HIV misdiagnosis:
Assuring the quality of test kits

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Likely drivers of misdiagnosis

- WHO systematic review showed misdiagnosis of HIV-positive status was common (range: 0.28-10.5%)

- WHO recommended testing strategy not used
  - use of Assay 3 as tiebreaker to rule in HIV infection
- National testing algorithm not validated
- Poor training and supportive supervision of testers
- Instructions for use issued by manufacturer not observed by end-users
  - Irregular reading of weakly reactive test lines
  - Reading results before minimum reading time
  - Incorrect storage of test kits

Misdiagnosis of HIV cont'd

Impact of ARVs on sensitivity

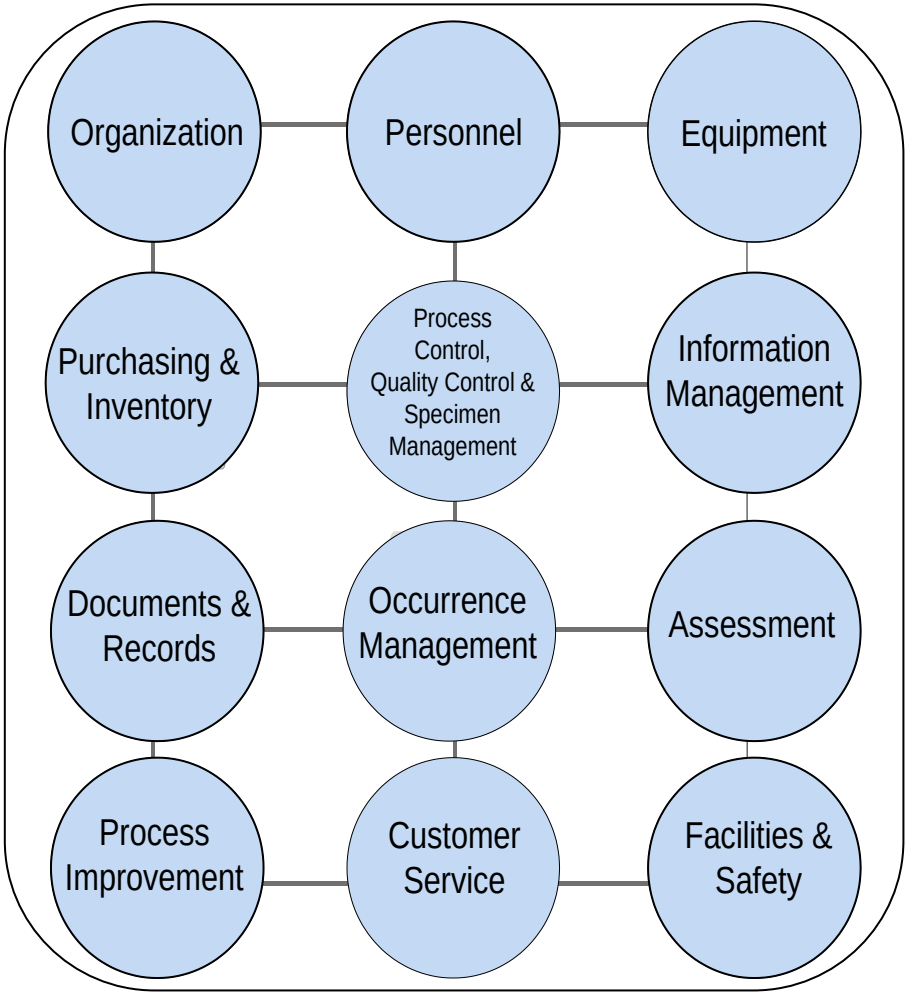
- Antibody production is affected by early initiation of ART
  - ↓ sensitivity for older generations of assays (1st/2nd)
  - ↓ sensitivity for oral fluid RDTs
- Detection of nucleic acid is affected by ARV
  - Plasma RNA is suppressed
  - But cell-associated DNA is not likely be affected by ARV

Impact of x-reactivity on specificity

- Same antigen sources used
- ↑re-branding arrangements, same assay is available under different brand names
- False reactive results due to interfering substances and concomitant infections

Importance of quality systems

- 12 aspects are critical to assure the quality of testing
  - Purchasing and inventory
    - Standards for test kits procured
  - Personnel
    - Training and supervision
  - Assessment
    - EQA (proficiency testing)
  - Post-market surveillance
    - Through records/documentation/ occurrence management



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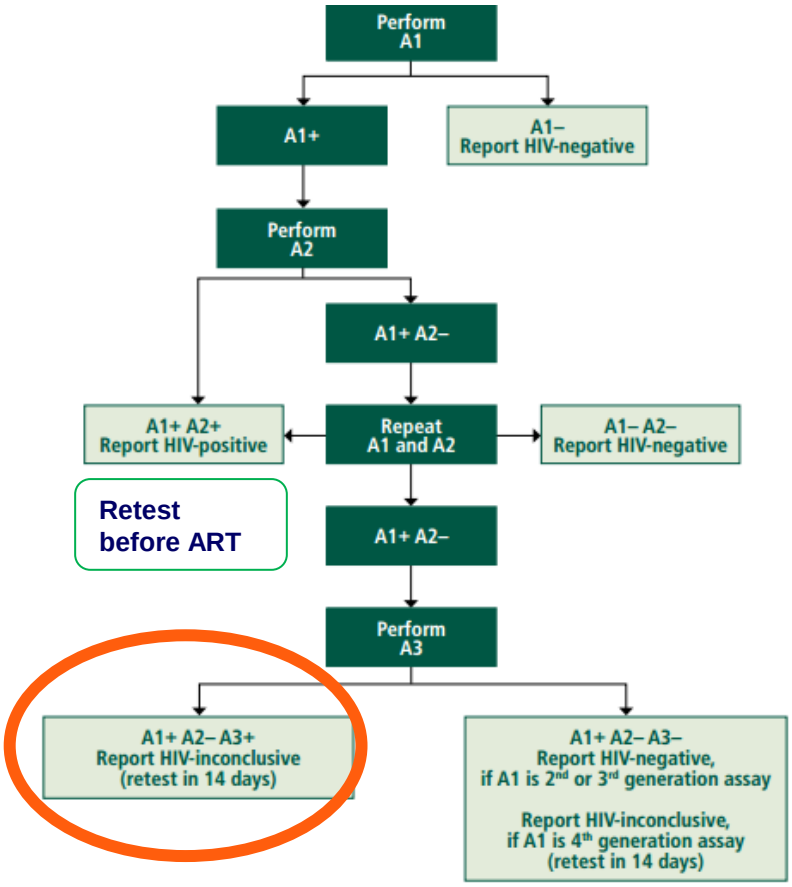
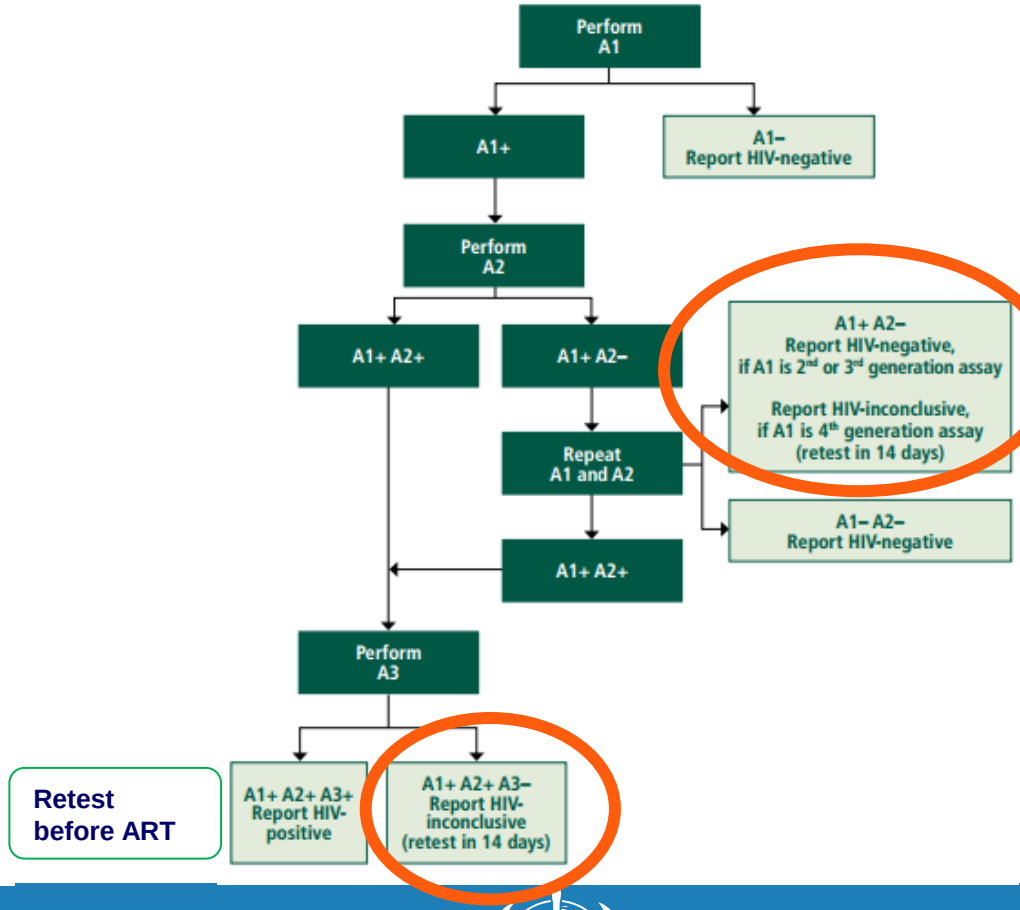
WHO testing strategies

High prevalence (>5 %)



Low prevalence (<5%)



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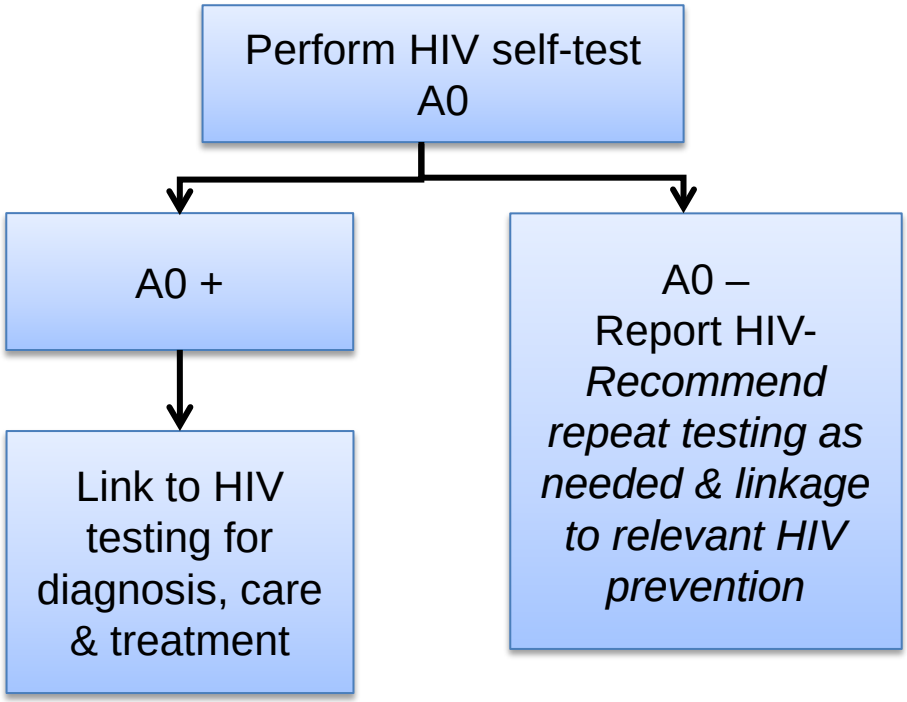
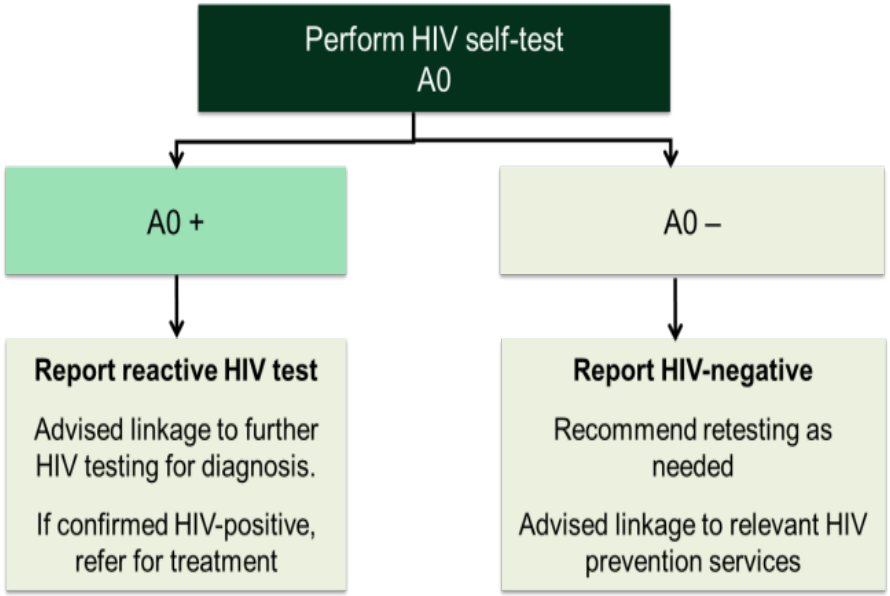
New HIV testing approaches

Test for triage



HIV self-testing



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Re-testing recommendations

- What is retesting?
  - Same testing algorithm, different specimen different testing site
- Objective?
  - To rule out/rule in seroconversion
  - To rule out operator error, test device error, transcription errors
- Who should be re-tested
  - Individuals with **HIV-inconclusive** status after 14 days
  - Individuals with **newly diagnosed HIV-positive** status prior to care and treatment;
  - Individuals with HIV**-negative** status with ongoing risk

What is WHO prequalification?

- WHO PQ independently reviews **safety**, **quality**, **performance** of HIV diagnostics (and others)
- WHO PQ is similar to regulatory approval, it can be used in settings where regulation of diagnostics is poor

- WHO PQ is also used by UN agencies and governments to make procurement decisions

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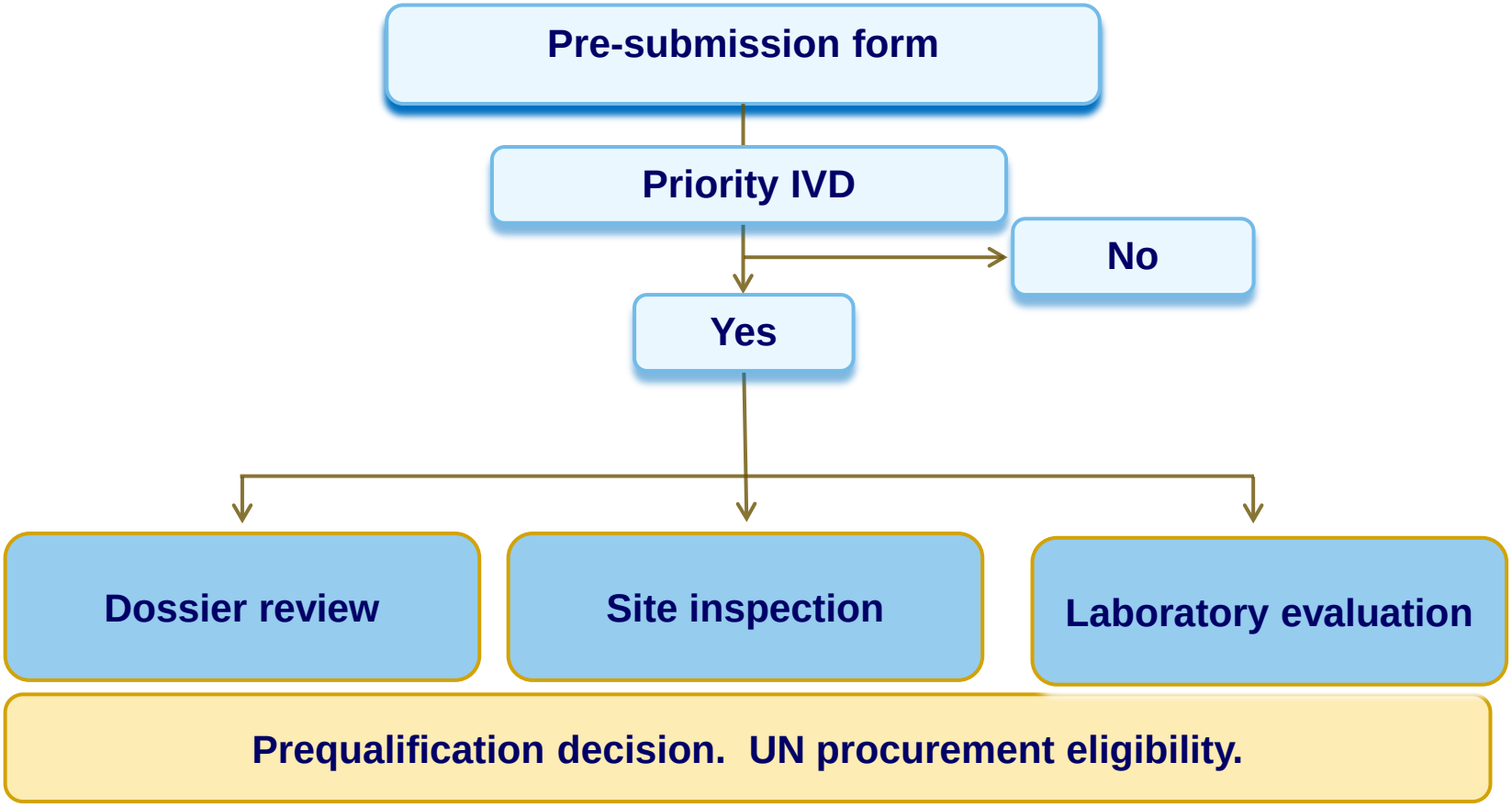
WHO prequalification process



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Post-market surveillance

An incident happens to the product
e.g. pouch of test kit is breeched, higher than expected rate of invalid tests

An adverse event happens to a person
e.g. false negative or false positive result where it leads to a misdiagnosis

- The instructions for use for the test kit will state expected sensitivity and specificity and other claims such as storage conditions, specimen collection, incubation times, etc.

- End-users are expected to report when the assay does not work according to the claims and for incidents/adverse events

Quality of HIV testing has a continuum

Test kit quality

- Poorly designed
- Poorly manufactured
- Production defect

Testing quality

- Stored incorrectly during transportation or use
- Test procedure not followed correctly

- Prequalification identifies test kits that don't meet WHO standards for quality, safety and performance
- Quality systems and post-market surveillance are critical to monitor test kit quality post-introduction

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