

Module Issue Investigation



 **Cepheid**[®]
A better way.

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Overview

- **Context**

- GeneXpert is being widely rolled out in every corner of the planet, in a variety of settings
- Some issues with modules have arisen and Cepheid is working on solutions to make the system more robust
- Given the complexity of the situation – remote locations, multiple possibilities, the investigation has been long

- **Principal issues leading to module replacement**

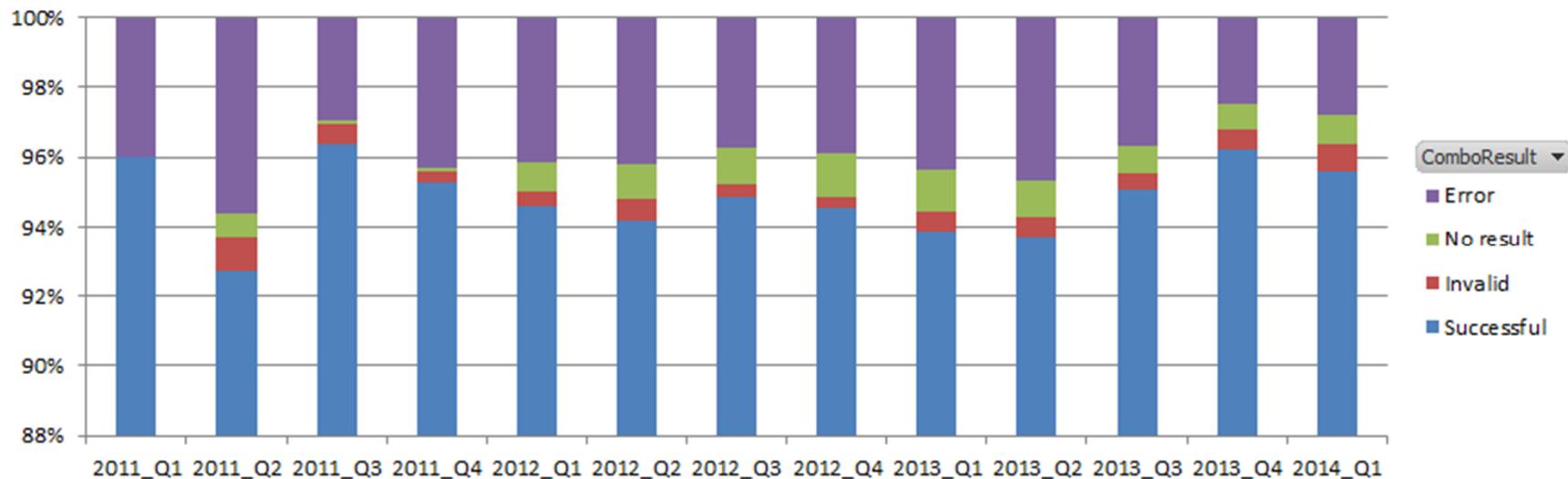
- **Error 5011 Signal loss in amplification curve**
 - South Africa 28% / Other HBDC 6% (cartridge issue, now addressed)
- **Error 4017 Thermistor**
 - South Africa 27% / Other HBDC 10% (loose connection, now fixed)
- **Error 5007 Probe check error – under investigation**
 - South Africa 22% / Other HBDC 16%

Actions to-date

- **Modules have been replaced under warranty**
 - Minimising disruption to the lab
 - A failed module does not mean a failed instrument
- **Engineering changes to provide durable solutions**
 - R1 (grey) to R2 (white) improvements
 - Air filtration
 - Larger cooling fan
 - Cable connectivity – replaced with permanently attached cable
- **Recommendations to users**
 - If a module produces more than 5% errors then contact Cepheid Technical support

The focus may be on issues but it should not be forgotten that it is not all bad news

- **South Africa: Test results 2011 to 2014**
 - Xpert MTB/Rif 96% success rate



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Nature of the Issue

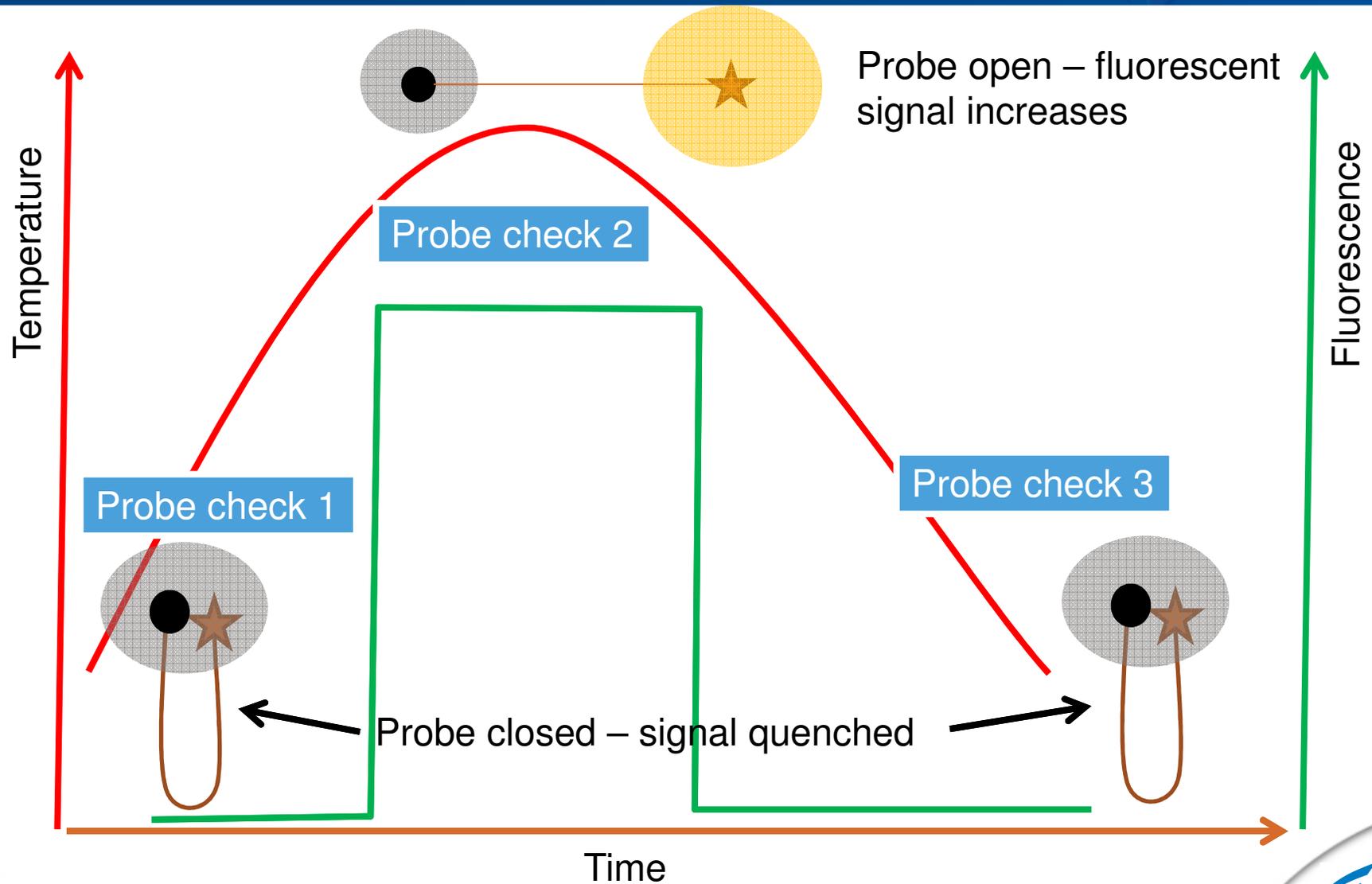
How the Error was Detected

- **FIND India collected study data and then with NHLS South Africa became pilot sites for the Remote Xpert remote monitoring system**
 - Managers could see the performance of every module
 - Errors generated by the GeneXpert were monitored and trended
- **Some modules exhibited progressively higher error rates over time**
 - The error code most often implicated was 5007
 - This relates to a Probe-Check failure
- **Whilst module performance can be tracked manually, Access to Remote Xpert will make the process far easier**

Probe-Check

- **Following sample purification and extraction, the reaction mix is transferred to the reaction tube.**
- **The fluorescence is measured across all channels to obtain a base-line**
- **The reaction mix is heated to 65C and the fluorescence measured again**
 - **At higher temperatures, the probe structure opens and separates the fluorophore and the quencher**
 - **The fluorescence signal increases**
- **The reaction mix is cooled and the fluorescence measured once more**
 - **The fluorescence signal decreases once more to the base-line**

Probe-Check



Probe-Check Errors (Error 5007)

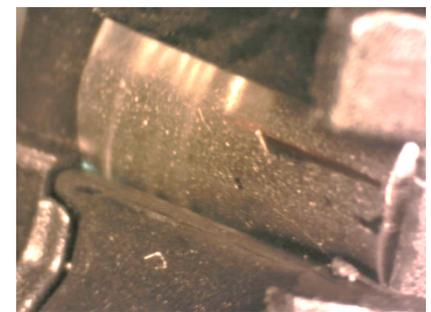
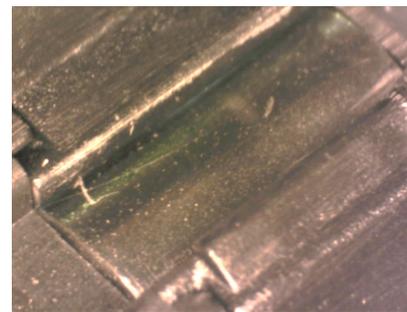
- The range of acceptable probe-check values are established for every lot and are transmitted via the bar-code to the GeneXpert
- If the values obtained during probe-check are outside of this range it signifies one of the following conditions:
 - A sample which is too viscous
 - A sample volume of less than 2ml
 - Air bubbles introduced during sample preparation
 - Inappropriate storage conditions have caused degradation of the probes
 - Manufacturing issue (very unlikely as Cepheid's QC procedures are very thorough)
- It is now clear that a rising trend of this error can be symptomatic of a previously un-encountered issue



Cause and Effect

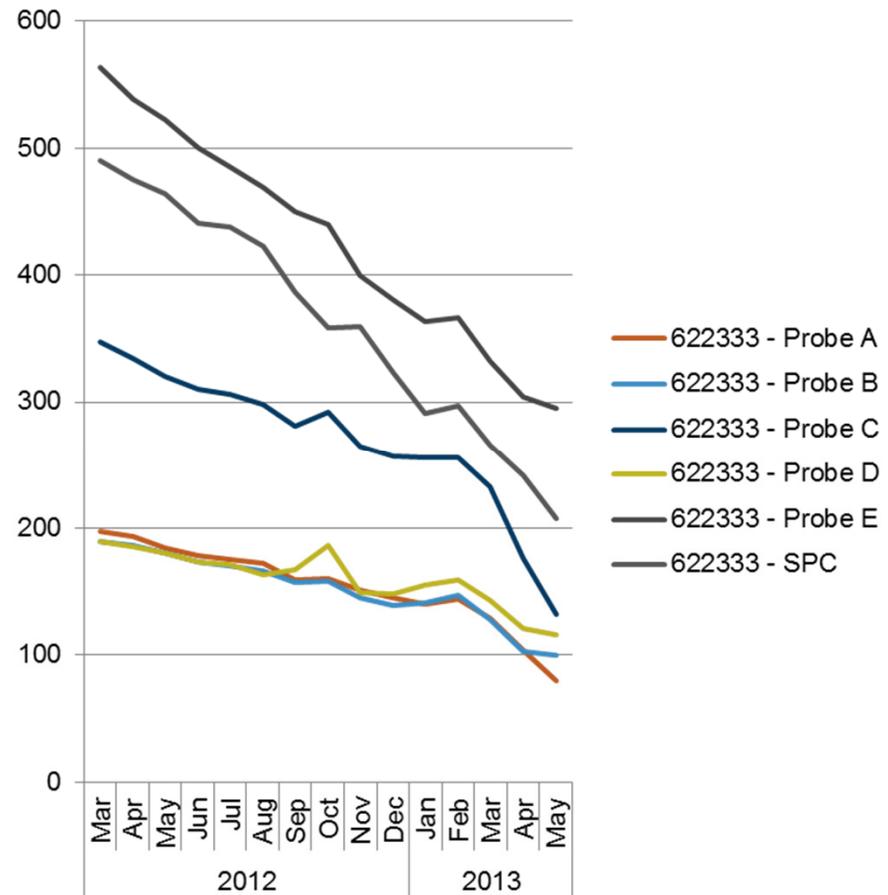
The Cause - Dust Incursion

- **Dust enters the instrument and forms a fine layer on the components**
- **Dust enters the module**
 - coating the windows of the emitter and detector blocks
 - Reducing the sensitivity of the module's optics
- **This is both preventable and reversible**



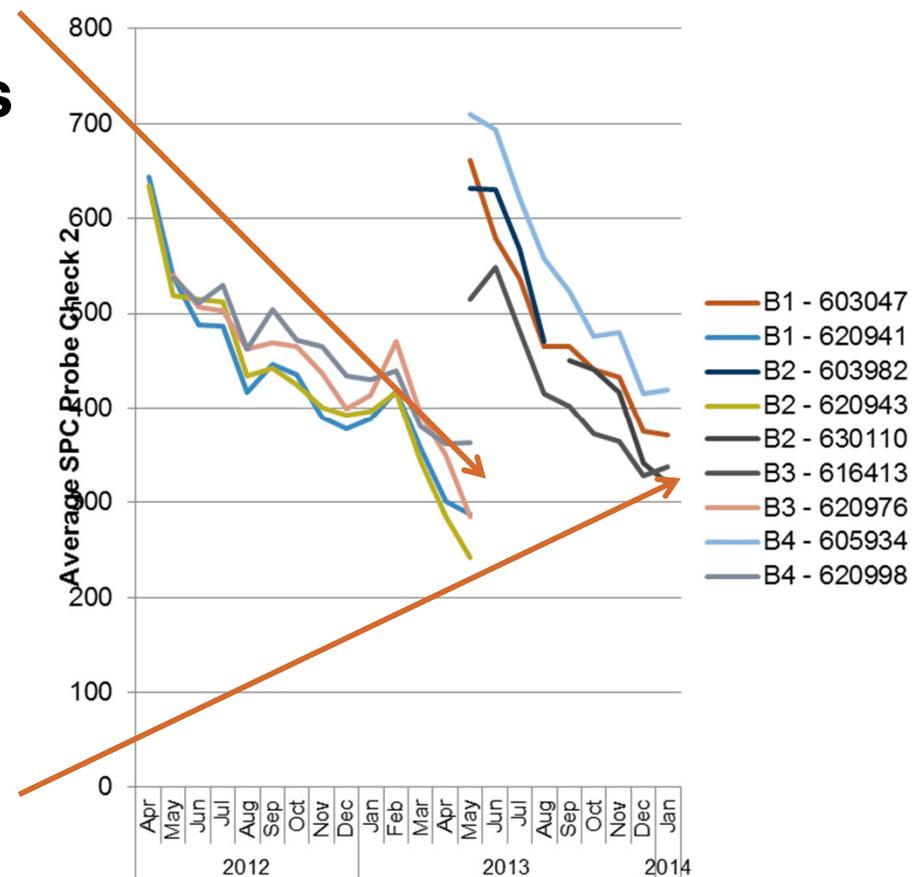
The Effect – Loss of Sensitivity Over Time

- **Sensitivity loss on all channels**
- **Eventually, the minimum fluorescence value is not achieved in one or more channels**
 - **Error 5007 reported**
 - **Cartridge is rejected as the reaction mix is assumed to be defective**



Why Many of the Failures Occur During Recalibration

- **Simultaneous loss of sensitivity in all modules of a system as dust builds**
 - System shares test load between modules
 - Modules aspirate similar quantities of dust
- **Calculated conversion factor is out of range**
 - All modules fail calibration
- **Replacement modules fail more rapidly due to dust-filled cabinet**



Fixing the Issue

Preventative and Corrective Actions

- **Preventative actions:**
 - Tools to be provided to users to allow periodic cleaning of the optical block lenses from outside the module
 - Sensitize users to the cleanliness of the area
- **Corrective actions:**
 - Preventing dust from entering the GeneXpert
 - Replacement rear panel
 - Filter holder relocated to the outside of the rear panel for easy access
 - Filter to be changed for one with a finer pore size
 - Spare filters provided for periodic replacement.
- **Remote Xpert will help to avoid future issues**

Take Home

Key Points

- **The module issue has been raised and acknowledged. Actions are taken to remedy this situation**
- **The sophistication of the GeneXpert probe-check signalled the issue and prevented incorrect patient results from being produced**
- **The power of Remote Xpert allowed the issue to be detected and empowered the investigation**
- **GeneXpert will gain additional robustness as solutions are deployed**

Thank you for your attention