

CYTOLOGY WORKLOAD ISSUES

Alberto Gutierrez, Ph.D.
Food and Drug Administration
Office of *In Vitro* Diagnostics and Radiological Health (OIR)

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Cytology Workload Regulation

Clinical Laboratory Improvement Amendments of 1988 (CLIA '88)

- ❑ “individual workload limits must be established by the technical supervisor and based on individual capabilities/performance”
- ❑ “maximum workload limit for manual screening is 100 slides in no less than an 8-hour day” (based on expert consensus opinion)
- ❑ “When performing evaluations using automated and semi-automated screening devices, the laboratory must follow manufacturer's instructions for preanalytic, analytic, and postanalytic phases of testing...”

FDA approved two semi-automated screening devices

- ❑ Hologic's ThinPrep Imaging System (TIS) for ThinPrep Pap slides – 2003
 - Hologic's Review Scope Manual+ (TIS+): Microscope with enhanced features to be used with the ThinPrep Imaging System for ThinPrep Pap slides – 2012
- ❑ Becton Dickinson Focal Point Guided Screening System (BD) for SurePath Pap slides - 2008

- ❑ For a Pap slide, imaging algorithm identifies Field of View (FOV) (field of diagnostic interest)

- ❑ Cytotechnologist (CT) reviews the FOVs
 - If no abnormality is identified during FOV review and there are no specimen adequacy limitations, then slide is Negative (NILM)

 - If abnormal cells or specimen adequacy limitations are identified during FOV review, CT performs a Full Manual Review (FMR)

 - If imager does not give any FOVs (Algorithm failed) then CT performs FMR

Pre-Market Clinical Study

- Imaging System for ThinPrep slides by Hologic
- Imaging System for SurePath slides by BD
- Both Imagers were evaluated with similar study design
- Both Studies (TIS and BD) had 2 parts:
 - Accuracy and
 - Workload

Workload Part of Study

For Manual arm and for Imager arm:

- ❑ Each day is considered as 8 hours (480 minutes) including bio-breaks

- ❑ Each day for each CT, the following were recorded:
 - Number of hours worked
 - Total number of slides reviewed
 - Total number of slides requiring FOV only
 - Total number of slides requiring FMR after FOV review (FOV+FMR)
 - Total number of slides requiring FMR because of no FOV

NOTE: In this study design, the time spent for each slide was not recorded (i.e. case set up time, slide review time, case complete time and in-between time)



Workload limits specified in the labeling for the FDA approved semi-automated cytology screening devices were based on data from the workload studies

TIS+ (Review Scope Manual+)

- ❑ TIS+ is an accessory to the ThinPrep Image processor
- ❑ Replacement of the desktop joystick console with a touch screen monitor which serves as the user interface
- ❑ In addition to all the functions that are present in the joystick console, the touch screen also provides real-time slide screening information such as slide ID, date scanned and a map of the fields of view (FOVs) for each slide and their location when the slide is being screened
- ❑ Addition of a review control knob to the microscope. The review control knob replaces the Navigator Pod on the joystick console and functions similarly to the Navigator Pod. It has a scroll wheel that enables the user to execute the main review functions (Next, Previous, Mark) while screening slides without having to take their eyes away from the binocular objectives of the microscope

TIS+

- ❑ The essential function of the TIS+ is to move the microscope slide to the coordinates identified by the accompanying ThinPrep Image Processor so the objects of interest are visible to the cytotechnologist.
- ❑ The changes to the TIS+ were considered minor and therefore workload studies were not needed

FDA Lab Tip - 2010

- ❑ There were inconsistencies with the way labs were counting slides when using these semi-automated devices
- ❑ FDA issued a laboratory safety tip: “How Laboratorians Can Safely Calculate Workload for FDA-Approved Semi-Automated Gynecologic Cytology Screening Devices” – July 2010
- ❑ Provided clarification about the method that should be used to count slides in order to calculate workload



FDA Slide Counting Method for Semi-Automated Screening Devices

- ❑ All slides with full manual review (FMR) count as **1 slide** (as mandated by CLIA'88 for manual screening) or 4.8 minutes per slide
- ❑ All slides with field of view (FOV) only review count as 0.5 or ½ slide or 2.4 minutes
- ❑ Slides with **both** FMR and FOV count as 1.5 or 1½ slides or 7.2 minutes
- ❑ Use these values to count workload, not exceeding the CLIA maximum limit of 100 slides in no less than an 8-hour day

CLIA/FDA Formula

| | FOV Only | FOV+FMR | FMR-non-imaged (or Imager error) |
|-------------|----------|---------|-------------------------------------|
| Time in min | 2.4 | 7.2 | 4.8 |

$$2.4 * FOV + 7.2 * (FOV + FMR) + 4.8 * FMR = 480 \text{ min}$$



| | FOV Only | FOV+FMR | FMR-non-imaged |
|---------|----------|---------|----------------|
| Weights | 0.5 | 1.5 | 1.0 |

$$0.5 * FOV + 1.5 * (FOV + FMR) + 1.0 * FMR = 100 \text{ slides}$$



CLIA/FDA formula is applied
for three systems:
BD, TIS, and TIS+.

CDC Study



□ 102 CTs

For each CT for each slide,

Total time includes

□ Case set-Up time

□ FOV time

□ FMR time

□ Case Complete time

□ Time till next slide

Time of work with slides for 8 hours = 480 minutes

For each of three systems:

(BD, TIS, and TIS+),

for each of three types of slide review:

(FOV, FOV+FMR, FMR),

Times for slides were analyzed and

25th percentile,

50th percentile (median)

75th percentile

were estimated (in minutes).

CDC Data for slides FMR-only.



In minutes

| | BD | TIS | TIS+ |
|-----------------------------|-------|-------|-------|
| 25 th percentile | 3.063 | 3.837 | 3.405 |
| median | 3.870 | 4.870 | 5.090 |
| 75 th percentile | 4.970 | 6.270 | 7.348 |

Weights* in counting for Limit of Slides=100

| | BD | TIS | TIS+ |
|-----------------------------|-------------|-------------|-------------|
| 25 th percentile | 0.64 | 0.80 | 0.71 |
| median | 0.81 | 1.01 | 1.06 |
| 75 th percentile | 1.04 | 1.31 | 1.53 |

- If FMR is counted as 1, then calculations based on medians are close to CLIA requirement of 100 slides
- If FMR is counted as 1 and one uses 75th percentiles of time in calculations => it can require a **change in CLIA requirement of 100.**

* Minutes are divided by 4.8 because working day is 480 minute

BD

CDC Data, time in minutes

| | FOV Only | FOV +FMR | FMR Only |
|-----------------------------|--------------|--------------|--------------|
| 25 th percentile | 2.017 | 4.385 | 3.063 |
| median | 2.617 | 5.615 | 3.870 |
| 75 th percentile | 3.398 | 7.018 | 4.970 |

6% of slides with FMR Only

BD



| % of FOV+FMR | CLIA/FDA | CDC Data (Median) | Over-work time (minutes) |
|--------------|----------|-------------------|--------------------------|
| 95% | 70 | 89 | |
| 90% | 73 | 92 | |
| 85% | 75 | 94 | |
| 70% | 84 | 103 | |
| 60% | 91 | 110 | |
| 50% | 100 | 117 | |
| 40% | 110 | 126 | |
| 30% | 123 | 136 | |
| 28.6% | 125 | 137 | |
| 20% | 139 | 147 | |
| 10% | 160 | 161 | |
| 9% | 163 | 163 | |
| 8% | 165 | 165 | |
| 7% | 168 | 166 | |
| 6% | 171 | 168 | +7.9 |
| 5% | 173 | 169 | +11.0 |



TIS



CDC Data, time in minutes

| | FOV Only | FOV +FMR | FMR Only |
|-----------------------------|----------|----------|----------|
| 25 th percentile | 2.033 | 4.867 | 3.837 |
| median | 2.587 | 6.297 | 4.870 |
| 75 th percentile | 3.363 | 7.897 | 6.270 |

3% of slides with FMR Only

TIS



| % of FOV+FMR | CLIA/FDA | CDC Data (Median) | Over-work time (minutes) |
|--------------|----------|-------------------|--------------------------|
| 95% | 70 | 79 | |
| 90% | 72 | 81 | |
| 85% | 75 | 84 | |
| 70% | 84 | 93 | |
| 60% | 91 | 100 | |
| 50% | 100 | 108 | |
| 40% | 111 | 117 | |
| 30% | 124 | 129 | |
| 28.6% | 126 | 130 | |
| 20% | 141 | 142 | |
| 10% | 163 | 159 | +12.7 |
| 9% | 166 | 161 | +14.7 |
| 8% | 169 | 163 | +16.7 |
| 7% | 172 | 165 | +18.8 |
| 6% | 174 | 167 | +20.9 |
| 5% | 177 | 169 | +23.2 |

TIS+



CDC Data, time in minutes

| | FOV Only | FOV +FMR | FMR Only |
|-----------------------------|--------------|--------------|--------------|
| 25 th percentile | 2.680 | 5.547 | 3.405 |
| median | 3.270 | 7.077 | 5.090 |
| 75 th percentile | 4.180 | 8.758 | 7.348 |

3% of slides with FMR Only

TIS+



| % of FOV+FMR | CLIA/FDA | CDC Data (Median) | Over-work time (minutes) |
|--------------|----------|-------------------|--------------------------|
| 95% | 70 | 70 | |
| 90% | 72 | 72 | |
| 85% | 75 | 74 | +2.5 |
| 70% | 84 | 81 | +14.9 |
| 60% | 91 | 87 | +25.0 |
| 50% | 100 | 93 | +37.1 |
| 40% | 111 | 100 | +51.8 |
| 30% | 124 | 108 | +69.9 |
| 28.6% | 126 | 110 | +72.8 |
| 20% | 141 | 118 | +93.1 |
| 10% | 163 | 130 | +123.6 |
| 9% | 166 | 131 | +127.2 |
| 8% | 169 | 133 | +130.9 |
| 7% | 172 | 134 | +134.7 |
| 6% | 174 | 135 | +138.7 |
| 5% | 177 | 137 | +142.8 |

TIS+

$$3.270 * FOV + 7.077 * (FOV+FMR) + 5.090 * FMR = 480 \text{ min}$$

This relationship can be presented in many ways

$$0.68 * FOV + 1.47 * (FOV+FMR) + 1.06 * FMR = 100$$

For simplicity, keeping the same weights as in the current formula (0.5, 1.5 and 1), what is limit of slides?

$$0.5 * FOV + 1.5 * (FOV+FMR) + 1 * FMR = ???$$



| % of FOV+FMR | FDA formula with 100 | FDA formula with 85 | FDA formula with 80 | | TIS+ (based on CDC data) |
|--------------|----------------------|---------------------|---------------------|--|--------------------------|
| 95% | 70 | 59 | 56 | | 70 |
| 90% | 72 | 61 | 58 | | 72 |
| 85% | 75 | 63 | 60 | | 74 |
| 70% | 84 | 71 | 67 | | 81 |
| 60% | 91 | 77 | 73 | | 87 |
| 50% | 100 | 85 | 80 | | 93 |
| 40% | 111 | 94 | 89 | | 100 |
| 30% | 124 | 105 | 99 | | 108 |
| 28.6% | 126 | 107 | 101 | | 110 |
| 20% | 141 | 120 | 113 | | 118 |
| 10% | 163 | 139 | 131 | | 130 |
| 9% | 166 | 141 | 133 | | 131 |
| 8% | 169 | 143 | 135 (+8.7 min) | | 133 |
| 7% | 172 | 146 | 137 (+11.8 min) | | 134 |
| 6% | 174 | 148 | 140 (+14.9 min) | | 135 |
| 5% | 177 | 151 | 142 (+18.2 min) | | 137 |

Proposal:

BD and TIS: No changes

The same weights, limit=100

$$0.5 * \text{FOV} + 1.5 * (\text{FOV} + \text{FMR}) + 1.0 * \text{FMR} = 100$$

TIS+:

No change in methodology (the same weights: 0.5, 1.5, 1),
number of slides (limit=80)

$$0.5 * \text{FOV} + 1.5 * (\text{FOV} + \text{FMR}) + 1.0 * \text{FMR} = 80$$

Individualized Approach



Each CT has his/her own weights

Basic points (without details):

- Weights are data driven weights
- Imager system calculates automatically number of reviewed slides using weights for this CT;
- Weights are set up in the beginning as “median” and then updated based on performance of this CT, for example, during previous 2-4 weeks;
- It can be that weights for CT can be only from some range of weights (times) for FOV, FOV+FMR, and FMR in CDC study data (for example, 25th -75th percentiles or 40th-75th percentiles).
- Pilot program and then implementation

Individualized Approach



Example of TIS+



| 25 th percentile | |
|-----------------------------|--------|
| Type of slides | Weight |
| FOV | 0.56 |
| FOV + FMR | 1.16 |
| FMR | 0.71 |
| Limit=100 slides | |

| 50 th percentile | |
|-----------------------------|--------|
| Type of slides | Weight |
| FOV | 0.68 |
| FOV + FMR | 1.47 |
| FMR | 1.06 |
| Limit=100 slides | |

| 75 th percentile | |
|-----------------------------|--------|
| Type of slides | Weight |
| FOV | 0.87 |
| FOV + FMR | 1.82 |
| FMR | 1.53 |
| Limit=100 slides | |

$2.680 * \text{FOV} +$
 $5.547 * (\text{FOV} + \text{FMR}) +$
 $3.405 * \text{FMR} = 480$

$3.270 * \text{FOV} +$
 $7.077 * (\text{FOV} + \text{FMR}) +$
 $5.090 * \text{MR} = 480$

$4.180 * \text{FOV} +$
 $8.758 * (\text{FOV} + \text{FMR}) +$
 $7.348 * \text{MR} = 480$

Individualized Approach (Example of TIS+)



| 25 th percentile | |
|-----------------------------|--------|
| Type of slides | Weight |
| FOV | 0.56 |
| FOV + FMR | 1.16 |
| FMR | 0.71 |
| Limit=100 slides | |

| 50 th percentile | |
|-----------------------------|--------|
| Type of slides | Weight |
| FOV | 0.68 |
| FOV + FMR | 1.47 |
| FMR | 1.06 |
| Limit=100 slides | |

| 75 th percentile | |
|-----------------------------|--------|
| Type of slides | Weight |
| FOV | 0.87 |
| FOV + FMR | 1.82 |
| FMR | 1.53 |
| Limit=100 slides | |

FDA formula with 80 gives
number of slides=73

Percent of
(FOV+FMR) =60%
Number of slides =
87

Percent of
(FOV+FMR) =60%
Number of slides =
69

FDA formula with 80 gives
number of slides=131

Percent of
(FOV+FMR) =10%
Number of slides =
130

Percent of
(FOV+FMR) =10%
Number of slides =
102



Alberto.Gutierrez@fda.hhs.gov