

Over-the-Counter Diagnostic Tests for the Detection of Pathogens Causing Infectious Diseases

Gina Conenello, Ph.D.

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Definition of Over the Counter Test

- Available WITHOUT prescription
- Can be independent of health care settings
- Performed by lay users
- Users self-select that the test is appropriate for symptoms or risk behaviors

Regulation of OTC Tests

- Each potential OTC assay to be discussed would be regulated under a separate analyte specific regulation.
- Under these regulations a device can be cleared as either 'prescription use only' or 'for over the counter use'

Studies for Qualitative Infectious Disease Diagnostics

510(k): Laboratory Setting



- **Analytical Studies:**
 - Limit of Detection
 - Cross-reactivity
 - Interfering substances
 - Reproducibility
 - Inclusivity
- **Clinical Study:**
 - Specimen collection by healthcare professional
 - Test performed by laboratorian

CLIA Waiver: Physician's Office



- **In addition to 510(k) studies:**
 - Flex Studies
 - Near the Cut-Off Study
- **Clinical Study:**
 - Specimen collected by healthcare professional
 - Test performed by untrained user employed at healthcare site

Over the Counter: Home setting

- **In addition to 510(k) Analytical Studies:**
 - Near the Cut-Off Study to be performed by lay users
 - Flex Studies
- **Clinical Study:**
 - Specimen collected by lay user
 - Test performed by lay user
 - Test interpreted by lay user

Current OTC Tests

- FDA has approved or cleared several OTC tests, e.g.:
 - Cholesterol
 - Fecal Occult Blood
 - Pregnancy
- Infectious Diseases: HIV tests are the only approved OTC collection and testing devices. Approved by CBER after extensive clinical and analytical studies and following discussion at three Advisory Panel Meetings.
- FDA has also approved OTC sample collection kits for:
 - HCV
 - HIV

Why are OTC Diagnostics for Infectious Diseases Different?

- Many analytes present a unique benefit/risk profile
 - This requires individualized approach to evaluation in most cases

FDA Considerations for Evaluating OTC Infectious Disease Tests

- Sensitivity & Specificity
- Positive & Negative Predictive Values
- How well the test performs in the hands of lay users:
 - Likelihood of lay users making errors
 - Due to device performance (i.e., compared to laboratory professionals)
 - Sample collection errors
 - Errors following directions
 - Incorrect result interpretation

Standard Risk Mitigation Strategies

- Human factors engineering
 - Test design
 - Clear directions
 - Robust procedure
 - Easy to interpret results
- Educational/supplemental material included with test

Public Health Considerations

- Will a tests increase or decrease the burden on our healthcare system?
 - For example: interactions with the healthcare community
- Will the availability of OTC tests significantly improve access to testing?
- Will OTC tests affect testing in professional settings?

Potential Benefits of OTC Testing for Influenza, GAS, and CT/NG

- **Greater access to testing and earlier disease detection:**
 - Potential for patients to seek earlier diagnosis (and accordingly, treatment)
 - Possibly reduced community spread
- **Home testing may decrease healthcare visits for:**
 - Users with negative results
 - Lower risk patients with positive results
- **Labeling /packaging gives an opportunity to educate**
 - Discourage inappropriate antibiotic use outside of health care intervention.
 - Means to avoid spread of infection
 - Educate high-risk individuals to seek medical care and potential treatment regardless of results (e.g., persons with diabetes, etc.)

Risks for OTC Tests (for Influenza, GAS and CT/NG)

- False Negative Result
 - Untreated infection can prolong symptomatic disease, and/or lead to complications
 - Increased community spread of infection
- False Positive Result
 - Unnecessary treatment with antibiotics or antivirals can result in adverse effects
 - Inappropriate use of antibiotics contributes to increased antibiotic resistance
 - Patient may not seek treatment for true cause of illness
- True Positive Result
 - Test could detect colonized individuals who do not necessarily need treatment (for GAS)
 - Patient may have superinfection (e.g., influenza) and may not seek treatment

Risks of an OTC Influenza Test

- Less professional testing could impact surveillance activities:
 - Fewer specimens tested may decrease tracking resistance and/or detection of novel influenza viruses
 - Missing data on prevalence of influenza-like illness visits
- Poor Positive Predictive Value when influenza has low prevalence
- Poor Negative Predictive Value when prevalence of influenza is high

Risks of an OTC GAS Test

- Specimen collection may be difficult for untrained users
 - The posterior pharyngeal area may be difficult to identify and/or sample, and may lead to false negative results or adverse events
- Colonization may be assumed to be infection

Benefits of OTC CT/NG Tests

- Greater access to testing and earlier testing
 - Earlier treatment
 - Reduced community spread
- OTC availability has the potential to expand testing:
 - Individuals concerned about confidentiality
 - Individuals who cannot readily access health care
 - Individuals who may want partners tested

Benefits of OTC CT/NG Tests (2)

- OTC testing would permit self-collection of genital samples as an option for women.
- Labeling gives an opportunity for user education
 - Review of safe sex practices and importance of testing for *all* sexually transmitted infections
 - Could allow patients to access material that promotes sexual health and other educational activities

Risks of OTC CT/NG Tests

- False Negative Result
 - Untreated infection in women can lead to complications, e.g., infertility
 - Patient may spread infection to partners
- False Positive Result
 - Unnecessary treatment with antibiotics and potential adverse reactions
 - Potentially significant emotional burden, i.e., significantly impact personal relationships

Risks of OTC CT/NG Tests (2)

- True Negative Result
 - Patient may interpret results as reinforcement of high risk sexual behavior
 - Patient may mistake this as evidence that they are free of all sexually transmitted infections
 - Other causes of symptoms may not be detected
- Less surveillance activities
 - Both CT and NG are reportable infections and OTC testing may not permit accurate disease tracking
 - Contact tracing not possible for unreported infections
 - Obtaining isolates for tracking resistance may be impaired

How Will OTC Test Results Be Integrated Into Medical Care?

- Will results be accepted by health care providers, i.e., will repeat testing be necessary?
- Can OTC results be captured in medical records?
- Are there means for test developers to encourage patients to seek appropriate follow up?

How Does Human Factors Engineering Influence Home Test Design

- People have different abilities to follow directions
 - e.g., may perform test incorrectly
- Lay users may not follow ‘ideal’ laboratory practice, e.g., washing hands, clean workspace, etc.
- Failure to obtain adequate or appropriate sample by untrained users
- Users may interpret results or implications of results incorrectly

Study Design

- FDA has considered the general study designs that should be performed for each of the analytes discussed
- Flex studies needed to demonstrate that potential OTC tests are robust; these may be unique by product
- Clinical study directed to OTC use, e.g., testing is conducted by patients in 'home' environment with careful attention to representative patient enrollment

Flex Studies

- Flex studies are performed to inform the potential for erroneous test results and the sources of errors for a given device
- Testing intended to challenge the assay procedure and test components based on possible deviations and variations that may occur with lay users. Goal is for a robust testing process and that mistakes result in an invalid test, not a false result

Flex Studies (2)

- Flex study approach is similar to that used for CLIA Waiver evaluation
- Flex study testing is performed by trained users in the laboratory to isolate individual sources of error such as test system failure and operator procedural errors.

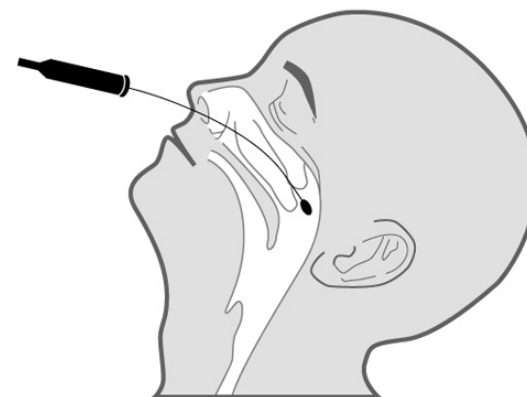
Specimen Collection

- Current specimen collection methods and/or sample types for influenza or GAS may not be appropriate for home users.
- Sample collection methods may be important across different patient populations, e.g., adults vs. children, varying education levels, etc.
- FDA would like to encourage manufacturers to research new sample types and collection methods

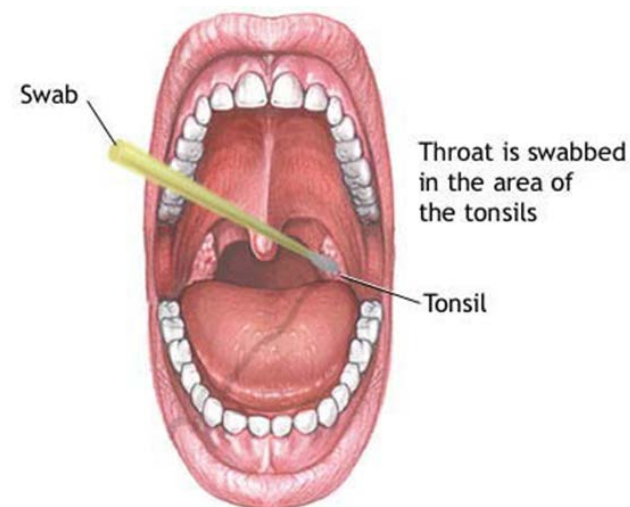
Example Clinical Study: Influenza and GAS Assays

Recruit at Urgent Care, Drug Stores, University Health Centers, Child Care Centers, etc.

- Healthcare professional obtains nasal/nasopharyngeal swab for influenza or pharyngeal swab for GAS for comparator assay
- Patient conducts test on themselves or with assistance (e.g., children) at home or other setting and interprets results

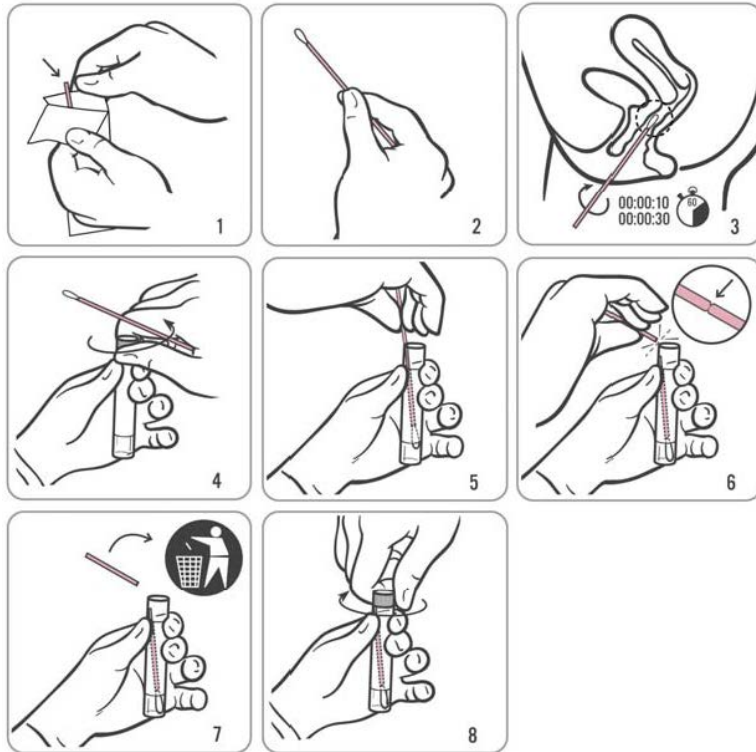


Nasopharyngeal Swab



Pharyngeal Swab

Clinical Study: STI Tests



Recruit at Urgent Care, STD Clinics, University Health Centers, etc.

- Patient collects sample and performs test
- Doctor or trained personnel collects reference sample for NAT assay

NC Sexually Transmitted Diseases Public Health Public Health Program Manual /Laboratory Testing & Standing Orders Self- Collected Swabs, April 2011

Clinical Study Design Concerns

- Need to recruit 'true' intended use population.
 - Titer of infectious agent may be different in those with symptoms severe enough to seek medical care vs. those seeking for OTC medication or diagnosis
 - Patients already seeking medical care may not represent OTC test population in behavior, education level, socioeconomic status

Clinical Study Design Concerns (2)

- While new sample type development is encouraged for OTC products, comparator should be conducted using the cleared clinical specimen type
- Does physician collection prior to patient self (or assisted) testing introduce 'education'

Questions

1. Do you agree with the benefits and risks described for OTC testing of each of the pathogens, and are there any other benefits or risks that should be considered?

Questions

2. What measures would be appropriate to mitigate the risks associated with OTC diagnostic tests?
3. What would be recommended minimum performance criteria for testing of each pathogen?

Questions

4. Please discuss recommendations for ensuring that individuals representing the appropriate intended use population are enrolled in the clinical studies to demonstrate the device performance and support OTC claims.

Questions

5. Please discuss appropriate ways to connect patients to healthcare services.
 - a) Are there any recommendations regarding potential patient access to additional resources that diagnostic test manufacturers should be responsible for, e.g., a hotline, etc.? Does this differ across the diseases described above?

Acknowledgments

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