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Audit 8227: Process Audit of the Automated DNA IQ™ System (including Off-Deck Lysis)

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Background

- Potential instances of well-to-well cross contamination were identified and investigated (OQI 19477, 19768, 19349).
- The exact cause of the contamination could not be identified.
- Audits of processes were already scheduled for a later date, but these were put forward.
- Audit team was formed consisting of Amy Cheng, Peter Clausen and Iman Muharam.

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Objective

To identify any steps in the automated DNA IQ™ protocol where a potential for quality breakdown was present, and also to identify areas of improvement that may benefit the protocol.

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Why perform audits?

- Internal audits:
  - Verify the integrity of the system to meet internal objectives.
  - Is the quality system effective and sustainable?
- Process audits:
  - Any activity, or set of activities, that uses resources to transform inputs into outputs.
  - Often, the output from one process will directly form the input into the next process.
- Factors affecting a process may include:
  - Environment.
  - Safety.
  - Documents.
  - Records.
  - Equipment.
  - People.
  - Output from the previous process.

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Audited batches (15-28 July 2008)

Batch ID	Protocol Type	MP II Platform	Auditor[s]	Date
[redacted]	Off-deck (RS)		IAM, AC	15 July 2008
	STORstar lysate		IAM	15 July 2008
	Off-deck (NRS)		IAM, AC	15 July 2008
	DNA IQ (Ref)	MP II B	IAM	16 July 2008
	DNA IQ (Ref)	MP II A	AC	16 July 2008
	Off-deck (NRS)		PAC	16 July 2008
	Off-deck (NRS)		PAC	16 July 2008
	DNA IQ (CW)	MP II B	IAM	17 July 2008
	DNA IQ (Ref)	MP II B	PAC	28 July 2008

Video footage was captured for some processes.
Training records for 16 staff members were also reviewed.

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Trends

Various trends were identified throughout the audit process:

1. KPC's for the off-deck lysis and STORstar components are not included in the DNA IQ™ training module (QIS 24896 R0), but are integral to the DNA IQ™ protocol.
2. The majority, but not all, training records (e.g. QIS 24450 Operation and Maintenance of the MultiPROBE® II PLUS HT EX Robotic Platform TM and QIS 24896 Automated DNA Extraction with the DNA IQ Kit TM) for staff members were either available in the QIS Professional Development module or ready for upload to QIS.
3. Staff in the Automation Project team, involved in the development of the SOP (QIS 24897) and Training module (QIS 24896), have either completed the training modules or possessed "Statements of Competence" records.
4. "Statement of Competence to Train" records were available for some but not all trainers. All trainers have previously attended Train the Trainer.
5. Staff members generally do not have a checklist system to ensure that they have performed a specific step within any particular protocol.
6. Staff members use different methods to transfer substrate matrices into spin baskets.

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Trends

7. Volume calculations for DNA IQ™ reagents are not checked by a different operator to confirm calculation results. The worksheet to record calculations (Appendix 18.1 of QIS 24897 R3) is often not used or not included with the DNA IQ™ worksheet (Appendix 18.2 of QIS 24897 R3).
8. The volume of critical reagents (e.g. TNE buffer) is not measured using calibrated volumetric devices.
9. Some procedures within the automated DNA IQ™ protocol, e.g. (1) transfer of supernatant to the storage plate and (2) the double elution steps, require a review and optimisation due to apparent inefficient pipetting parameters.
10. Operators are consistently required to manually secure the 96-well plate on to the magnet when performing the automated DNA IQ™ protocol.
11. The MP II maintenance log for each MP II platform is used effectively to document maintenance schedules that are performed, including any work performed by the PerkinElmer engineer. Day-to-day work and observations is recorded appropriately in specific logs for each platform.
12. Some staff members that were questioned feel that they are frequently exposed to changes in protocols and methods, and are required to adapt quickly. Although some staff members were comfortable with this environment, others feel slightly overwhelmed.

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Audit recommendations

1. Add KPC's for off-deck lysis and STORstar components into the DNA IQ training module (QIS 24896 R0).
2. As part of DNA IQ™ training delivery and the associated training module, incorporate more aspects into the background and theory of the system, including discussions on the composition and function of each buffer reagent.
3. A Training Delivery Plan needs to be developed for training in the automated DNA IQ™ extraction process. Note that a TDP already exists for training on the use of the MultiPROBE® II platforms (used in conjunction with QIS 24450).
4. "Statement of Competence to Train" records must be finalised for appropriate Automation Project team members.
5. Review the expected timeframes to complete training modules QIS 24450 (Operation and Maintenance of the MultiPROBE® II PLUS HT EX Robotic Platform) and QIS 24896 (Automated DNA Extraction with the DNA IQ Kit).
6. Trainers and supervisors need to progress the completion of training modules with staff. Consider adding progress reports as an agenda item in weekly team meetings or an appropriate alternative.

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Audit recommendations

7. Apart from staff identified as trainers, it is recommended that all DNA Analysis staff attend Trainer the Trainer. This will assist with 1) trainer and trainee responsibilities, 2) adult learning styles, 3) introduces the FSS Learning and Development Manual (QIS 23651).
8. A re-evaluation of pipetting skills should be performed in order to benchmark and standardise techniques. The evaluation can incorporate demonstrations on differences in the pipetting behaviour of hot, warm and cool liquids; reagents containing a high proportion of solvents (e.g. ethanol), etc. A SOP and TM detailing and assessing pipetting techniques (e.g. forward versus reverse pipetting) should be created, if not yet available (e.g. see QIS 23899). The re-evaluation should also assess the use of multichannel and multistep pipettors in combination with various tip types.
9. The issue of overworked staff in the Analytical Section needs to be investigated further.
10. In-tube sample submissions to the Analytical Section must contain the appropriate amount/length of sample in the first instance, in order to eliminate the need for reprocessing and reduce the risk of contamination.
11. If proceeding with a checkerboard format for DNA extractions, the method for preparing the water blanks must be reviewed and standardised (see point 2.2.3).
12. Standardisation of the method for transferring substrates to spin baskets should be considered (see 2.2.6).

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Audit recommendations

13. Investigate the isolation of all DNA IQ™ reagents and off-deck lysis protocols in one working area. The authors are aware, however, that the current physical design of the DNA Suite may not allow this.
14. Investigate the advantages of separating the DNA IQ™ SOP (QIS 24897) into two separate documents, e.g. off-deck lysis (including STORstar) and automated DNA IQ™, and implement as appropriate. The SOP needs to be updated to reflect changes and correct minor errors (e.g. see points 2.4.7, 2.4.13.2, 2.4.13.13).
15. Finalise configuration of the appropriate AUSLAB worksheets for use throughout the DNA IQ™ method, so that operators are using the correct worksheets and are able to record all of the necessary batch details in designated fields.
16. The automated DNA IQ™ protocols must be reviewed and further optimised to increase liquid handling performance (e.g. incorporate the use of different syringe sizes and tip types) with the assistance of a qualified PerkinElmer specialist (e.g. see points 2.4.13.7, 2.4.13.9, and resin transfer in points 2.5.9, 2.5.16). The optimised protocol should be tested and verified prior to routine use, as per current practice.

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Audit recommendations

17. Further to 16, the applicability of a different magnet in order to minimise the need to manually secure the plate to the magnet should be investigated. Alternatively, a 96-deep well plate that is not prone to heat warping should be sourced.
18. The option for using pierceable film or septa on plates during the automated DNA IQ™ protocol should be investigated (see point 2.4.13.14).
19. A procedural checklist should be considered for each protocol so that individual operators can keep track of each specific step as they are performed. This checklist can be added as an appendix to SOP's in QIS that can be printed out by operators prior to performing the procedure. Alternatively, the checklist can be configured in AUSLAB and printed out together with the batch worksheet.
20. Checking of calculation results for reagent volumes by a different operator should be introduced, as should the dispensing of reagents into the correct troughs.
21. The use of "working" containers and aliquots should be enforced where appropriate so that the possible contamination of stock solutions is minimised.
22. Appropriate calibrated volumetric devices should be sourced to measure the volume of critical reagents such as TNE buffer.

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Audit recommendations

23. A process to change syringes more frequently at regular intervals should be implemented. Because of this, the process to calibrate or check new syringes will be time consuming and therefore alternative calibration or pipetting verification systems should be sourced (e.g. Artel MVS).
24. The BSD Duet 600 instrument can be moved to a different location in order to decrease human traffic and increase the amount of working space available around the MP II extraction platforms. A portable biohazard hood can be introduced into Room 6125 to enable some sample processing outside of the MP II hoods (e.g. manual addition of DNA IQ™ resin).
25. Investigate the use of a tip catcher that is made of a material not prone to rusting (e.g. plastic).
26. The procedure for washing and drying the MP II tip chutes must be reviewed (see point 2.4.13.18). Designate a rack position or location for drying of the tip chute and tip catcher, separate from the rack used for reagent troughs. Furthermore, a spare tip chute can be made available for each MP II, therefore used tip chutes can be allowed to decontaminate in a Decon bucket to fully decontaminate the tip chute, without compromising throughput of the MP II.
27. The cleaning regime of the MP II, including surroundings and enclosure (e.g. top of MP II hood), must be reinforced.
28. As a continuous QA/QC measure, the supervisor should observe the DNA IQ™ protocols at regular intervals for critical assessment and possible re-evaluation of the impact and suitability of changes in the methods.

OQI's

- Three OQI's were raised as an outcome of the audit.
  - 20367: Automated DNA IQ process, including documentation.
  - 20368: Enhancement of MP II platforms, including environment.
  - 20369: Training and personnel related to the DNA IQ process.

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Audit handover

- Audit findings were presented to Allan, Cathie and Tom on 11 August 2008.
- The report (including video footage disc) was handed over to Quality Management.
- Some recommendations were already being investigated and changes implemented at the time of handover.

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