

In clinical protocols in which the PK/PD procedure represents a higher risk of hospitalization (e.g., more than 1% chance), PK/PD procedures may be included if scientifically necessary. The PK/PD procedure should be listed as part of the protocol's primary or secondary objectives. The IRB has set the following criteria for these protocols:

- **Phase 1:** PK/PD procedures may be required for participation in the protocol.
- **Phase 2:** PK/PD procedures may be a required or an optional part of the study as determined by the IRB.
- **Phase 3:** PK/PD procedures may be allowed based on assessment of risk and potential for direct benefit for study participants.

Examples of PK/PD procedures that represent a higher risk of hospitalization include:

- Conscious sedation anesthesia
- Liver biopsy

Possible Actions of the IRB for Non-Compliance with this Policy:

The IRB actions may include, but are not limited to the following:

- Accepting an investigator's corrective action plan, and requiring no further action
- Requiring the investigator to make changes to the Informed Consent Document
- Requiring the investigator to make changes to the protocol, and other study documents
- Requiring re-consenting or informing of current and/or previously enrolled research participants (to occur whenever the information may relate to the participants' willingness to continue participation in the research)
- Requiring steps to reduce immediate risks to participants or others
- Requiring modification of the continuing review schedule
- Suspending or terminating the research protocol (according to the IRB policy for suspension and terminations)
- Requesting additional information
- Conferring with other institutional departments (e.g., Legal Services, Institutional Compliance, Research Education and Regulatory Management, or the Institutional Official)
- Requesting a targeted audit of the investigator’s research protocols
• Consulting with the investigator's Division or Department Chair
• Assigning oversight of the protocol to an independent monitoring board (e.g., Data Safety Monitoring Board or outside entity, if appropriate)
• Requiring education and training of investigator and research staff
• Initiating other actions appropriate for the local context

Within 30 days of notification, the IRB will report any serious or life-threatening issues related to the research to the Institutional Official, the supporting agency and/or OHRP, as required by this policy.

Penalties for Non-Compliance:

Failure to comply with this policy may result in temporary or permanent suspension of the research and/or the investigator's research privileges.

In accordance with 45 CFR 46.113, any suspensions or terminations of approval will be reported promptly to the investigator, to the appropriate institutional officials, and possibly the federal department or agency head responsible for oversight or funding of the research.

1 For purposes of this policy, a determination that a procedure is “minimally invasive” is not equivalent to a determination of “minimal risk” as defined in the Code of Federal Regulations (45 CFR 46.110 and 21 CFR 56.110).

REFERENCES

21 CFR 56.111
45 CFR 46.111

REVISIONS

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This policy has been revised as of February 24, 2010. The revised, IRB approved policy can be found below. The policy is effective March 3, 2010, and thus will not affect currently activated studies or those studies that have already received IRB approval.

For a copy of the previous policy, please see (2002-06-02: IRB Memorandum Regarding the Inclusion of Pharmacokinetics in Clinical Research).