HIV Self-Testing in South Africa

MOVING FROM PRODUCT TO POLICY TO PROGRAMMES

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03.06.2017
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From 2005 – 2015, there was a sharp increase in HIV-positive diagnoses in Africa. From 2010—2014, > 600 M people received HTS in 122 low- and middle-income countries – nearly half all tests were in Africa.
Why are we talking about HIV Self-Testing (HIVST)?

Source: UNAIDS, Gap report 2014
Why are we talking about HIV Self-Testing (HIVST)?

Source: UNAIDS, Gap report 2014
There is a testing gap.

Source: UNAIDS, Gap report 2014
Proposed UNAIDS “90-90-90”

- **PLHIV**: 100%
- **PLHIV who know their status**: 90%
- **PLHIV on ART**: 90%
- **PLHIV virally suppressed**: 90%

**Source**: UNAIDS, Ambitious treatment targets, 2014
Global Progress Toward the First 90, 2015

40% of PLHIV still remain undiagnosed worldwide

- 60% of PLHIV diagnosed
- 46% of PLHIV on ART
- 38% of PLHIV on ART & virally suppressed

Source: UNAIDS, 2016 – based on 2015 measure derived from data reported by 87 countries, which accounted for 73% of people living with HIV worldwide; 2015 measure derived from data reported by 86 countries. Worldwide, 22% of all people on antiretroviral therapy were reported to have received a viral load test during the reporting period.
Estimated progress toward the first 90 in the African Region, 2015

Eastern & southern Africa

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLHIV Diagnosed in Africa</td>
<td>62%</td>
</tr>
<tr>
<td>PLHIV on ART</td>
<td>54%</td>
</tr>
<tr>
<td>PLHIV on ART Virally Supressed</td>
<td>45%</td>
</tr>
</tbody>
</table>

Western & Central Africa

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLHIV Diagnosed in Africa</td>
<td>36%</td>
</tr>
<tr>
<td>PLHIV on ART</td>
<td>28%</td>
</tr>
<tr>
<td>PLHIV on ART Virally Supressed</td>
<td>12%</td>
</tr>
</tbody>
</table>

Source: UNAIDS, 2016
So who are we missing?
New adult HIV infections globally, 2015

~1.9 M new adult HIV infections in 2015

44% new HIV infections are among key populations and their partners

Source: UNAIDS, 2016. Data is for populations 15 years of age and above.
Women

Make Up
Approximately of Those 70% Tested in 2014

Much of all HIV testing is in ANC – even in low HIV prevalence settings

Source: WHO 2015, 76 reporting low and middle income countries. Data is for populations 15 years of age and above.
~90% of the world’s HIV-positive adolescents (10–19 years of age) are in sub-Saharan Africa, where testing coverage remains low.

Testing coverage is often low due to:

- Age of consent laws
- Structural barriers
- Unfriendly services
- Stigma and discrimination
Innovation Needed to Close the Testing Gap
What is self-testing?

Collects

Performs

Interprets
So what is HIV Self-Testing?

- HIVST is a process by which an individual wanting to know his or her HIV status collects a blood or oral fluid specimen, performs a HIV test, and interprets the results by him or herself.

- WHO: HIVST is defined a “screening test” or Test for Triage
So what is HIV Self-Testing?

• As a new innovation that has significant potential to extend beyond the limitations of the HIV testing infrastructure and address existing barriers to testing, HIVST could play a substantial role in accelerating progress towards this goal of 90-90-90.
HIVST has been touted as a supplementary strategy to reach key and under-tested populations.

It is a concept that requires optimization for the ‘lay’ person out in the community.
What is HIVST NOT?

• It is not here to replace traditional HTS, and facility based HTS should continue to be the main modality through which the majority of the population learn their status.

• It is not a definitive test, but rather the first step towards learning a status. All POSITIVE results must be confirmed using the national algorithm and negatives retested in 3 months. MESSAGING MUST BE CLEAR.
What has been the greatest barrier to market entry in SA?

• South Africa does not have a Medical Devices Regulatory Authority, or evaluation framework

• SAHPRA formally constituted 02 JUNE 2017

• Yogan Pillay DDG Health “NDOH will not allow HIV Self-Tests into Public Health which have not been approved by the WHO PQ process”
Wits RHI HSTAR Programme

The HSTAR Programme, currently funded by the BMGF and AIDS Fonds, is evaluating HIV self-testing in the South African market, actively engaging with policy makers and communities, to pave the way for several well-tested products to enter the market, and facilitate the process towards World Health Organisation Pre-Qualification and National Guidance on ST.
Challenges faced by the industry

- Final WHO PQ Technical Specifications were not available until Dec 2016
  - Uncertainty regarding the requirements
- Manufacturers did not have the capacity to do evaluations in-country
- Independent evaluators to conduct clinical research were not easily accessible
- Many other market entry barriers including high cost of R&D paired with high uncertainty around policy
Why WHO Pre-Qualification?

- Prequalification is an assessment made by WHO regarding the quality, safety, performance and suitability of an IVD/MD when it is used in WHO Member States.
- WHO prequalification is a risk-based procedure founded on best regulatory practice.
- WHO undertakes a comprehensive assessment of individual IVDs/MDs through a standardized procedure aimed at determining if the product meets PQ requirements.
Why WHO Pre-Qualification?

- The PQ decision is used by UN bodies and procurement agencies as a means for quality assuring IVDs/MD and other health products.

- The PQ decision can be used by Member States without strong regulatory systems or with limited resources to provide assurance of quality, safety and performance.

- The PQ decision is used by health implementing programmes to guide product selection.
But PQ only finalised the TSS in Dec 2016

• The FDA had approved Orasure in 2012 after a lengthy, robust and intense evaluation process
• Biosure received CE marking in UK in 2015

• Using a combination of study designs from these two Regulatory Authorities, the programme was designed which was proposed to WHO PQ. The essence of the programme remained:
  - Usability of products
  - Label Comprehension
  - Mock Result interpretation
  - Product performance by Untrained Users vs Lab Gold Std
Programme designed to mirror PQ

HIV Self-Testing RDT Evaluation

Non Clinical studies

LEVEL 1 Usability Assessment

LEVEL 2 Trained User Assessment

LEVEL 3: Intended Use Assessment

LEVEL 4 Expected Use Assessment

WHO PREQUALIFICATION TEAM: DIAGNOSTICS

Technical Specifications Series for submission to WHO Prequalification – Diagnostic Assessment

Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional use and/or self-testing
Product Pipeline
HSTAR 001 – USABILITY ASSESSMENT

The purpose of the Usability Assessment is to document if “lay” people, non-professional and inexperienced in HIV self-testing, can successfully perform the steps to use a HIV Self-Test device, without product familiarization

- gain data regarding the including any error[s] that may occur including modes of error, critical and non-critical errors, in a simulated “private” setting.

- Stratified for Age, Gender, Education level

Primary Objectives are to document and record:

• Label comprehension
• Usability / user interaction with the devices and accuracy of testing process
• Results interpretation (contrived results, no actual diagnosis will be made)
5 Devices: 3 Finger Stick, and 2 Oral Fluid

Table 1: Demographics of usability studies (N=200 for each device study, 5 devices total)

<table>
<thead>
<tr>
<th>Gender</th>
<th></th>
<th>Nationality</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>48-57%</td>
<td>SA</td>
<td>63-70%</td>
</tr>
<tr>
<td>Female</td>
<td>43-52%</td>
<td>Zimbabwe</td>
<td>24-32%</td>
</tr>
<tr>
<td>Age Band</td>
<td></td>
<td>Other</td>
<td>3-13%</td>
</tr>
<tr>
<td>18 – 25 years</td>
<td>19-33%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>26 – 35</td>
<td>31-44%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36 – 45</td>
<td>15-32%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>46 – 55</td>
<td>6-11%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>56 – 65</td>
<td>1-6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>65+</td>
<td>0-1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education Level</td>
<td></td>
<td>Last HIV Test</td>
<td></td>
</tr>
<tr>
<td>≤ Grade 7</td>
<td>30-33%</td>
<td>Tested in 2016</td>
<td>35%</td>
</tr>
<tr>
<td>≥ Grade 8 to Grade 12</td>
<td>34-37%</td>
<td>Tested in 2015</td>
<td>23%</td>
</tr>
<tr>
<td>Grade 12 +</td>
<td>33-34%</td>
<td>Tested in ≤2014</td>
<td>31%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Never</td>
<td>11%</td>
</tr>
</tbody>
</table>
1) Accuracy of testing process

- Participant provided test kit and instructions for use
- NO demonstration/familiarization provided
- Observer will record device specific step performance
- Tests were all mocks (no result conferred)

<table>
<thead>
<tr>
<th>Question</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Did the participant read/use the IFU?</td>
<td>94%</td>
<td>6%</td>
</tr>
<tr>
<td>2. Did the participant have difficulty removing the test tube from the test pack?</td>
<td>82%</td>
<td>18%</td>
</tr>
<tr>
<td>3. Did the participant the remove the buffer pot and stand in upright in slot?</td>
<td>76%</td>
<td>24%</td>
</tr>
<tr>
<td>4. Did the participant have difficulty lancing their finger?</td>
<td>78%</td>
<td>22%</td>
</tr>
<tr>
<td>5. Did the participant have difficulty forming a blood droplet?</td>
<td>78%</td>
<td>22%</td>
</tr>
<tr>
<td>6. Was the participant able to fill the tube with adequate amount of blood?</td>
<td>78%</td>
<td>22%</td>
</tr>
<tr>
<td>7. Was the participant able to push the test tube right to the bottom of the buffer pot?</td>
<td>68%</td>
<td>32%</td>
</tr>
<tr>
<td>8. Was a control line present?</td>
<td>86%</td>
<td>14%</td>
</tr>
</tbody>
</table>

**AVE** 80%

**BLUE: CRITICAL STEPS**

**AVE** 75%
Since mock devices were used to assess the product in terms of each process step individually, we could not ascertain whether under- or over loading of the specimen would result in a actual result being obtained.

Table 2: Key observer data for HIVST process

<table>
<thead>
<tr>
<th>Observer checklist:</th>
<th>FS1</th>
<th>FS2</th>
<th>FS3</th>
<th>OF1</th>
<th>OF2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did the participant read/use the IFU?</td>
<td>96.5%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Did the participant have any difficulty with the kit packaging?</td>
<td>11.5%</td>
<td>5%</td>
<td>1%</td>
<td>10%</td>
<td>1.5%</td>
</tr>
<tr>
<td>Was the participant able to obtain and transfer the specimen?</td>
<td>79%</td>
<td>85.5%</td>
<td>63%</td>
<td>76%</td>
<td>97%</td>
</tr>
<tr>
<td>Did the participant quit the process at any point?</td>
<td>11%</td>
<td>0.5%</td>
<td>1.5%</td>
<td>0.5%</td>
<td>0%</td>
</tr>
<tr>
<td>Critical IFU steps completed</td>
<td>81.3%</td>
<td>96.3%</td>
<td>85.5%</td>
<td>87.5%</td>
<td>98.3%</td>
</tr>
<tr>
<td>All IFU steps completed</td>
<td>84.2%</td>
<td>97.3%</td>
<td>89.1%</td>
<td>91.3%</td>
<td>93.6%</td>
</tr>
</tbody>
</table>
Types of errors

• Critical errors were noted when participants had difficulty obtaining and transferring the specimen.

• For the FS devices, the most common sampling errors including:
  • lancing the thumb instead of finger,
  • not acquiring enough of a blood droplet, or
  • not filling the transfer capillary to the fill mark.
  • There were several cases where the lancet was not pressed firmly against the finger, resulting in a too-shallow cut. Notably, many of the “quits” were because of lancet misfire.

• For the OF devices, the most common sampling errors came from placing the sample collector in the mouth instead of moving/swiping, or inserting the wrong end of the collector.
2) Interpretation of contrived results

- To evaluate the participant’s ability to read and interpret the device results, contrived tests were provided by each manufacturer to represent the four possible test outcomes:
  1) non-reactive/negative,
  2) reactive/positive,
  3) weak positive, and
  4) invalid (no control).

- Participants were provided with all four contrived devices (serially, in random order) to interpret each result.
Interpretation scores

Correctly Read Contrived Results

- Non-reactive /Negative: FS1 (93%), FS2 (91%), FS3 (99%), OF1 (99%), OF2 (99.5%)
- Reactive /Positive: FS1 (99%), FS2 (99.5%), FS3 (98%-96%), OF1 (98.5%), OF2 (98.5%)
- Weak Positive: FS1 (74.5%), FS2 (86.5%), FS3 (49.5%), OF1 (70%), OF2 (70%)
- Invalid (no control line): FS1 (97%), FS2 (96%), FS3 (93%), OF1 (96%), OF2 (98%)

The bar chart illustrates the interpretation scores across different conditions and methods.
Observations

• Participants achieved the best result interpretation when the test device could be placed next to “life sized” examples of the possible test outcomes in the IFU.

• Overall, participants could correctly interpret the non-reactive/negative and reactive/positive results accurately for each of the devices.

• For the weak positive result, some devices were contrived darker and easier to read, others were quite faint – there was no universal standard for intensity of a weak positive. Most of the weak positive errors were called as non-reactive/negative.

• The invalid test result was called correctly in most cases, but for some participants this was a new and confusing concept, and several of the invalid tests were marked as “not sure.”
3) Label Comprehension

• How long should you wait before reading the test?
• What is the maximum time to read the result?
• How should you dispose of a used test kit?
• What should you do if you have a negative/non-reactive result?
• What should you do if you have a positive/reactive result?
• What should you do if you have an invalid result?
• What should you do if you do not know/unsure of your result?
### Results

#### Table 3: Participant responses for what to do after HIVST

<table>
<thead>
<tr>
<th></th>
<th>FS1</th>
<th>FS2</th>
<th>FS3</th>
<th>OF1</th>
<th>OF2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>What should you do if you have a non-reactive/negative result?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Re-test in 3 months</td>
<td>29.5%</td>
<td>81%</td>
<td>81%</td>
<td>51%</td>
<td>82.5%</td>
</tr>
<tr>
<td>Condomize</td>
<td>43.5%</td>
<td>13%</td>
<td>16%</td>
<td>22.5%</td>
<td>17.5%</td>
</tr>
<tr>
<td>Other (no answer, partner test, celebrate)</td>
<td>27%</td>
<td>6%</td>
<td>3%</td>
<td>27%</td>
<td>0%</td>
</tr>
<tr>
<td><strong>What should you do if you have a reactive/positive result?</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit clinic/seek treatment/counselling</td>
<td>94.5%</td>
<td>99%</td>
<td>99.5%</td>
<td>94%</td>
<td>100%</td>
</tr>
<tr>
<td>Other (condomize, re-test, stress, acceptance)</td>
<td>5.5%</td>
<td>1%</td>
<td>0.5%</td>
<td>6%</td>
<td>0%</td>
</tr>
</tbody>
</table>
Observations

• Most of the IFUs provided simple recommendations for test results with the pictured examples, such as “go to clinic” for a reactive/positive result, and “re-test in 3 months” for a non-reactive/negative result.

• Some IFUs did not include recommendations for the non-reactive/negative test result, and the corresponding study participants had a higher percentage of “other” responses, suggesting the value of a clear IFU recommendation in lieu of a detailed explanation about the window of seroconversion.

• In the “other” category, some participants provided an emotional response: celebrate if good news (negative test result), with stress or acceptance if bad news (positive test result).
Recommendations and responses...eg.

a. **Issue: Buffer pot not been placed upright in the slot provided**

The majority of participants, after opening the packaging, do not open the IFU as one would a booklet, but rather as a leaflet. Figure 6 below demonstrates this.

![Figure 6: Opened as leaflet (left) vs. Opened as booklet (right)](image)

As a result, some participants are not locating the slot (red circle) as easily as they would if opened as a booklet (blue circle). Therefore, those participants not locating the slot are standing the buffer-pot on the table, or holding it in their hands. This is not critical; however it does allow the possibility of falling over, spillage and not pushing the tube in correctly.

We recommend that the arrows pointing to the slot be made bolder and more visible however...
HSTAR 003 Objectives

*Primary Objectives*

- The primary objective of this study is to evaluate the ability of untrained users to obtain accurate HIV test results using the XXXXX Rapid HIV Self-Test when compared to professional users and ELISA. (UNASSISTED HIVST)

*Secondary Objectives*

- To evaluate the untrained users’ interaction with the device in terms of effectiveness and efficiency, i.e. successful / unsuccessful completion and difficulty of the critical steps as per the Instructions for Use
- To assess the ability of the untrained users to correctly comprehend key messaging from device packaging and labelling, including the Instructions for Use
- Participants will be surveyed for user experience, and satisfaction with the overall process; in addition, users will be asked for comments and recommended improvements for test process
## Confirmatory Data Comparison

<table>
<thead>
<tr>
<th>HIV Self Test</th>
<th>Confirmatory Test (EIA + DNA)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive: 76</td>
<td>Negative: 3</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive: 0</td>
<td>Negative: 321</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIV Self Test</th>
<th>RDT Algorithm</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive: 76</td>
<td>Negative: 3</td>
</tr>
<tr>
<td>Negative</td>
<td>Positive: 0</td>
<td>Negative: 321</td>
</tr>
</tbody>
</table>

### Sensitivity and Specificity Calculation

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>True Positive</td>
<td>76</td>
</tr>
<tr>
<td>False Negative</td>
<td>0</td>
</tr>
<tr>
<td>True Negative</td>
<td>321</td>
</tr>
<tr>
<td>False Positive</td>
<td>3</td>
</tr>
</tbody>
</table>

**Sensitivity**: 100%

**Specificity**: 99.1%
Constraints/Barriers to Market Entry

• Barrier 1: Undefined Regulatory landscape†
• Barrier 2: High cost of risk and uncertainty‡
• Barrier 3: Lack of demand for quality-assured HIVST translating into concrete purchase orders~
• Barrier 4: Price pressure form donors and governments~
• Barrier 5: Lack of incentives to innovate for further product development~
• Barrier 6: Lack of ownership of and investment in key market functions‡~

† Majam (2016), ~ PSI (2016)
Barriers? What barriers?
Public health vs Private Sector Strategies
South African Pharmacy Council ruling

(g) All clients require and deserve the full attention of the person interviewing them. Rushed appointments, abbreviated counselling sessions and inadequate record keeping in no way serves the best interest of the patient.

(h) Pharmacists must not sell HIV tests for patients to perform at home.

(i) It is preferable that the infected person should tell his/her partners and family themselves. A counsellor can be pre-

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23 Dec 2016

MINIMUM STANDARD FOR THE SELLING OF HIV SCREENING TEST KITS

1. Purpose

In April 2010, South Africa launched an HIV Counselling and Testing (HCT) campaign that, among other things, sought to increase the number of people who knew their HIV status and received treatment. This is in line with the goals laid out in the country’s National Strategic Plan (NSP) for HIV, Sexually Transmitted Infections and Tuberculosis, which aims to significantly reduce the number of new infections and expand access to appropriate treatment, care and support to people diagnosed with HIV.

The minimum standard for the selling of HIV screening test kits aims to provide guidance on how the pertinent issues and concerns relating to HIV home testing should be addressed. These pertinent issues and concerns are the reliability of testing instrument, consent and counselling-related concerns.

2. General Considerations

Pharmacists must only sell HIV test kits for screening which have been approved by WHO or such suitable authority.

3. Pre-test Counselling

Buying a HIV home test kit is deemed to be consenting to testing. Individuals using the tests, however, may not have considered their options and the consequences of the result. Since the person will be performing the test him/herself, access to counselling shall be available to:

(i) prepare the person for the result of the test;

(ii) inform the patient that the self-test should not be taken as a conclusive diagnosis and

(iii) inform the patient that the diagnosis of HIV infection is dependent on a confirmatory test.
On the market
The difference...

---

**INSTI HIV SELF TEST INSTRUCTIONS**

**Questions?**  +1-800-204-6784

**INSIDE YOUR TEST KIT**

- BOTTLE 1
- BOTTLE 2
- BOTTLE 3
- TEST DEVICE POUCH
- LANCET

---

**PREPARATION**

1. Open test device pouch.
2. Place the test device down on a flat surface.
3. Remove cap of Bottle 1. Place on flat surface.

---

**STEP 1: COLLECT BLOOD**

1. Twist off tip. Throw away tip in waste bin.
2. Rub finger until warm.
3. Place lancet on the side of finger tip.
4. Rub finger to get larger round drop of blood.
5. Let 1 drop fall into Bottle 1.
6. Twist on cap of Bottle 1.

---

**INTERPRETATION OF RESULTS**

- **Negative**
  - This result indicates that at present in the sample tested there are no HIV-1 and HIV-2 antibodies or that the concentration of HIV antibodies is below the detection limit of the test. A negative result at any time does not preclude the possibility of an HIV infection.

- **Positive**
  - Two colour lines are visible, one in the Control (C) region and one in the Test (T) region. If the T line is a light color, this should be considered as a possible positive result and should be followed up with a laboratory test. A positive test result indicates the presence of antibodies to HIV in the sample. Any positive results should be followed up with a laboratory test.

- **Invalid**
  - If there are no visible colour lines, the result is invalid. Proper procedures may not have been followed in performing the assay, or the kit may have deteriorated. The sample should be re-tested with a new test.

**WARNINGS**

ALL POSITIVE TESTS MUST BE FOLLOWED UP BY A VISIT TO A HEALTHCARE PRACTITIONER FOR CONFIRMATION. TO BE USED IN CONJUNCTION WITH PRE AND POST COUNSELLING.

KEEP OUT OF REACH OF CHILDREN.

For OTC and professional in vitro diagnostic use only. Do not use after the expiry date. Do not eat, drink, or smoke in the area where the specimens or kits are handled. Do not reuse test if pouch is damaged. Handle all specimens as if they are infectious agents. Observe established precautions against microbiological hazards throughout the procedure and follow the standard procedures for proper disposal of specimens. Humidity and temperature can adversely affect results.

**STORAGE INSTRUCTIONS**

Store at room temperature or refrigerated (15 °C - 30 °C). Keep from direct light. Do not freeze the test.

**PRODUCED FOR**

**Instilocks South Africa (Pty) Ltd**

1040 Sable and Pontiac Streets, Cape Town, 8001
South Africa

Tel: 021 4601826
ST manufacturers have brought innovation to a stagnant industry

All in one test

Flow through technology
Results in seconds
National Dept of Health Supportive

- HIVST included in the National HTS Policy 2016
- Supplement to HTS 2016 on HIVST in production
- HIVST included in the NSP 2017 – 2022
- Minister of Health included HIVST in his IMC slides in Feb 2017