Pregnancy Tests for Family Planning

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receive the contraceptive method. Another obstacle to use of IUCDs and injectable and implantable contraceptives is delaying the start until the menstrual period begins—even sometimes limited to a specific day. In truth, these methods can be started any time if non-pregnancy is established.

-“Medical Barriers to Access to Family Planning”
Shelton, Angle and Jacobstein, Lancet, 1992

It appeared that some providers gave methods only to women who were menstruating. Seven of 35 current or past contraceptive users in the qualitative sample reported either being asked to show proof of menstruation or being told to return during their next period. While 6 women indicated receiving a method on their first visit, at least 7 others reported having to return, sometimes multiple times, mostly because they were not menstruating during the clinic visit or to obtain pregnancy test results. A large proportion (43%) of survey respondents agreed with the statement that the nurse would ask to see their menstrual pad if they went for family planning.

-“Getting to 70%: Barriers to modern contraceptive use for women in Rwanda”
Brunie, Tolley, Ngabo, Wesson, Chen, 2013
When you get there, they ask if you are having your period. When it is ‘no,’ they give you another appointment. When it is ‘yes,’ they give you cotton wool and you go somewhere discreet to put some blood [on it] and come back to show it to the provider. It is only then that the provider shows you the methods.

49-YEAR-OLD DMPA USER, RWANDA
Lack of menstruation a barrier to contraceptive service delivery – providers use menses to rule out pregnancy; clients turned away for same-day FP services

Many new family planning clients are not menstruating when they visit the clinic

Few non-menstruating clients are actually pregnant

According to WHO, no known harm occurs to either a pregnant woman or a fetus from exposure to hormonal family planning methods*

*In case of the IUD, it is important to rule out pregnancy because inserting an IUD in a woman who is already pregnant may result in septic miscarriage, which is a serious complication.
As of 2006...

- The Pregnancy Checklist was adopted in at least 15 countries and available in five language (English, Spanish, French, Romanian, and Kiswahili)

- Included in the Global Handbook for Family Planning and the WHO Decision-Making Tool

However...

- There are instances when the checklist cannot exclude pregnancy

- Some providers don’t like/trust the checklist
Pregnancy tests complement Pregnancy Checklist

Pregnancy tests available for purchase for \( \leq \) US$0.10

Additional benefits:
- FP demand generation
- Social marketing
- Tool for improving continuation of progestin-only methods
- Contribute to decrease in gestational age for clients seeking ANC and abortion services
Pregnancy Tests: Research in Zambia (FHI 360)

% New, Non-Menstruating Clients Denied Effective Method

2015 Innovation Fund project: Price of ‘least expensive’ pregnancy test available in US dollars by facility type

<table>
<thead>
<tr>
<th>Facility Type</th>
<th>Mali (n=30)</th>
<th>Malawi (n=39)</th>
<th>Kenya (n=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>*Mean calculated among facilities that reported charging for the test. Reflects the “least expensive” pregnancy test available at each facility.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Private</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean* [range], US$</td>
<td><strong>1.99 [0.41-3.28]</strong></td>
<td><strong>0.95 [0.35-1.77]</strong></td>
<td><strong>1.94 [0.98-5.87]</strong></td>
</tr>
<tr>
<td>sample size</td>
<td>n=14</td>
<td>n=19</td>
<td>n=20</td>
</tr>
<tr>
<td><em>No charge for test</em></td>
<td>(n=1)</td>
<td>(n=2)</td>
<td>(n=5)</td>
</tr>
<tr>
<td><strong>Public</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean* [range], US$</td>
<td><strong>1.72 [0.82-2.46]</strong></td>
<td><strong>0.35 [0.35-0.35]</strong></td>
<td><strong>1.86 [0.98-4.89]</strong></td>
</tr>
<tr>
<td>sample size</td>
<td>n=10</td>
<td>n=9</td>
<td>n=15</td>
</tr>
<tr>
<td><em>No charge for test</em></td>
<td>(n=1)</td>
<td>(n=8)</td>
<td>(n=10)</td>
</tr>
<tr>
<td><strong>Pharmacy / Drug shop</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean* [range], US$</td>
<td><strong>2.12 [1.15-2.46]</strong></td>
<td><strong>0.66 [0.35-0.88]</strong></td>
<td><strong>0.84 [0.49-1.96]</strong></td>
</tr>
<tr>
<td>sample size</td>
<td>n=6</td>
<td>n=11</td>
<td>n=7</td>
</tr>
<tr>
<td><em>No charge for test</em></td>
<td>(n=0)</td>
<td>(n=0)</td>
<td>(n=0)</td>
</tr>
</tbody>
</table>
Innovation Fund Project: Are Women Ever Sent Away to Buy Tests? (Public & private facilities only)

Results from following question: “If there are either occasional stock-outs of pregnancy tests or if pregnancy tests are never available at this facility, are women ever instructed to purchase pregnancy tests elsewhere?

Mali (n=27)
- Sometimes: 20%
- Never: 80%

Malawi (n=38)
- Sometimes: 60%
- Never: 40%

Kenya (n=38)
- Sometimes: 40%
- Never: 60%
Innovation Fund Project: Awareness, availability and use of Pregnancy Checklist (public & private facilities)

- Ever heard of checklist
- Copy of checklist at facility
- Providers typically use checklist
New Clinical Job Aid for Providers – When to Use Checklist versus Pregnancy Tests

Figure 2. Job Aid for Ruling Out Pregnancy Prior to Contraceptive Initiation

<table>
<thead>
<tr>
<th>Client with amenorrhea</th>
<th>Client between two regular menses</th>
<th>Client with late/missed period</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Implants, pills, ring, injectables, or patch</strong></td>
<td><strong>Implants, pills, ring, injectables, or patch</strong></td>
<td><strong>IUDs</strong></td>
</tr>
<tr>
<td><strong>IUDs</strong> Copper or LNG</td>
<td><strong>IUDs</strong> Copper or LNG</td>
<td><strong>IUDs</strong> Copper or LNG</td>
</tr>
</tbody>
</table>

- Take history using pregnancy checklist. If pregnancy is ruled out, provide method.
- If pregnancy is not ruled out, use pregnancy test.
- If pregnancy test is negative (or test is not immediately available), provide the method now. Schedule a follow-up pregnancy test in 3-4 weeks.
- If pregnancy test is positive, refer the woman to her regular provider.

- Do not use a pregnancy test (in most cases, it is too early for it to be effective). Take history using pregnancy checklist.
- If pregnancy is not ruled out, use pregnancy test.
- If pregnancy test is positive, refer the woman to her regular provider.
- If pregnancy test is negative (or test is not immediately available), provide the method now. Schedule a follow-up pregnancy test in 3-4 weeks, then repeat the pregnancy test.
- If the test is still negative, provide an IUD.

- Within 7 days of onset of her next menses or within 12 days for a copper IUD; but in the interim, use COCs, DMPA, or condoms or abstain.
- If test sensitivity is not specified, assume lower sensitivity.

Counsel all women to come back any time they have a reason to suspect pregnancy (e.g., miss a period).

DRAFT
Currently under review for publication
J. Stanback, I. Yacobsen, L. Harber
Family Planning Client by Menstrual Status

- Menstruating
- Between menses
- Amenorrheic
- Post-abortion

Zambia, Ghana, Guatemala, Senegal, Mali
International procurement is split across a number of buyers – relatively ‘low volume and low value,’ which often translates into no dedicated resourcing for quality assurance, limited sharing of information and pooling of resources.

Through the 2015 RHSC Innovation Fund project, stakeholders highlighted a number of concerns related to quality:

- concerns about fake, counterfeit and questionable CE-marked products entering markets
- uncertainty and confusion around quality assurance standards
- limited regulatory approval/oversight
- limited visibility for procurers on the supply side

New Guidance Document for Procurement of Pregnancy Tests
We cannot give you the data of how many [inaccurate results]. There is quite a bit that goes on. This is really an area of concern for us....
Guidance Document For Procurement of Pregnancy Tests: Scope of Project

FHI 360 with USAID funding through the *Envision FP* project, and in consultation with RHSC MDAWG workstream and expert procurement committee, are developing a guidance document for procurers of pregnancy tests.

- **Goals:**
  - Factor in best practices from a number of key documents describing global standards and performance criteria for rapid in vitro diagnostics.
  - Broadly outline requirements for quality standards and provide details on technical specifications to optimize the selection of high quality pregnancy tests.

- **Intended audience:**
  - Individuals responsible for the procurement, supply, and quality assurance of pregnancy test kits at a global, national and/or local level including procurement officers, health officers and supply chain managers responsible for selecting, procuring or assisting in the procurement of pregnancy tests for use in the public and private sectors.
Pregnancy Tests: Areas of Guidance Covered

Classification of self-test pregnancy test
Class II (USA)/Self-Test (EU) medical device

Premarket submission types for approval

US FDA 510(k)
Determination of substantial equivalence

EU requirements
Declaration of conformity to ISO 13485

Rest of the World
Varying requirements

Proof of substantial equivalence

Approval by a Notified Body and CE mark

Market approval and registration; additional country level registration requirements

Manufactures’ submission to procurers for assessment

Approval of quality standards

Certificate of Analysis and/or Technical Files

Accelerated Stability Study Report

Labeling requirements

Proof of 510(k) clearance
Copy of ISO13485 certification & CE declaration of conformity

References provided for requirements of other Stringent Regulatory Authorities

- Test Format and ancillary items
- Sensitivity
- Specificity
- Accuracy
- Other quality control criteria (limitations, interferents, etc.)

Shelf-life

Primary packaging/product insert and secondary packaging
Pregnancy Tests - Best Practice, Acceptable Practice & Current General Status

**Standards**
- Interfering agents
- % Accuracy

**Analytical & Diagnostic Performance Data**
- Sensitivity
- Specificity

**Instructions for Use (IFU) & Result Interpretation (RI)**
- Product Insert
  - Performance data
  - Limitations
  - Summary & principle of test
  - Quality control measures
  - Safe use and disposal

**Labeling**
- Catalog number
  - Declaration
  - Address
  - Lot number

**Desiccant**
- Replacement of non-indicating desiccants with humidity-indicator desiccants

**Heat Stability**
- 2-40 °C

**Best Practices**
- Or FDA approval

**Acceptable Practices**
- Printed on Pouch
  - IFUs with illustrations
  - Complete RIs with illustrations
  - Declared reading time
  - Stability of results

**Current General Status**
- Or FDA approval
  - Sensitivity
  - Printed on Pouch
  - IFUs printed on pouch: always
    - RIs: often incomplete
    - Declared reading time: sometimes
    - Stability of results: rarely

- Trade name of device
  - Where not obvious, intended use
  - Required but not provided items

- Desiccants with air-permeable packaging with printed warnings

- 2-30 °C

- Low prevalence
# Pregnancy Tests – Checklist and Tools for Procurers

## Annexes

### 15.1 Annex 51: Checklist for procurers

Procurers may use this checklist to verify manufacturer’s compliance with acceptable standards as part of the product selection process. Items shaded in green are those listed under ‘best practices’, and therefore, are recommended to adopt as the country regulatory infrastructure improves or at procurer’s discretion based on organizational risk analysis.

<table>
<thead>
<tr>
<th>Commercial name of pregnancy test</th>
<th>Yes</th>
<th>No</th>
<th>NA</th>
<th>Comments/problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lot number</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Date of assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Name of assessor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**List of Documents to be Provided by Manufacturer**

- ISO 13485 Certification
- CE Declaration of Conformity (if applicable)
- FDA 510 Clearance (if applicable)
- Product Stability Documentation
- Certificate of Analysis
- Technical File
- Test results from independent Quality Control Tests (if applicable)

### Quality Standards

- Manufacturer compliant with ISO 13485...
- Compliant with a different standard (state the standard under comments)
- Product is CE marked
- CE mark is accompanied by the identification number of the notified body
- Product is US FDA regulated
- Product is regulated by another party (state the party in the comments column)

#### Labeling/Marking on Secondary Packaging (Carton and Boxes)

- Commercial name of the test included
- Batch/lot number included

**Example of cassette with a well for urine sample**

- Cassette-type
  - The strip is encased in a plastic cassette. Key features are: control line (C), test line (T) and a sample-well indicating where urine sample is to be added (S)
  - Ancillary item
    - Dropper (D), clean cup/tube
  - How test is to be used: Collect urine in a clean cup/tube → Using the dropper, transfer a specified volume of urine into the sample-well, placed on a flat surface with result window facing up → Read results after the specified period of time

**Example of dipstick**

- Dipstick
  - The strip is mounted on a laminated strip. Key features are: control line (C), test line (T), and absorbent pad to wick the urine (A)
  - Ancillary item
    - a clean cup/tube for urine collection (V)
  - How test is to be used: Collect urine in a clean cup/tube → Dip the dipstick in urine up to the line indicated by arrows (A) for the specified period of time → Place the dipstick flat on a surface, with the result window facing up, for the specified period of time for results to develop

Includes a number of useful tools for procurers
Pregnancy Tests - QA Work Instructions

- **Goal**: to develop work instructions for QA of specificity, sensitivity, accuracy, and package seal integrity

- **Intended audience**: any laboratory interested in evaluating pregnancy tests (i.e., Africa, Asia, and South America)

- Information obtained from publically available sources, and not from proprietary sources (i.e., manufacturers / suppliers)

- **Sampling plans / criteria for different scenarios:**
  - product qualification
  - pre-shipment testing
  - post-shipment testing
  - stability study evaluations
# Pregnancy Tests - QA Work Instructions

## Overall Sampling Plans and Specifications for Different Testing Scenarios

<table>
<thead>
<tr>
<th>Assumed Lot size (35,000 – 150,000)</th>
<th>Product Qualification</th>
<th>Pre / Post / Stability Time Point</th>
<th>Small Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category 1</strong> (Performance)</td>
<td>Large Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Controls (hCG x 6)</td>
<td>Sensitivity – ≥ 95% positive</td>
<td>28 units at high conc.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Specificity – Accept ≤ 3 failures</td>
<td>20 units at label claim</td>
<td></td>
</tr>
<tr>
<td>Negative Controls (Blank + interferences)</td>
<td>Accuracy – % of true pos./neg. per number tested</td>
<td>16 Blank &amp; 16 Glucose</td>
<td></td>
</tr>
<tr>
<td>Category 2 – Package Integrity</td>
<td>Accept ≤ 2 failures</td>
<td>13 units</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Sensitivity** – ≥ 95% positive
- **Specificity** – Accept ≤ 3 failures
- **Accuracy** – % of true pos./neg. per number tested
- **Accept** ≤ 2 failures
- **Accept** ≤ 1 failure