ICMR Bioethics Unit

INDIAN COUNCIL OF MEDICAL RESEARCH

GUIDANCE ON ETHICAL REQUIREMENTS FOR LABORATORY VALIDATION TESTING

JANUARY 2024

Ethical Requirements for Laboratory Validation Testing

1. Background:

1.1. Laboratory validation tests are used to ensure that laboratory test data and results are accurate, consistent, and precise. These are processes that are documented and standardized to establish that the methods or instruments used will provide consistent results within the prescribed acceptance criteria to be clinically applicable. Validation is defined as e*stablishing documented evidence that provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes*.

1.2. Validation test or processes in laboratory medicine may typically refer to the multi-tiered process of evaluating the performance of a new instrument or test methodology, that is currently in use for diagnostics. A validation may be extensive, e.g., to validate a newly developed in-house method, or it could be narrow in scope, e.g., to validate a commercial method that is already in use and has had minor modifications. Validation is different from evaluation which is used to describe the measurement of performance capabilities of a test method and is a systematic and extensive process.

2. Scope:

2.1. This guidance refers to the Laboratory Validation Tests which may include tests to ensure reproducibility, sensitivity, specificity, accuracy, reliability, fitness for purpose, quality control/assurance purposes etc. done using residual/ archived/ unlinked/ anonymous samples.

2.2. It does not include independent evaluation of novel products/ innovations for which clinical evaluation is required and may involve regulatory pathways.

3. Laboratory Validation Testing vs Biomedical and Health Research Involving Humans:

3.1. Biomedical and health research on humans includes studies are designed primarily to increase the scientific knowledge about diseases and conditions (physical or socio-behavioral), their detection, cause, and evolving strategies for health promotion, prevention, or amelioration of disease and rehabilitation including clinical research. Therefore, biomedical research explores scientific questions related to human health and disease.

3.2. Lab validation testing typically focuses on lab methods undertaken in a controlled environment to ensure the accuracy and reliability of results and not for exploring broader scientific questions to understand human health and diseases.

3.3. All laboratory tests must be validated before being introduced for patient testing to ensure that the values reported will meet clinical expectations with a desired degree of

reliability. It involves standard clinical/ laboratory diagnostic practices or the advancement of standard practices, without any active recruitment of participants.

3.4. The validation testing must not in any way influence patient diagnostics, management, or treatment and has no bearing on health-related outcomes for a patient.

4. Ethical Considerations:

4.1. Laboratory Validation Testing employs samples or biological materials or biological specimens such as blood, urine, tissue, cells, saliva, DNA, etc. Often these could be pooled samples collected from multiple individual samples. The samples must not have been collected specifically for this purpose but are available as archived samples which are dis-associated/ delinked/ unidentified/ pooled/ anonymous samples and available without any patient information and thus pose no risk to patient's confidentiality.

4.2. If the biological samples are linked to different types of personal identifiers (name, address, etc.) or with health-related data (chronic illnesses, prior hospital stays), and other types of potentially sensitive data (travel history, family history) there is a risk for breach of confidentiality and such samples are not recommended for Lab Validation Testing without ethics approval from ethics committee (EC).

4.3. The laboratory must not tend to collect or extract more samples to be used for future validation testing (for example, draw more blood volume for use later) than would typically be needed for the diagnostic procedure. Any extra blood draws would require appropriate ethics approval and informed consent of the patient.

4.4. At the time of sample collection, if there is a probability of future usage of samples, appropriate informed consent must be obtained from the patients. The informed consent must clearly mention the plan for future testing purposes or storage.

4.5. The investigator undertaking Laboratory Validation Testing must keep the ethics committee informed regarding use of leftover/ archived/ anonymous samples. The laboratories involved in the validation of tests/ methods, may be exempted from ethical approval using leftover archived and anonymized samples.

4.6. Regulatory testing carried out at National Control laboratories, involving leftover or stored samples in biorepositories (hospitals, diagnostic labs, blood banks, IRCS, etc.) may require administrative approvals from institutional authority and not necessarily ethical approval provided the samples are anonymized and no extra sample is drawn from patients.

5. Administrative approval:

5.1 Sites participating in the Lab Validation Testing must ensure that institutional authorities are kept duly informed before undertaking any Laboratory Validation Testing.

5.2 The investigator must commit to Good Laboratory Practice Guidance, fill the checklist (Annexure II) and provide a self-declaration to the ethics committee and to the department/ or the relevant institutional authorities/ Head of the Institution.

5.3 The commercial implications related to Lab Validation Testing must not compromise the scientific integrity and all efforts must be taken to avoid biases in the lab validation testing.

5.4 After completion of Lab validation testing, a summary of the number and type of samples used in validation testing should be provided to the institutional authorities as well as the ethics committees.

Recommendations:

- **If the Laboratory Validation Testing involves the use of anonymous or de-identified samples and focuses on parameters such as sensitivity, or specificity, etc., without the intention of conducting research or influencing patient treatment/ management and does not involve any novel/ innovative diagnosis/ technology, the proposal for laboratory validation testing is exempted from ethics committee review.**
- **A self-declaration form (Annexure-II) to be submitted by the investigators to the institutional authorities and ethics committee for information.**

References:

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Annexure I

Potential Scenarios of Laboratory Validation Tests

SN	Type of study	Scenarios	Implications on patients	Examples	Risk assessment	Privacy and confidentiality	Informed consent	Ethics approval
1	Analytical validation	Studies that use residual or stored samples	None	Stored residual sputum or blood samples used for testing analytical sensitivity/ specificity of test kit	No harm/ discomfort	Samples anonymized	Not required	Not required
2	Clinical validation	Sample collected from patient/ healthy donors as per routine practice. No additional sample is collected for the study.	None	Sputum sample is collected for routine diagnosis of TB. One part of the sample is used for clinical diagnosis as per routine practice. One part of the sample is used for performance evaluation of test kit	No harm/ discomfort	Samples anonymized	Not Required	Not required
3	Clinical validation- Non-invasive samples	Additional sample collected with no discomfort to patient	Possibility of negative implications	Extra volume of sputum sample collected for the study	Minimum harm/ discomfort	Samples anonymized	Required	Required (Expedited review by the EC)
4		Additional sample collected with minimum discomfort	Possibility of negative implications	Extra volume of induced sputum or extra nasal swab collected for the study	Minimum harm/ discomfort	Samples anonymized	Required	Required
5	Clinical validation- Invasive samples	Additional sample collected with no discomfort to the patient	Possibility of negative implications	Extra volume of blood drawn at the same time with no additional needle prick	Minimum harm/ discomfort	Samples anonymized	Required	Required (Full EC review)

6		Additional sample collected with minimum discomfort	Negative implications	Extra needle prick or insert required for the study	Minimum harm/ discomfort	Samples anonymized	Required	Required (Full EC review)
7	Repeat tests- Non-invasive samples	Additional sample (sputum or swab) collected with extra visit	Negative implication	Patient is called for additional visit to collect repeat sputum or swab sample (to resolve discrepancies, indeterminate/ inconclusive results, contamination etc)	Minimum harm/ discomfort	Samples anonymized	Required	Required
8	Repeat tests- Invasive samples	Additional sample collected (blood) with extra visit	Negative implication	Patient is called for additional visit to collect repeat blood sample	Minimum harm/ discomfort	Samples anonymized	Required	Required (Full EC review)
9	Additional lab investigations	Additional lab investigations performed for the study from the sample collected for routine diagnosis	None	Quantification of cytokines or CD4 count from the serum or blood collected for routine diagnosis	No harm/ discomfort	Samples anonymized	Required	Information to EC/ Institutional head/ Authorities
10	Concordance testing	Concordance testing of new version/ system/ make with existing version/ system using residual or stored samples	None	Concordance of fully automated version with partially automated version, high throughput version vs modules with lesser samples	No harm/ discomfort	Samples anonymized	Not required	Not required

Annexure II – Self Declaration Form to be filled by the Investigator and checklist for Laboratory Validation Tests projects/protocols

Title:

S No.	Criteria	Yes	No
1.	Lab Validation Tests will be conducted on samples that are dis-associated/ delinked/ unidentified/ pooled/ anonymous samples irreversibly without any patient information.		
2.	Lab Validation Tests utilize samples already collected for routine laboratory practices and would involve testing related to accuracy, sensitivity, specificity, reliability, reproducibility, precision, fitness for purpose and quality control/ assurance.		
3.	Lab Validation Testing/ management is the sole purpose of this process and research/ hypothesis testing/ publication is not an intent.		
4.	Lab Validation Tests does not require the collection of clinical information or additional samples from patients.		
5.	Lab Validation Tests doesn't directly or indirectly identify or impact patient health, disease treatment or management or other similar scenarios in present or at a future date.		
6.	Lab Validation Testing doesn't involve using any new diagnosis/ innovative/ novel methods or technology/ discovery/ drug development.		

If the answer to all the above-mentioned criteria is 'Yes', you can proceed with the declaration.

☐I am hereby declaring that the above-mentioned information about this Lab Validation Tests is true to best of my knowledge.

Place: Signature:

Date: Name:

Head of the department Head of the institution

Note:

1. *If the answer to all the above-mentioned criteria is 'Yes', this form should be submitted to the ethics committee for information attested by the head of the department and head of the institution before undertaking Lab Validation Test.*
2. *If the answer to any of the above-mentioned criteria is 'No', the proposal should be submitted for ethics committee review and approval before undertaking the Lab Validation Test.*

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