POSTER # 227

# Evaluation of traceability in various TB&NK workflows to assess stages of errors proneness and auditability

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## Introduction

Specimen and reagent traceability is integral to Good Laboratory Practice (GLP). Current staffing challenges and increased workloads demand high traceability. Various flow cytometry workflows employ specimens and reagent barcodes and audit trails throughout the process for both GLP and enhancing workloads: (1) manual methods with visual confirmation or logs; (2) semi-automation enables increased auto-traceability; and (3) fully integrated automation systems have high auto-traceability.

BD Multitest™ 6-color TBNK kits are widely available in flow cytometry as IVD(R). These include robust documentation from the manufacturer to support standardized processing of specimens that enables an objective assessment of traceability and auditability. Assessment methods, applied to these workflows for traceability evaluation, can inform automation selections to enhance GLP.

## Methods

The three workflows assessed were paired with three representative configurations for which documentation was available and are utilized in the clinical laboratory for performing TB&NK enumeration *(Table 1)*. The reagent used in this simulation was the BD Multitest™ 6-Color TBNK Reagent with BD Trucount™ Tubes technology.

Assumptions included all possible features for traceability and auditability by the respective workflows being utilized, and all workflows utilized middleware to transfer results to the LIS (no manual entry).

*Table 1: Workflow and representative configurations used*

| Flow cytometry workflow | Configuration used for assessment |
|---|---|
| (1) manual methods with visual confirmation or logs; | manual to BD FACSLyric™ Flow Cytometry System |
| (2) semi-automation enables increased auto-traceability | BD FACS™ Sample Prep Assistant (SPA) III to BD FACSCanto™ II Clinical Flow Cytometry System |
| (3) fully integrated automation systems have high auto-traceability | BD FACSDuet™ Sample Preparation System to BD FACSLyric™ Flow Cytometry System |

Six Sigma attributes methodology was utilized to score the TB&NK workflow stages of (a) preparation, (b) middleware involvement (utilized throughout the process), and (c) acquisition/analysis. These were then further sub-staged *(Table 2)* using manufacturer product-specific Instructions for Use (IFU), Product Inserts, User Guides (UG) and other available documentation (e.g. website Quick Reference Guides (QRG)).

The various components of specimen and reagents traceability with a scoring system as follows

1. A score of "0" was assigned with visual confirmation only being used
2. Score of "1" with a manual entry into software or paper log; and
3. Finally, a score of "2" for barcode enabled auto-entry

Each stage was then classified as auditable and/or error prone.

*Table 2: Workflow and substages*

| Workflow Components | Examples of Sub-Steps (non exhaustive list) |
|---|---|
| (a) preparation | • Reagent lot and expiry<br>• Specimen information<br>• BD Trucount™ Tubes lot and expiry<br>• Lysing reagent lot and expiry<br>• Dispensing of samples and reagents |
| (b) middleware involvement (BD FACSLink™ Software or BD FACS™ Workflow Manager) | • Creating worklists<br>• Exporting of worklist from sample prep to flow cytometer<br>• Transfer of results to LIS |
| (c) acquisition/ analysis) | • Specimen tube to position logged<br>• Secondary tube positions logged per specimen<br>• Report with operator information<br>• Approval of results |

The scoring system will be completed using the available information in the relevant IFU's and experienced BD Applications Specialist inputs with verification in publicly available BD documentation (e.g., Instructions for Use, User Guides etc). No samples or systems were run.

## Results

A total of 51 distinct substages, or individual opportunities for traceability and audit trail development, were identified across the three methods that were assigned an attribute score. The (1) manual preparation to BD FACSLyric™ Flow Cytometer System acquisition method had a total of 24 substages, the (2) semi-automated BD FACS™ SPAIII to BD FACSCanto™ II System had 36 substages, and the (1) fully integrated and automated BD FACSDuet™ System to BD FACSLyric™ System had 31 substages.

- The (1) manual method had the highest percentage of workflow **traceability** employing visual checks by the operator (45.8%) occurring primarily in the sample preparation stage, resulting in a over all score of 0.76/2.00. Visual checks would include stages such as verifying the sample ID, checking the lot number of reagent and BD Trucount™ Tubes used. Once the specimen moved to the acquisition and analysis stage, traceability by the flow cytometer software and worklists to LIS increased scoring. Of note, this second phase of the workflow relies on the integrity of the first phase or sample preparation workflow. Traceability increase with (2) semi-automation and is greatly increased with fully-automated systems *(Table 4)*.
- Automation, whether semi or full, increases traceability and the **auditability** of each of the substages. This is achieved either using electronic logs into which data can have manual/semi-automated software logged entries (score of 1) or fully automated barcoded entries (score of 2). The instance of auditable stages is lowest for the (1) manual method (41.7%) and highest for the (3) fully automated system (80.6%). Examples of auditability were worklists and reports that contained specimen and reagent components used in the processing of the TB&NK workflow. Examples of non-auditable stages in the fully automated were relating to reagent recall or stages not requiring an audit (removal of samples from the system) and may not result in lack of information in the audit trial or be categorized as an error prone stage.
- The (1) manual method had the highest number of **error prone** stages, as it relates to traceability, of the three methods assessed at 75.0% error prone. The least error prone method was the (3) fully-automated process at 6.5%.

**FREQUENCY TABLES:**

The frequencies of each score for each method assessed can be **quantified** and represented in various forms providing information on the relative differences between the methods *(Figure 1)*.

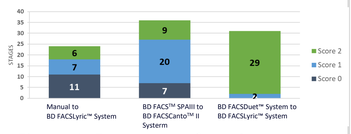


*Figure 1: Frequency of scoring*

Almost half, or 45.8%, of traceable stages in the (1) manual process involve a visual check only (score of 0). Whereas in the (2) semi-automated process it was 19.4%, which is a 41.7% improvement over the manual method. The (3) fully integrated process has 100% traceability of its workflow (score of 1 and 2) with 93.5% of traceability that is automated using barcodes, middleware, and worklist functionality.

**MAPPING TRACEABILITY SCORES:** These data can also be **visualized** to demonstrate the workflow substages where the traceability scores were applied as depicted in Figure 2.

Automated systems, whether (2) semi-automated or (3) fully automated, utilized LIS capabilities from the start of the process through to the end of the results verification stage. This increases the number of substages relative to the manual method (manual to BD FACSLyric™ System method) of 24 substages, the semi-automated (BD FACS™ SPAIII System to BD FACSCanto™ II System) with 36 substages, and the fully-automated (BD FACSDuet™ System to BD FACSLyric™ System) with 31.

The reduction in substage from (2) semi-automated to (3) fully automated was influenced by the automated flow of worklists, with partial countering with improved use of barcodes capabilities for both sample and reagents across the process. It was noted that non-mandatory manual entry by the operator in the (2) semi-automated method could be opted out reducing traceability, which could introduce potential variation between operators within a lab. In the fully automated system, such entries were automatic and information provided automatically in audit trails.

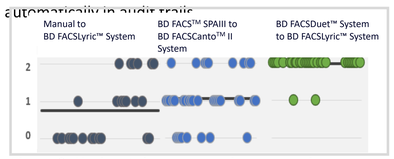


*Figure 3: Horizontal score mapping comparison*

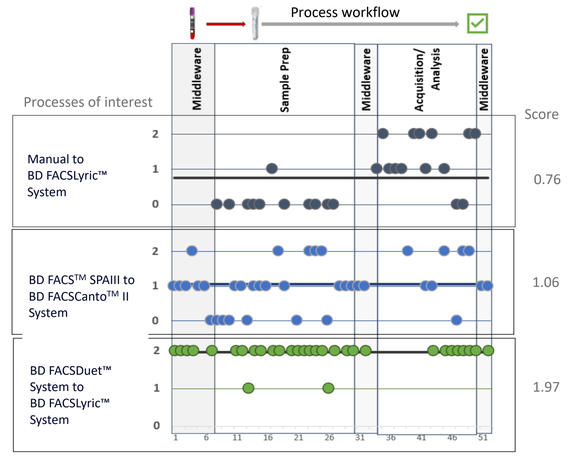


*Figure 2:Traceability detailed score mapping*

This data visualization (Figure 2) demonstrates a clear picture of the substages category assignment and can be represented horizontally for further assessment (Figure 3). In the (1) fully automated workflow for TB&NK, there were only two data points that scored as 1. The first was attributed to the entry of the BD Trucount™ Tubes into the BD FACSDuet™ System where the lot number, expiry and bead counts could be scanned in using the barcode on the pouch, but the operator would verify the lot in use upon starting a worklist. While the system has secondary tube barcode scanning, BD Trucount™ Tubes are not lot barcoded for auto-verification by automation. The second was the ability of the BD FACS™ Lysing Solution lot number and expiry date to be entered into the BD FACSDuet™ System, with the dilution of the 10X solution to be verified and expiry assigned (every 30 days). The BD FACSDuet™ System lysing container location has no barcode as this container is not limited to BD FACS™ Lysing Solution (used in the TB&NK processing), thus the operator would verify upon launching a worklist

*Table 4: Final results*

| Score | Manual to BD FACSLyric™ System | BD FACS™ SPAII to BD FACSCanto™ II System | BD FACSDuet™ System to BD FACSLyric™ System |
|---|---|---|---|
| Traceability | 0.76/2.00 | 1.06/2.00 | 1.97/2.00 |
| Auditability | 41.7% | 62.9% | 80.6% |
| Error Prone | 75.0% | 62.9% | 6.5% |

Graphic display of the **progression of steps** in relation to error proneness and auditability across the workflow provides a **visual comparison** of the three TB&NK representative configurations (Figure 4). The (1) manual workflow graph shows the error prone nature of the sample preparation stages (grey bars meeting the task line), which is slightly improved upon moving to the flow cytometer along with increased auditability. In contrast, the (3) fully automated has an improved relationship between auditability for each task while demonstrating minimal error proneness across all stages of the workflow.

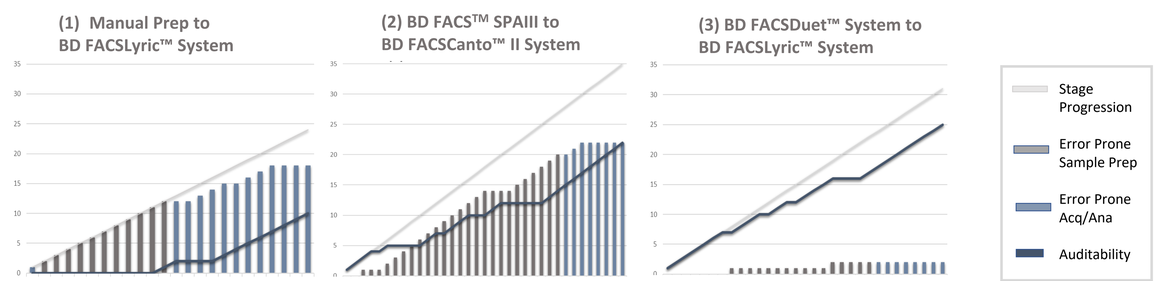


*Figure 4: Cumulative Error Prone & Auditability to stage progression*

The (2) semi-automated graph, with the BD FACS™ SPAIII and BD FACSCanto™ II System, illustrates an increased number of sub-stages relative to the (1) manual method as automation adds preparation device software tools and worklist creation earlier in the workflow. Traceability tools in software were further developed and streamlined into (3) fully automated workflows where automatic barcode readers and auto-transfer of worklist information is employed. *(Reduction in stages between (2) and (3) was seen due to variety of factors noted in the mapping section.)*

## Conclusions

Using an objective attributes assignment method, the (3) fully integrated automation system running TB&NK testing provided the highest traceability score (1.97/2.00), followed by (2) semi-automation with a score of 1.06 and then (1) manual methods with 0.76. In addition, (3) employs automatic barcodes reading with audit trails to ensure consistency in practice and documentation. The tools in this methodology are simple to apply when evaluating next generation systems to adhere to Good Laboratory Practice.