Planning and managing validation: A Generic Validation proforma

1. Validation / Verification Details

- Section 1 should be completed as far as possible to establish the goals and general format of the validation / verification.
  - Sections 1.1 “**Intended use or application**” and 1.2 “**Requirements**” *must* be completed at the start of the procedure. The assessment of the validation/verification depends formally on confirmation, through the provision of objective evidence, that these requirements have been fulfilled.
  - If mentioned (1.2), the “Expected Performance” should be distinguished from the “Requirements”, which must be shown to have been fulfilled.

E.g. *The statement “should detect all known point mutations of hemophilia A” could be included as a guide in the Expected performance; if stated as a requirement, however, it would need to be proved.*

1.1 Test details

Test name	Internal descriptive name	**Reference**	Internal ref.

Intended use or application	Outline the intended results of the test and how they will be used including any interpretative considerations; linked to 1.2 Performance Requirements.
Locus / Gene / Marker	Specify analyte[s]
Reference Sequence	e.g. NCBI accession number
Outline methodology	Describe the technology and how it will be employed
SOP	Reference internal SOP
References	List any relevant documentation both internal and external indicating the derivation of the test and including performance specifications, publications and any previous validations

1.2 Validation details

Overall Aims	State clearly the overall aim of the validation
Requirements	Define the levels of performance that must be attained (accuracy, precision and any other performance requirements such as robustness or maximum failure rate). Linked to 1.1 Intended Use or Application and
Validation / Verification	State whether the study is a validation or verification and the justification for this course of action.
Type	State the type of test and if the validation is to be performed at implementation or on an ongoing basis.
Scope / limitations	List any pre existing limitations (e.g. test to be performed on DNA extracted from EDTA peripheral blood samples only)
Turn around time	The required TAT
Other considerations	List any other factors that may affect the utility of the test for the intended purpose. Expected performance can be mentioned here.

2. Validation of Utility

- Section 2 covers the validation of utility which should be carried out for all validations and verifications. In the majority of cases this section can be completed on objective evidence from developmental work, design procedures (e.g. SNP checking primers) or by the use of limitations or controls in the on-going test. Where this is not the case, work plans for relevant parameters should be prepared as in 3 below.

2. Validation of Utility

Applicability of measurements	Is what is being tested appropriate and sufficient to achieve the desired results?
Selectivity	Detail any test specific selectivity issues together with limitations and/or control measures taken to ensure test utility. A validation work plan (section 3) should be drawn up for any specific potential selectivity issues that cannot be eliminated by limitation or control measure[s].
Interferences	Detail any test specific interference factors together with limitations and/or control measures taken to ensure test utility. A validation work plan (section 3) should be drawn up for any specific potential interference that cannot be eliminated by limitation or control measure[s].
Cross-reactivity	Detail any test specific cross-reactivity together with limitations and/or control measures taken to ensure test utility. A validation work plan (section 3) should be drawn up for any specific potential cross-reactivity that cannot be eliminated by limitation or control measure[s].

3.*n* Validation / Verification for [insert parameter]

- Appropriate parameters for experimental investigation should be identified with the aid of the table appendix A – a checklist is also provided at the top of section 3. For each parameter required, the investigating scientist develops a work plan based on section 3 (these are referenced 3.1, 3.2 to 3.*n*) by completing copies of sections 3.*n*.1 ('Aims', 'Samples' and 'Methodology'). It is suggested that these be maintained in a single document.

☐ **Sensitivity**	☐ **Trueness**	☐ **Reproducibility**	☐ **Limit of quantification**
☐ **Specificity**	☐ **Repeatability**	☐ **Robustness**	☐ **Linearity**
☐ **Accuracy**	☐ **Intermediate precision**	☐ **Limit of detection**	☐ **Measurement uncertainty**

3.*n* Validation / Verification for [insert parameter]

- The work plan[s] should be agreed and authorized by the investigating and the senior scientist by signing and dating in the boxes provided.
- The experimental work is performed and analysed by the investigating scientist who should then complete the 'experimental results' and 'interpretation' sections 3.*n*.2.
- The 'outcome and limitations' should be agreed between the investigating and senior scientists by signing and dating in the boxes provided.
- Points 3 to 6 should be repeated for each parameter to be tested.

Authorization	Name	Signature	Date
Investigating scientist			
Senior Scientist (Authorization)			

3.*n*.1 Work plan

Section aims	Describe the specific aims of this section of the validation
Samples	Describe the samples to be used including [where relevant] numbers and type[s] of mutations present, relevant physical characteristics and how the sample status has been derived (i.e. the reference or 'gold standard' test). It may be appropriate to reference another document or database here.
Methodology	Describe the method to be used to evaluate the specific parameter

3.*n*.2 Partial results and conclusions

Experimental results	Summarise the experimental results Cross-reference to or include the data.
Interpretation	Summarise the interpretation of experimental results (e.g. estimated level of accuracy with confidence limits)
Outcome / limitations	➲ State whether the results fulfil the validation requirements listed in 1.2 ➲ List any specific derived limitations to reproduce the outcome (e.g. controls and how they should be used)

3.1.2 Partial results and conclusions

- If there is any non compliance between the experimental results and the required performance specification detailed in section 1.2 the parameter in question should to be re-examined to determine if the methodology can be changed or new limitations introduced to rectify the non-compliance. Any further work should be recorded in a new section 3 work plan. Alternatively the implementation can be abandoned.

4. Validation / Verification Final Conclusions

- Once all the parameters have been satisfactorily investigated the investigating and senior scientist can agree and sign off the final conclusions in section 4.

Authorization	Name	Signature	Date
Investigating scientist			
Senior Scientist (Authorization)			

4. Validation / Verification Final Conclusions

Overall Conclusion	State explicitly if the requirements in 1.2 have been fulfilled; Give any other relevant conclusions.
Estimates of accuracy and measures of uncertainty	Give experimentally-derived values for the relevant metrics. Comment on the potential influence of the uncertainty on the reliability of the result.
Limitations and/or predictable interferences	List all limitations and control measures required to maintain the on-going test performance
Internal QC	Detail internal quality control measures to be implemented, addressing in particular the limitations and interferences identified.
External QA	Details of external quality assurance measures

Implementation plan

- Assuming the validation / verification has been completed satisfactorily an implementation plan can be drawn up. Appendix B provides a basis for an administrative checklist for the implementation.

Administrative checklist

- [ ] Validation completed and approved
- [ ] Complete SOP
- [ ] Order reagents
- [ ] Health and safety aspects (personal, reagents)
- [ ] Equipment (electrical testing, maintenance)
- [ ] Subscribe to EQA
- [ ] Update request forms
- [ ] Update website and any directory listings
- [ ] Billing procedure
- [ ] Training
- [ ] LIMS functionality
- [ ] Worksheets
- [ ] Inform clients
- [ ] Report template