Introducing a new laboratory technique: NGS HLA Typing

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What is involved?

1. **Planning:**
   - What test?
   - Why?
   - Budget?
   - Who will be involved?
   - Time scale
   - Change management

What is involved?

2. Investigating and evaluating:

- Tendering
- Validation
- Optimisation

What is involved?

3. Implementation:

- Training
- Competency assessment
- Equipment purchasing
- Laboratory organisation / workflow
- Documentation – SOPs, risk assessment, COSHH, MoU, competency documents, validation write up, change controls
- Informing users
- Deciding on billing
- LIMS – Reporting system

What is involved? A LOT!

4. Continual monitoring / quality assurance:

- Key performance indicators
  - Turnaround times
  - Repeat rates
  - CAPA
  - Audit
- Accreditation (EFI/UKAS)
- NEQAS scheme

PLANNING

- **What test and why?**

  - RCPath guidelines: “Evaluating and introducing new diagnostic tests: The need for a national strategy”

    - How much will it cost?
    - What is the benefit?
    - Will we be able to discontinue outmoded tests?
    - What are the risks if we do nothing?
    - Do we have the necessary resources do implement this test?
    - How will we provide ongoing quality assurance?
    - Is there scientific evidence of the validity of the test?

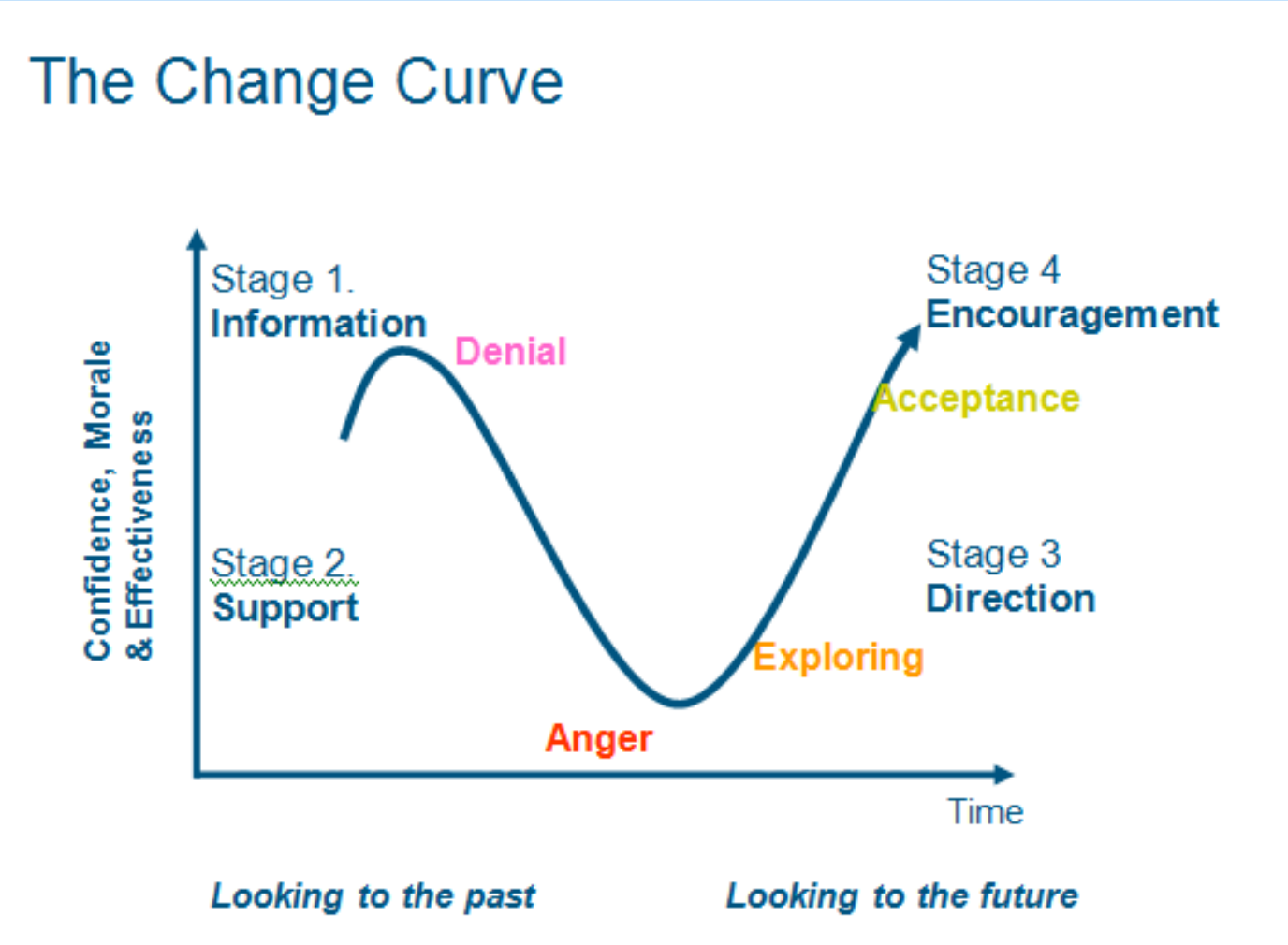
- **Budget?**

  - Will more staff be required
  - New equipment costs
  - Kit costs
  - Business case

PLANNING

- **Who will manage this process?**
  - Team leader
  - Staff to perform validation tests
  - Staff to provide training
- **Time scale**
  - Tender deadline
  - Validation tests deadline
  - Planned implementation date
- **Change curve**
  - Something to be aware of

SIDENOTE: Change curve



GO OUT TO TENDER

Tender document: Written invitation sent out to potential suppliers of a good or service to inform them about the information required for the buyer to choose among them

Considers:

Section	Total Maximum Score
SPECIFICATION COMPLAINACE	40%
PRODUCT SUPPORT & SERVICE	10%
REPORTING	20%
CLINICAL EVALUATION	Pass/Fail
PRICE EVALUATION	30%

NGS Tender

- Tender process identified 2 kits as suitable for our needs:

- Both companies demonstrated kits in our labs
- We compared:
  - Hands-on time & total assay time
  - Complexity of process
  - Flexibility of protocol (safe stopping points etc.)
  - Ability to batch samples
  - Equipment required to purchase
  - Consumables required
  - Cost
- It was **very** close but Illumina won overall

VALIDATION

Make a plan first!

- Test the claims made by the manufacturer – Does the test do what they say?
- Select appropriate samples to test
  - Cover a range of scenarios
  - Previously tested samples
  - NEQAS samples
  - Samples tested by another lab

Review results

- Are they concordant
- Are they acceptable resolution/ meet standards?

Review the technique

- Can the lab work be performed in a normal working day?
- Is the test robust and practical?
  - Will it suffer from batch to batch variation due to slight variances in technician
  - Is it practical test to perform week in week out

VALIDATION - NGS

April 2015: TruSight HLA v1 kits

- Tested 60 samples and compared results with gold standard sanger sequencing
- Identified kits not compliant with EFI standards and some software problems

March 2016: TruSight HLA v2 kits

- Tested 66 samples and compared results with gold standard sanger sequencing

Samples included: variety of HLA types, previously tested NEQAS, known unusual/problem samples, DNA extracted from buccal/saliva/blood

Concluded:

- Compliant with EFI standards, software bugs appeared to be fixed
- Robust test
- Laboratory staff able to perform technique without problems
- Plan to implement

IMPLEMENTATION: Training

- Who will provide it and who will receive it
  - Representative from company?
  - Staff member attending training course?
  - All staff or selected staff
- Competency assessment
  - What will it consist of?
  - How will it be documented?
- NGS example
  - Illumina staff visited lab to train 3 members of staff in lab work and data analysis
  - These staff members can provide cascade training to others
  - Not all staff are competent at NGS

Google image "Lab Training"

SIDENOTE: Competency assessment

- Documentation of staff competency is a requirement of ISO15189:2012
- Used to assess both laboratory technique and analysis/reporting
  - Ensure staff member follows procedures properly and can generate accurate, reliable results.
- Reassessment of competence periodically to ensure staff maintain competence
  - Maintain high standards
  - Good for confidence too

IMPLEMENTATION: Equipment

- ***Purchasing (£££):***
  - New computers and external hard drive (IT department)
  - Hybex microsample incubator
  - Plate shaker
  - Pipettes
  - Magnetic stand
  - Consumables

- ***Service level agreements:***
  - Stratified Medicine Core Laboratory (SMCL) team, University of Cambridge
  - Molecular Genetics Department, Addenbrooke's Hospital

IMPLEMENTATION – Laboratory organisation and optimisation

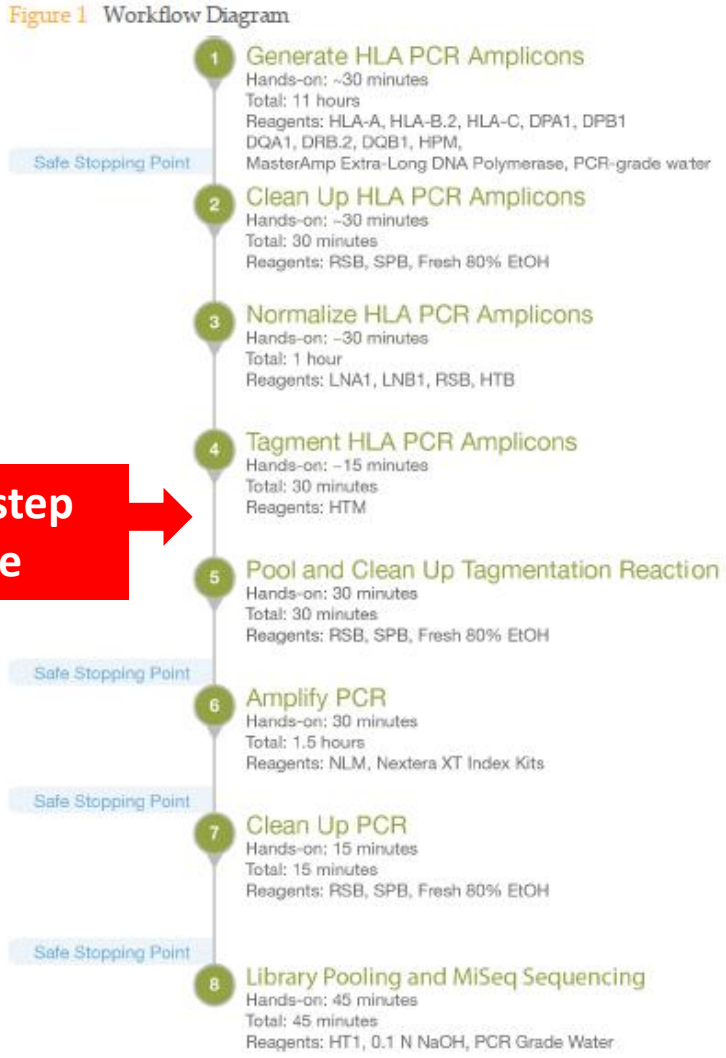
Laboratory organisation:

- Workflow (this was a big part of NGS implementation)
- When to test and how often
- Who will perform test

Optimisation (using validation data):

- Modification of protocol
- Software settings
- Set quality control acceptance criteria

Extra freeze step added here



IMPLEMENTATION: Documentation

- Standard Operating Procedure,
- Risk assessment,
- COSHH,
- Determine the Measurement Uncertainty
- Competency documents
- Validation write up
- Batch QC

IMPLEMENTATION: Other

- **LIMS – Reporting system**
  - How will the results be recorded?
  - Are changes needed to the IT system?
  - Can the process be streamlined?
  - What is the safest way?
- **Decide on billing**
  - What will the test cost?
- **Inform users**
  - What are the changes
  - Timescale

IMPLEMENTATION: Example timescale

Introduction of NGS was part of a wider plan to update our HLA genotyping strategy.

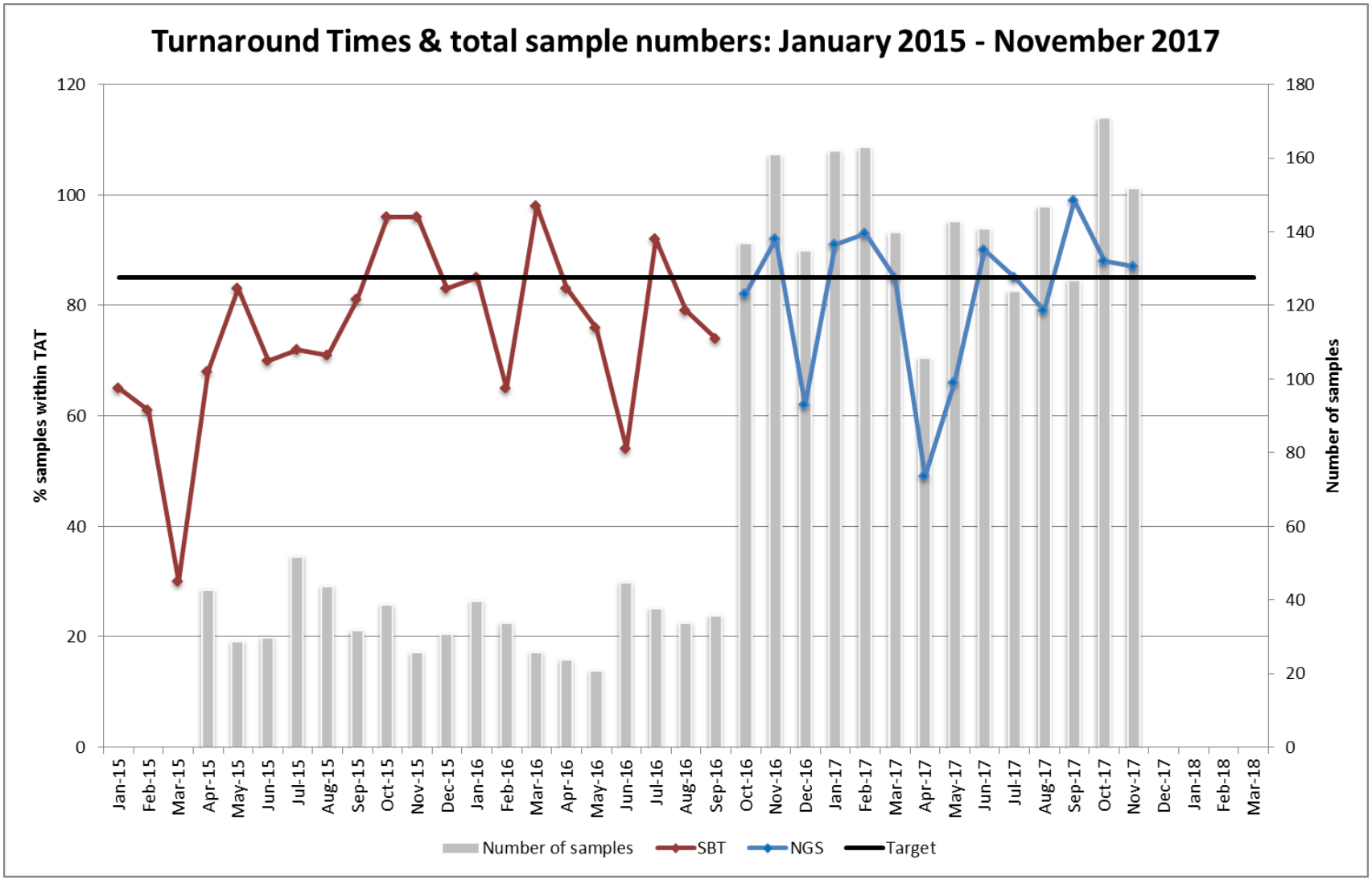
- **March 2016** – Completed validation tests
- **July 2016** – Switched all deceased donor typing to RT-PCR
- **September 2016** - Switched all HSCT and solid organ Full HLA typing to NGS. Continued PCR-SSO for overflow and disease association tests.
- **December 2016** – UKAS inspection
- **May – August 2017** - Design and validation of new PCR-SSP kits for disease association tests – HLA-B27, -B51, -DQ2/8 and HLA-B*57:01
- **August 2017** – Stopped PCR-SSO. UKAS extension to scope authorised.

CONTINUAL MONITORING / QUALITY ASSURANCE

- **Is there an appropriate NEQAS scheme?**
- **Perform audit using UKAS standards**
  - Identify and respond to non-conformities
- **Monitor turnaround times**
  - Are they being met?
  - Are they realistic?
  - Monitor change as technique beds in – Allow for teething problems in first few months
- **Apply for UKAS extension to scope**

Remember to feedback to your team and celebrate their success!

Performance: SBT vs. NGS



Questions?