

Testing Strategies

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Because no anti-HIV test is absolutely sensitive or specific combinations of tests must be used to achieve close to the required 100% predictive values for the results on all testing. The blood transfusion services have adopted a no risk policy and demand close to 100% sensitivity with extremely high levels of specificity. Diagnostic laboratories demand error-free diagnoses. Thus, tests have been selected to identify any sample containing antibody whether true antibody or cross-reactive antibody, as reactive (Figure). Further other tests incorporate antibody so that either antibody or antigen is identified making the likelihood of missing early infection, less. Supplemental testing aims to differentiate true from false reactivity. Different strategies have been used in different situations.

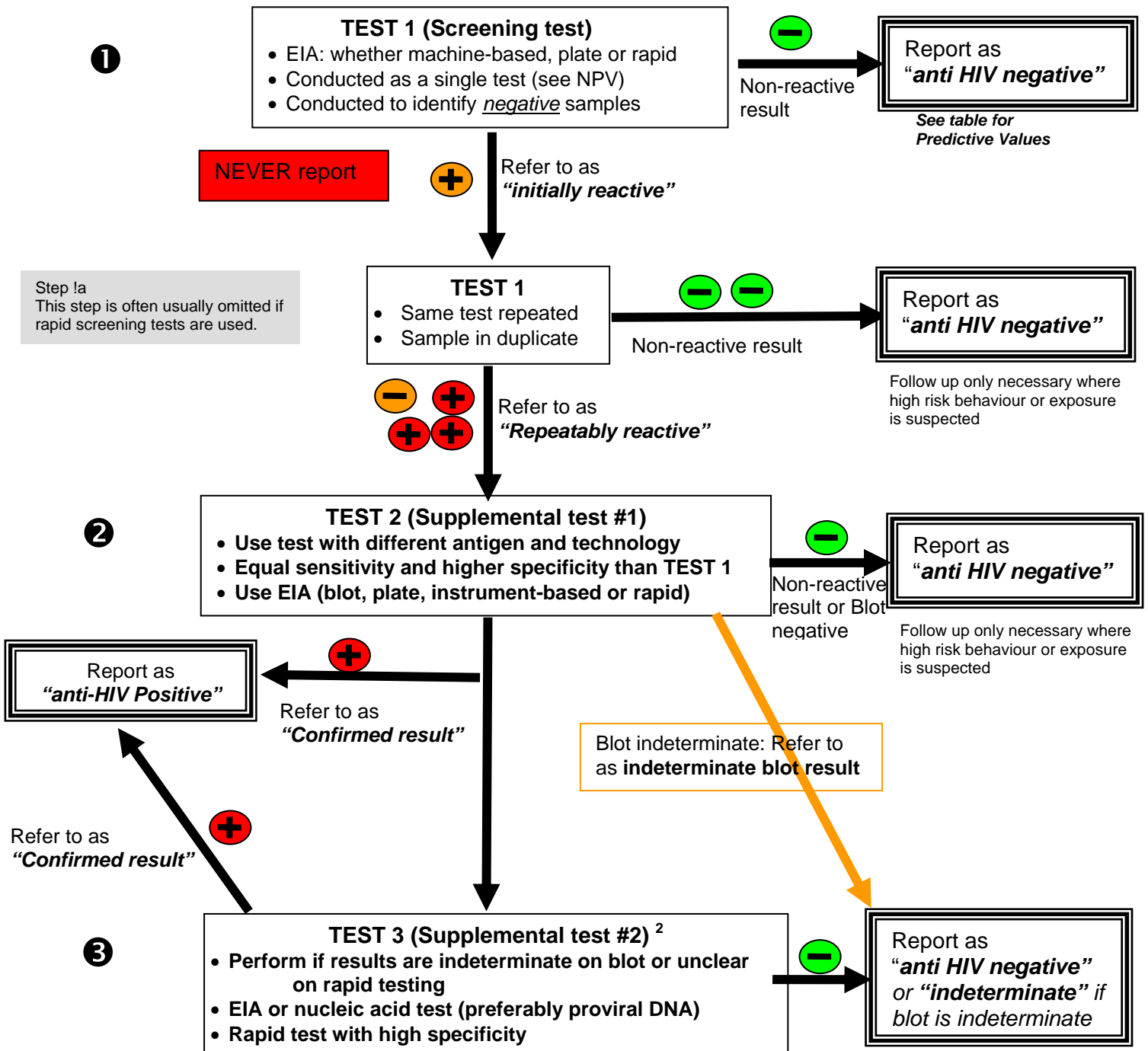
Diagnosis of HIV Infection

The diagnosis of HIV Infection is usually carried out by first performing a screening EIA on a serum or plasma sample. A negative result in an EIA can confidently be diagnosed as "Anti-HIV Negative" because of the extremely high negative predictive values in these tests. It is often written and said that false negative EIA results occur very early or very late in infection when antibody levels are low. Strictly speaking these results are not false negative results *of the test* but of the strategies because if antibody is not present or below the limit of detection obviously the screening anti-HIV EIA cannot detect it! Thus screening strategies employing NAT, to push back the time of diagnosis when antibody is absent or below detection have been adopted in blood screening strategies (see below). A Western blot is carried out in samples that give a reactive screening result. If the band pattern on a blot fulfils the criteria for a positive result the sample is confirmed as "Anti-HIV positive". However, Western blots are only specific by virtue of the combination of band patterns. Therefore it is quite common to have "indeterminate" patterns and the problem of dealing with the reporting of these has not satisfactorily dealt with in other countries. The National Serology Reference Laboratory (NRL), Australia developed strategies for dealing with indeterminate results in 1989-1990. Four groups of indeterminate results were found in a retrospective follow-up of plasmas with indeterminate results. It was found that only about 25% of samples from individuals with a p24 band sero-converted while those with gp41 bands had a high likelihood of sero-conversion⁵. These were designated Groups III and IV respectively. Cross-reactive band patterns that are common (e.g. p18 and p32) and that do not predict sero-conversion (Groups I and II in the original classification), are now no longer regarded as significant when they appear in isolation or with nonspecific bands, and the sample is given the status of "Anti-HIV negative". If an individual is sero-converting, the Western blots used presently will show changes within a very short time (days). There fore the tests may be repeated in close proximity and are best understood if the testing of the second sample is rerun in parallel with the first, so that the changes can be assessed without the complicating factor of inter-run variation. Individuals who give the same indeterminate band patterns on follow-up after a reasonable time (e.g. 3 months) are given a report of "Anti-HIV negative."

It should be noted that if a sample is found to be anti-HIV positive for the first time, a second sample from that person should be obtained and tested to assure that there was no sample mix-up through the process.

It is worth noting that a poorer performing kit used properly will give more reliable results than a high performance kit used poorly. There are many indications that the quality of performance in many laboratories is not optimal. There is a need for quality management systems and quality assurance (the mechanisms for supplying indicators of quality management) to be implemented and maintained. It is not recommended that any testing strategies be implemented without appropriate evaluation of the kits and verification that they operate appropriately in combination – no matter what the test or test type.

The Logic of HIV Testing Strategies¹



¹ A testing “strategy” is a generic name. When the actual tests to be used are specified, the term is a testing “algorithm”.

² Western blot testing proficiency should be maintained in national reference laboratories.