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Table 1. Criteria for the use of omics-based predictors in NCI-supported clinical trials

Domain	Criterion
Specimen Issues	1. Establish acceptable methods for specimen collection and processing and appropriate storage conditions to ensure the suitability of specimens for use with the omics test.
	2. Establish criteria for screening out inadequate or poor-quality specimens or isolated analytes prior to performing assays.
	3. Specify the minimum amount of specimen required.
	4. Determine the feasibility of obtaining specimens that will yield the quantity and quality of isolated cells or analytes needed for successful assay in clinical settings.
Assay Issues	5. Review all available information about standard operating procedures (SOPs) used by the laboratories that performed the omics assays conducted as part of the developmental studies, including technical protocol, reagents, analytical platform, assay scoring, and reporting method, to evaluate the comparability of the current assay to earlier versions and to establish the point at which the omics test was definitively locked down.
	6. Establish a detailed SOP for the conduct of the assay, including technical protocol, instrumentation, reagents, scoring and reporting methods, calibrators and analytical standards, and controls.
	7. Establish acceptability criteria for quality of assay batches and for results from individual specimens.
	8. Validate assay performance by using established analytical metrics such as precision, accuracy, sensitivity, specificity, linear range, limit of detection, and limit of quantification, as applicable.
	9. Establish acceptable reproducibility among technicians and participating laboratories and ensure adherence to a detailed SOP.
	10. Establish a turnaround time for test results that is within acceptable limits for use in real-time clinical settings.
Model Development, Specification, and Preliminary Performance Evaluation	11. Verify all data used in the process for developing the predictor model or conduct a retrospective evaluation to check for accuracy, completeness, and outliers.
	12. Assess the developmental data sets for technical artifacts (e.g., effects of assay batch, specimen handling, assay instrument or platform, reagent, or operator), focusing particular attention on whether any artifacts could potentially influence the observed association between the omics profiles and clinical outcomes.
	13. Evaluate the appropriateness of the statistical methods used to build the predictor model and to assess its performance.

Domain	Criterion
	14. Establish that the predictor algorithm, including all data preprocessing steps and cutpoints (if any), are completely locked down and identical to prior versions for which performance claims were made.
	15. Evaluate whether previously reported clinical validations of the predictor were analytically and statistically rigorous and unequivocally blinded.
	16. Establish the reproducibility of the predictions, including verification that the prediction algorithm can be applied one case at a time and does not depend on other specimens processed simultaneously.
	17. Summarize the expected distribution of predictions in the patient population to which the predictor will be applied, including the distribution of any confidence metrics associated with the predictions.
	18. Review any studies reporting evaluations of the predictor's performance and determine their relevance for the setting in which the predictor is being proposed for clinical use.
	19. Search public sources to determine whether any questions have been raised about the data or methods used to develop the predictor or assess its performance, and ensure that all prior questions have been adequately addressed.
Clinical Trial Design	20. Provide a clear statement of the target patient population and intended clinical use of the predictor and ensure that the expected clinical benefit is sufficiently large to support its clinical utility.
	21. Determine whether the clinical utility of the omics test can be evaluated by using banked specimens from a completed clinical trial (e.g., prospective–retrospective study).
	22. If a new prospective clinical trial will be required, evaluate what aspects of the proposed predictor have undergone sufficiently rigorous validation to allow treatment decisions to be influenced by predictor results; where treatment assignments are randomized, provide justification for equipoise.
	23. Develop a clinical trial protocol that contains clearly stated objectives and methods and an analytic plan that includes justification of sample size; lock down and fully document all aspects of the omics test and establish analytic validation of the predictor.
	24. Establish a secure clinical database so that links among clinical data, omics data, and predictor results remain appropriately blinded, under the control of the study statistician.
	25. Include in the protocol the names of the primary individuals who are responsible for each aspect of the study.
Ethical, Legal, and Regulatory Issues	26. Establish communication with the individuals, offices, and agencies that will oversee the ethical, legal, and regulatory issues that are

Domain	Criterion
	relevant to the conduct of the trial.
	27. Ensure that informed consent documents to be signed by study participants accurately describe the risks and potential benefits associated with use of the omics test and include provisions for banking of specimens, particularly to allow for "bridging studies" to validate new or improved assays.
	28. Address any intellectual property issues for use of the specimens, markers, assay, and computer software used for calculation of the predictor.
	29. Ensure that the assay is performed in a CLIA-certified laboratory if the results will be reported to the patient or his or her physician at any time, even after the trial has ended or the patient is no longer participating in the study.
	30. Ensure that appropriate regulatory approvals have been obtained for investigational use of the omics test.