IN VITRO DIAGNOSTIC (IVD) RISK DETERMINATION WORKSHEET

MIAP (MICHR IND/IDE Investigator Assistance Program)

INSTRUCTIONS

The following worksheet is intended to help UM Sponsor-Investigators determine if an IDE application to the FDA may be required prior to initiating a new clinical study. This document should be completed for all of the IVD(s) utilized in your study, and then provided to the IRB in support of an eResearch application prior to initiating a Clinical Trial.

- Complete only for IVDs utilized in your study that do not meet the exemption criteria (see section 16.2.6 of the eResearch application).
- This worksheet must be completed & signed by the UM Sponsor-Investigator.
- Contact MIAP @MICHRMIAP@med.umich.edu for questions or assistance with completing this form.

FDA DEFINITIONS

Significant Risk: "A significant risk device presents a potential for serious risk to the health, safety, or welfare of a subject. Significant risk devices may include implants, devices that support or sustain human life, and devices that are substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment to human health.

Non-Significant Risk: "Non-significant risk (NSR) device – a device that does not meet the definition of significant risk (SR) device.

In Vitro Diagnostic (IVD): "In vitro diagnostic (IVD) products – those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

Links to FDA guidance

- IVD Device Studies - FAQs
- Investigational IVDs Used in Clinical Investigations of Therapeutic Products

UM SPONSOR-INVESTIGATOR / SPONSOR NAME: _____

DEVICE NAME: _____ **HUM #:** _____

PROTOCOL/STUDY TITLE:

_____

IVD RISK DETERMINATION CRITERIA	Yes	No
1. Does the specimen collection procedure present a risk that is not part of standard of care procedures for the subjects?	☐	☐

Base this determination on the nature of the harm that may result from sampling. The risks related to tumor tissue biopsy depend upon the site of the tumor, the procedure used, and the patient population. For example, the FDA considers the following significant risk procedures: including (but not limited to) biopsies of major organs, bone marrow, or endoscopic procedures extending beyond the esophagus, stomach or bowel. Depending upon the population, FDA considers sampling procedures that require use of general anesthesia, or placement of a blood line access to an artery or large vein (subclavian femoral, or iliac) to present a significant risk.

Please explain your answer to #1

	Yes	No
2. Will use of the results from an investigational IVD lead to some study subjects foregoing or delaying a treatment that is known to be effective?	☐	☐

For example, in an investigation for a population that has no other treatment options, has exhausted all other treatment options, or for which standard of care provides only marginal benefit, the potential harm caused by an erroneous result from the investigational IVD use may be lower than for subjects who are newly diagnosed.

Please explain your answer to #2

	Yes	No
3. Could misdiagnosis and/or error in treatment caused by inaccurate results be life-threatening, or could it result in permanent impairment of a body function or permanent damage to a body structure to study subjects?	☐	☐

For example, false positive results can lead to unnecessary confirmatory testing, unnecessary treatment that can be invasive or have harmful side effects, and/or unnecessary psychological trauma when serious or life-threatening diseases or conditions are involved. False negative results can lead to a delay in establishing the correct diagnosis, failure to start or continue needed treatment, false security that may prevent timely follow-up and re-testing, and contribute to the potential spread of infectious agents to others.

Please explain your answer to #3

Does your research involve the use of an investigational IVD as part of a study of a therapeutic product (Investigational drugs or biologics)?

If **yes,** answer questions **4** and **5 below.**	If **No,** go directly to **Conclusion.**

CLINICAL INVESTIGATIONS OF THERAPEUTIC PRODUCTS	Yes	No
4. Will use of the results from an investigational IVD expose study subjects to safety risks (e.g., adverse events from the investigational therapeutic product) that exceed the risks encountered with the control arm therapy or non-trial standard of care?	☐	☐

When a drug has minimal side effects, for instance, the risk associated with the use of the investigational IVD for enrollment or assignment to treatment arms will generally be lower because an erroneous test result would not be expected to cause serious harm. However, in a study of an investigational therapeutic product with significant toxicity, the risk associated with the investigational IVD use will generally be greater because an erroneous test result could unnecessarily expose a subject to the therapeutic product's toxicity.

Please explain your answer to #4

	Yes	No
5. Is it likely, based on existing knowledge about the relationship between the biomarker and the investigational therapeutic product, that incorrect results from the investigational IVD would present a potential for serious risk to study subjects?	☐	☐

For instance, if there is strong (e.g. clinical) evidence that an investigational therapeutic product with serious side effects may be effective only in a marker-positive population, then an investigational IVD used to identify marker-positive subjects is likely to be of higher risk, regardless of the relative safety and efficacy of the standard of care alternative therapies.

Please explain your answer to #5

CONCLUSION

Significant Risk	Non-Significant Risk
If you answered **Yes** to any of the above questions, the use of the IVD in this study could be considered **Significant Risk (SR).** In addition to IRB approval, SR device studies must have an IDE application approved by the FDA before they may proceed.	If ALL of the questions were answered **No,** then the use of the IVD in this study may be considered **Non-Significant Risk**. NSR device studies do not require an IDE application. If the IRB agrees with the NSR assessment and approves the IRB application, the study may proceed under an abbreviated IDE under 21 CFR 812.2(b).

Signature	Name	Date
☑ UM Sponsor-Investigator ☐ Sponsor		