The NLA PTP Workshop

4th October 2018

Why do PTP at all?

- Because we must?
  - Someone else dictating requirements
  - If doing something someone else has decided on, the action is REACTIVE, not PROACTIVE
- Because we care?
  - Conscious decision / planned activities are PROACTIVE
  - That has to be the reason

Does it matter whether the test result is right?

- Why? / Why not?

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How do we know the answer is right?

- Because we care?
  - If you are "put on the spot" to prove your results are correct, are you being reactive or proactive?
  - If you have the support for your results on hand, (evidence, data) are you in a better position or a worse position?
    - Reactive or proactive?

Who is responsible for the correctness of your lab's test results?

- Accreditation body?
- Calibration lab?
- University?
- The PTP provider?

- Lab management and staff?

What are the consequences of issuing erroneous results?

- Safe / unsafe?
- Well / ill?
- Life / death?
- Relaxation/Litigation?
- Sleeping well / preparing a defence?

The facts of the matter

- PTP is just one piece of the puzzle in the world of appropriate testing practices

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The facts of the matter

- PTP gets a disproportionate amount of attention by AB's (and others), because it is an easy way to get information about the lab's performance.
  - It is also a good talking point for other quality management activities

The facts of the matter

- Consequently, the labs that are not proactive and look after their own quality, also focus disproportionately on PTP

Common PTP problems

- Labs getting outliers are disappointed and in disbelief that they have room for improvement.
- Common outcomes
  - Blame the PTP samples, or
  - Demand the PTP provider tells the lab staff what they did wrong

Blaming the PTP samples

- If the provider is accredited, they need to have data that backs them up.
- They understand the position their customers are in and the impact a bad outcome has for labs.
- The outliers are not issued lightly.

Demand the provider tells the lab where they went wrong

- Sorry, no can do.
  - The provider was NOT in your lab at the time the tests were being conducted.
  - The provider did not watch the test being conducted.
  - The lab should have QA/QC records of test conduct sufficient to recreate the test. Therefore, the lab should have this information at their disposal.

The reality is

- Over 90% of PTP outliers occur because quality assurance practices are lacking in some way.
- Usually, PTP samples are given special treatment
- When the above 2 points are true, there is a very high chance that the proportion of customer reports containing errors is higher than the proportion of PTP outliers.

ISO/IEC 17025 REQUIREMENTS

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6.4 Equipment

- **6.4.1 The laboratory shall have access to equipment (including, but not limited to, measuring instruments, software, measurement standards, reference materials, reference data, reagents, consumables or auxiliary apparatus) that is required for the correct performance of laboratory activities and that can influence the results.**

6.4.5

- **The equipment used for measurement shall be capable of achieving the measurement accuracy and/or measurement uncertainty required to provide a valid result.**
  - *This means that the reference materials, being "equipment" also need to support the conduct of the test to provide a VALID result.*

- So, CRMs (reference materials) are part of the lab’s equipment “tool cupboard” and should exist in every lab’s arsenal.

7.2.1 Selection and verification of methods

- 7.2.1.1 The laboratory shall use appropriate methods and procedures for all laboratory activities and, where appropriate, for evaluation of the measurement uncertainty as well as statistical techniques for analysis of data.

- 7.2.1.5 The laboratory shall verify that it can properly perform methods before introducing them by ensuring that it can achieve the required performance. Records of the verification shall be retained. If the method is revised by the issuing body, verification shall be repeated to the extent necessary.

7.5 Technical records

- 7.5.1 The laboratory shall ensure that technical records for each laboratory activity contain the results, report and sufficient information to facilitate, if possible, identification of factors affecting the measurement result and its associated measurement uncertainty and enable the repetition of the laboratory activity under conditions as close as possible to the original. .....

Old 17025

- **5.9 Assuring the quality of test and calibration results**
- 5.9.1 The laboratory shall have quality control procedures for monitoring the validity of tests and calibrations undertaken. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to the reviewing of the results. This monitoring shall be planned and reviewed and may include, but not be limited to, the following:

- a) regular use of certified reference materials and/or internal quality control using secondary reference
- materials;
- b) participation in interlaboratory comparison or proficiency-testing programmes;
- c) replicate tests or calibrations using the same or different methods;
- d) retesting or recalibration of retained items;
- e) correlation of results for different characteristics of an item.

New 17025

- **7.7 Ensuring the validity of results**
- 7.7.1 The laboratory shall have a procedure for monitoring the validity of results. The resulting data shall be recorded in such a way that trends are detectable and, where practicable, statistical techniques shall be applied to review the results. This monitoring shall be planned and reviewed and shall include, where appropriate, but not be limited to:

- a) use of reference materials or quality control materials;
- b) use of alternative instrumentation that has been calibrated to provide traceable results;
- c) functional check(s) of measuring and testing equipment;
- d) use of check or working standards with control charts, where applicable;
- e) intermediate checks on measuring equipment;
- f) replicate tests or calibrations using the same or different methods;
- g) retesting or recalibration of retained items;
- h) correlation of results for different characteristics of an item;
- i) review of reported results;
- j) intralaboratory comparisons;
- k) testing of blind sample(s).

- **7.7.2 The laboratory shall monitor its performance by comparison with results of other laboratories, where available and appropriate. This monitoring shall be planned and reviewed and shall include, but not be limited to, either or both of the following:**
- a) participation in proficiency testing;
- b) participation in interlaboratory comparisons other than proficiency testing.

- 7.7.3 Data from monitoring activities shall be analysed, used to control and, if applicable, improve the laboratory's activities. If the results of the analysis of data from monitoring activities are found to be outside pre-defined criteria, appropriate action shall be taken to prevent incorrect results from being reported.

THE BASICS OF QUALITY ASSURANCE

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Process analysis

- Understand each step in a process and work out what can go wrong
- Put things in place to mitigate the risk of things going wrong, or
- Put things in place that assist to deal with things identified to have gone wrong.
  - *(avoiding and/or identifying departures from the expected process)*

Test performance

- All tests are affected by:
  - Systematic factors
  - Random factors

  - Systems (causing systematic factors) can be adjusted and optimised
    - Equipment, methods, test approach
  - Random factors can be minimised by procedure and control
    - Human, training, environment, faulty equipment

- The point is to assure ourselves the effect of all factors remains within pre-determined limits *(viz., has not departed from the expectations)*

PROCESS ANALYSIS FOR TEST PERFORMANCE (IN GENERAL TERMS)

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method

- Choice of equipment & method
- Ability to carry out method

media

- Recovery of strains (quantitative & qualitative)
- Age, water content, pH other QC parameters

°C

- Actual temp
- Temp fluctuation

Skill

- Training
- Dexterity

Interpret

- Reading, confirmation
- Interference
- Understanding

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Typically,

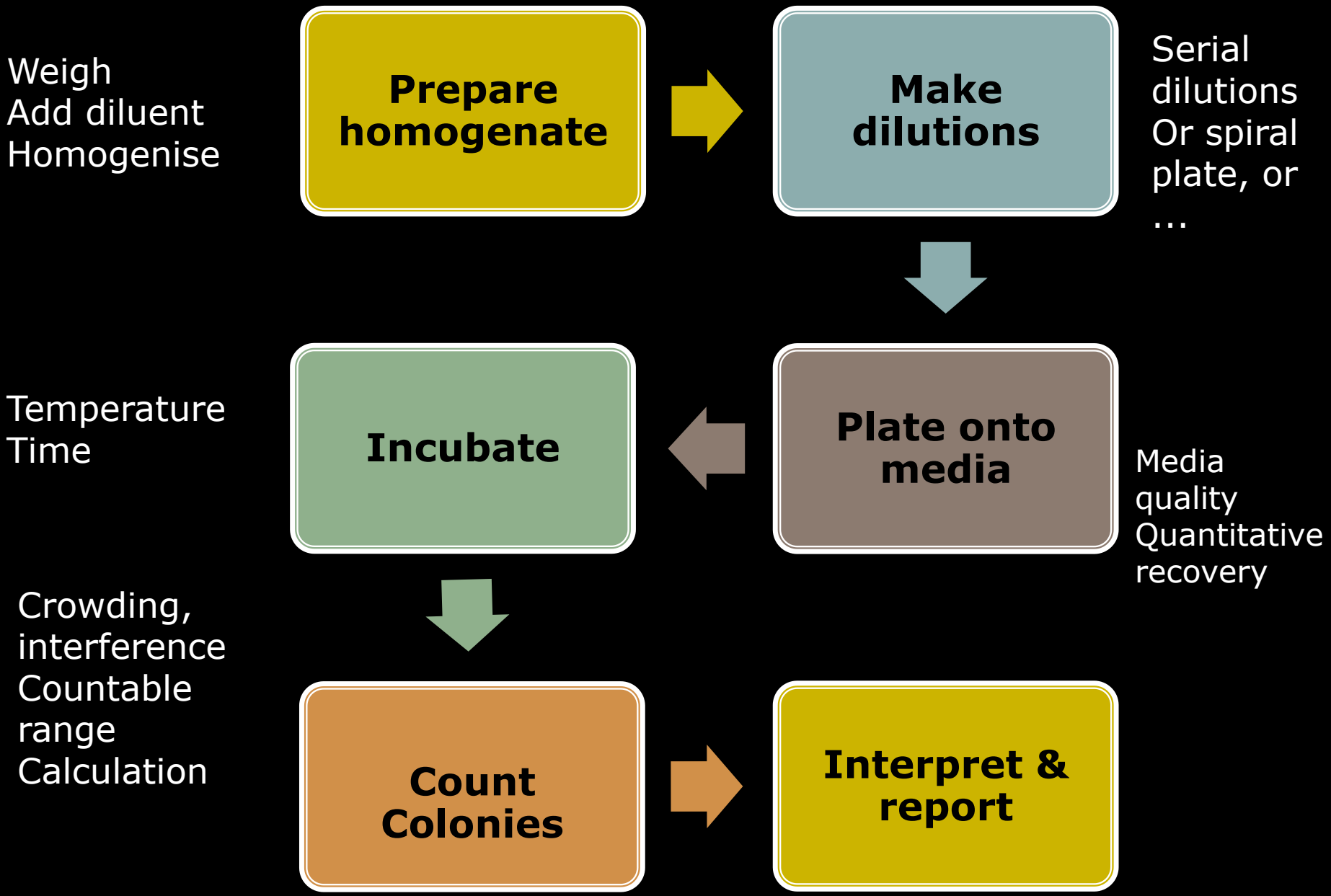
- Microbiology Lab uses **reference cultures** to check whether:
- Media supported the growth of the organism on the test day
- Temperatures were not too high or too low
- Or to pass a batch of media before use

- Do the test with the sample
- Streak a control plate
- Periodically, maybe monthly, a reference sample is tested
- Less frequently, maybe 2x or 4x /year, a proficiency test program is engaged in.

The aim is to:

- Change the paradigm – labs do not achieve their objectives by using unquantified single organism reference cultures
- Unquantified references only help at the most basic level and do nothing at all for a quantitative test.

- Let’s explain.....


Weigh
Add diluent
Homogenise
Prepare homogenate
Make dilutions
Serial dilutions
Or spiral plate, or ...
Plate onto media
Media quality
Quantitative recovery
Incubate
Temperature
Time
Count Colonies
Crowding, interference
Countable range
Calculation
Interpret & report

How does this

Help with this?

- **Prepare homogenate**
- **Make dilutions**
- **Plate onto media**
- **Incubate**
- **Count Colonies**
- **Interpret & report**

Separately:

- Many standards require specific strains to be used.
- These strains are the type strain.
- This ignores the fact that atypical organisms exist (e.g., we miss at least 15 % of *E. coli* by looking for indole production and lactose fermentation at 44.5 °C)
- It also means we may ignore an organism we see on a plate that is "not quite" exactly the same as the type strain.
- There is an argument for collecting organisms from the local environment and using these as controls..... (we're not going there today....)

Un-quantified (single organism) reference cultures

- Are usually robust happy critters – grow reliably (+ passages x 10^6 before receipt)
- Look completely typical
- Are "perfect" when they are alone on a plate
  - If they don't grow – you REALLY have problems
  - But if they do grow, there is no guarantee there are no problems....

Un-quantified reference cultures

- Do not look at interference between the sample, the matrix / chemicals and the target organisms
- Do not check the whole test system from start to finish

Quantified matrix based reference materials

- Can check the entire system as stand alone materials
- Can be used as internal standards when “sample effects” need to be checked
- Remove the need to streak control plates during the test, because they can be treated as whole samples

Quantified matrix based reference materials

- Can save a lot of time and effort
- Allows the laboratory to meet more aspects of 17025 in an efficient way
- When treated as a sample, they assure the quality of the whole system
- Reduces the need for extensive maintenance of a culture collection.

How often should quantified reference materials be used?

- How often do you perform test work?
- If you only use CRMs once per week, or once per month – what about the other days?
- What about the other sample types tested?

Daily Controls

- These are meant to be:
- FUNCTIONAL
- ECONOMICAL
- RELIABLE
- EASY TO USE

- Used daily

- The point is NOT always to be perfect.
- The point is to know that – all things considered – all aspects controlled – all variables known – that the testing system is in control and therefore:
- The test results are valid and have accuracy within a defined limit

Using CRMs

1. must be a planned activity
2. should be done on every testing day (in some form or another)
3. must address the quality of the tests conducted
4. assist to determine CONSISTENCY of test performance
5. results are MEASURED OVER TIME

The IFM Story...

- After a 17025 audit (in 2011), we were required to ***implement*** the use of quantified reference materials under clause 5.9.1 (of the previous edition of 17025)
- We thought – no problem! We make them, monitor them, certify them and use them, we just need to "make it official"

- This proved difficult.
- The arguments following were raised by our lab supervisor at the time our journey began.
- The lab supervisor was thinking in “specification mode” rather than “quality mode”.

- Of course, our accreditation body was right. Implementing quantified reference materials was not only necessary for us, but also an efficient way for us to meet our needs.
- The barriers we faced to their successful implementation were all “mental”. (…. “But we always did it this way”)

Barriers to using CRMs

- “I don’t have time to do another test.”
- “I cannot afford to use a separate CRM for every analysis.”
- “I don’t want to be spending time entering and analysing data to prove all is OK.”
- This is just “another thing” we have to do in a long list of things we already do.

"I don't have time to do another test."

- ***Counter-argument:*** If there is no time to assure validity of test results, there is no point in testing at all.

- ***Solution:*** If the test took about the same amount of time as streaking a control plate, would that be acceptable?

"I cannot afford to use a separate CRM for every analysis."

- ***Counter-argument:*** If the test approach, including its validity checks do not support the revenue, the business plan needs to be adjusted.

- ***Solution:*** If it didn't actually cost that much, could we do it?

"I don't want to be spending time entering and analysing data to prove all is OK."

- ***Counter-argument:*** If we are agreed there is no point in testing unless the result is valid, by default, QA activities are priority.
- ***Solution:*** Good planning and protocols can be implemented to avoid such activities from causing additional work.

This is “just another thing” we have to do amongst a long list of things we already do.

- ***Counter-argument:*** This QA activity can replace other activities. ... Provided that QA activities are already in place, using CRMs should not result in there being MORE to do.

- ***Solution:*** Working smarter, not harder

IFM lab staff agreed with and understood all of that, but

- There were still the practicalities of actually using it.....
- Note that NOT using CRMs was not an option for us. It was a requirement from the AB.
- Chemists have been using CRMs "forever".
- We believe the only reasons biologists have not been using them is for lack of reliable cost effective supply.

We began by "booking in" CRMs as a normal sample

- Considered by staff to be useful.
- We would get through the entire test day, and THEN someone would remember they had not yet set up QA samples

- ..... Oh dear

Rule 1. Using CRMs is planned

- The job of preparing CRMs was given to the staff making media. At the beginning of every day, each required CRM was made up and placed in the cool room, "ready to go". Media staff were some of the main users of CRMs, so it made sense to give them this responsibility

Confusion about how to prepare and how to use

- Sometimes 4-6 analytes on the CRM certificate with different concentration levels. Staff want to "follow" - not think.
- This was "left over" from the "bad old days". There is little thought required to streak a plate. Suddenly we needed to think about:
  - what we were doing,
  - how we were doing it
  - and why.

- Allowed the staff to make their own judgements (act professionally)
  - This was a bit confronting!

- In time, staff found they liked the responsibility. Implementation was not perfect, but satisfying when it was mastered.

- Then we started collating the results
- The test certificates showing results for chosen CRMs and methods were just “lumped together” for someone to sort out at the end of the week

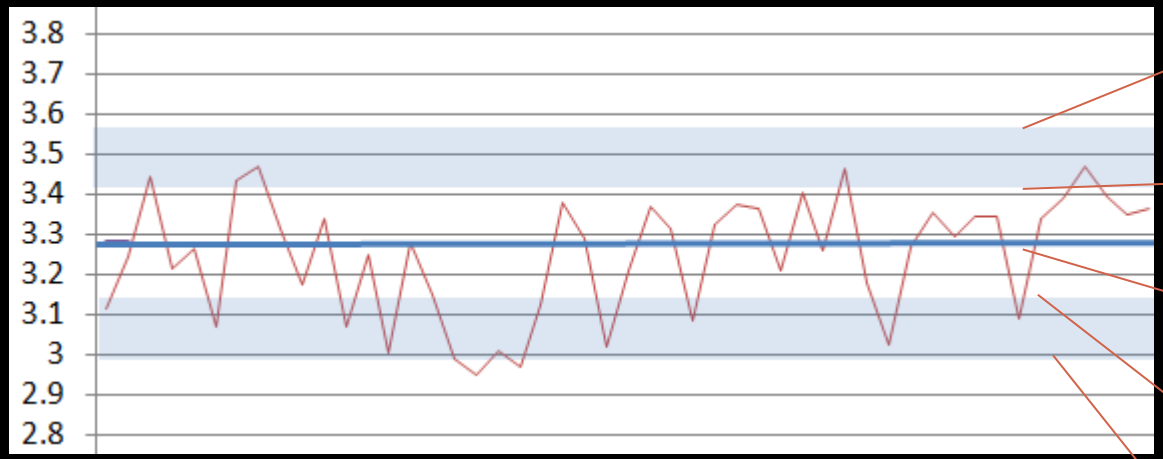
- the “I am too busy” arguments started again when someone was faced with a week’s worth of data

This approach was counterproductive

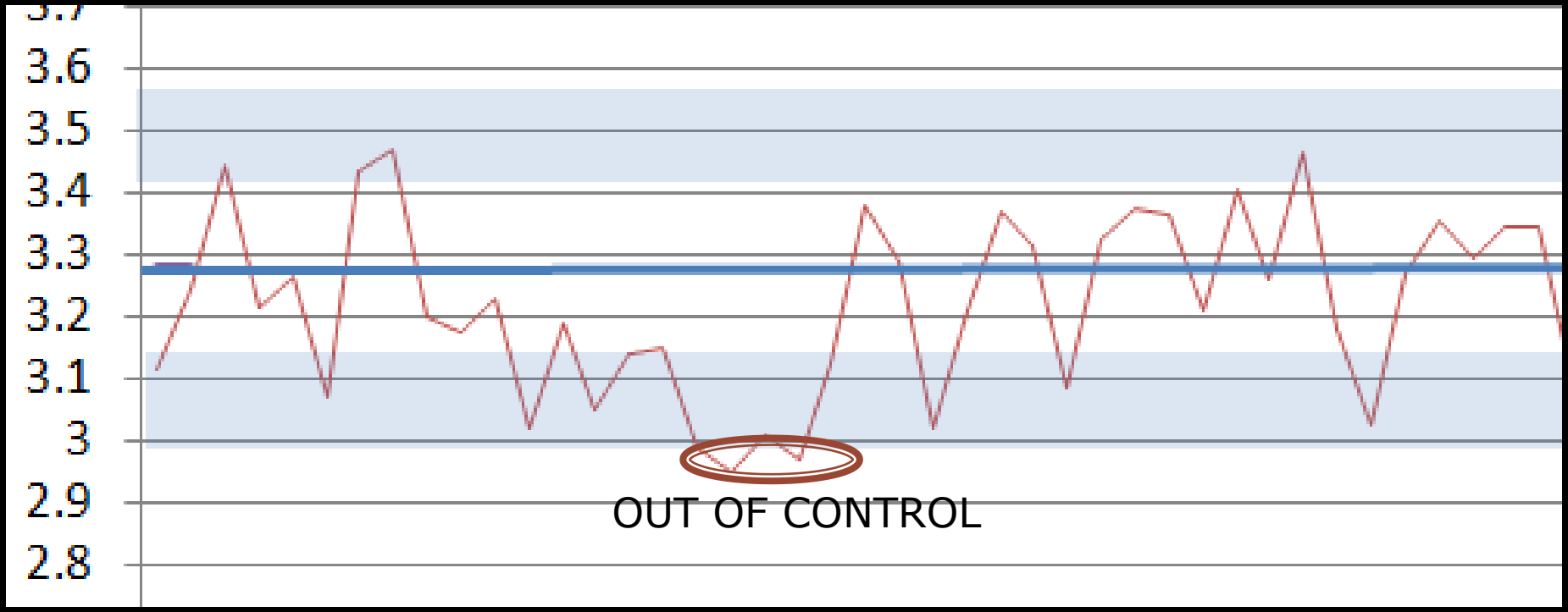
- Waiting until the end of the week (or longer) to deal with the data does not serve the purpose of using a CRM.
- The data needs to be dealt with immediately.

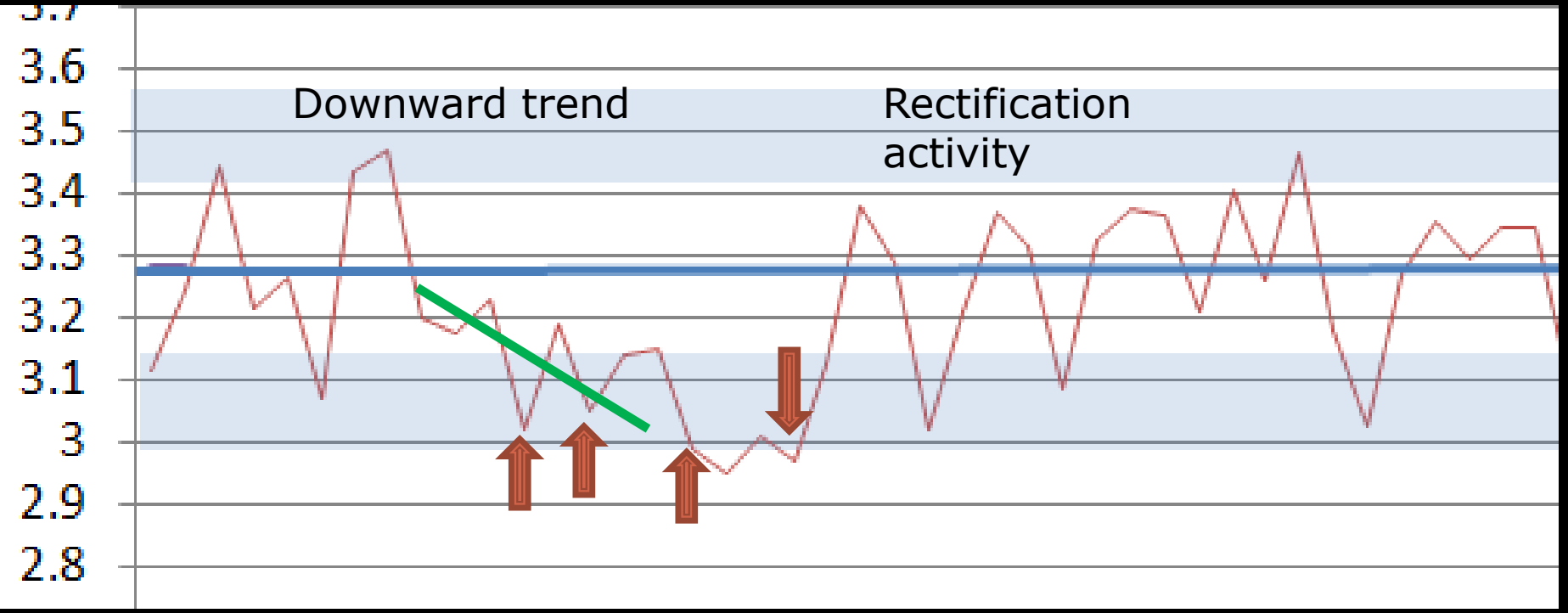
- We started using a spreadsheet like a control chart
  - Control charts are basically just a collection of data plotted over time.
  - Statistical limits are shown on the chart
  - Enable users to see how the system is going “at a glance”
  - The beauty of a control chart is the fact all aspects of the system are looked at as a whole.

Typical Control Chart



- Upper Limit
- “Hi- warning”
- Target
- Lo-warning
- Lower limit


3.6
3.5
3.4
3.3
3.2
3.1
3
2.9
2.8
OUT OF CONTROL


3.6
3.5
3.4
3.3
3.2
3.1
3
2.9
2.8
Downward trend
Rectification activity

Control chart concept was accepted (YAY!!)

- But : "we are too busy to keep it up". Someone has to find time to finalise the test report, open the control charts and add the data points.
  - AND THEN ANALYSE THIS DATA....
- The data from the testing of CRMs was just left to the end of the day and staff wanted to go home rather than doing this "just another task".

We were sagging at the finish line

- So much effort, so many stumbles
- Deep thinking was required.

Modified control chart

- Doubles as the worksheet for CRM testing and make-up

TOTAL COUNT CONTROL SHEET

Method name	Total Count	O_2 / AnO_2	O_2
Name of RM	FM2032-501	Certificate Issue Date	1/7/14

TOTAL COUNT

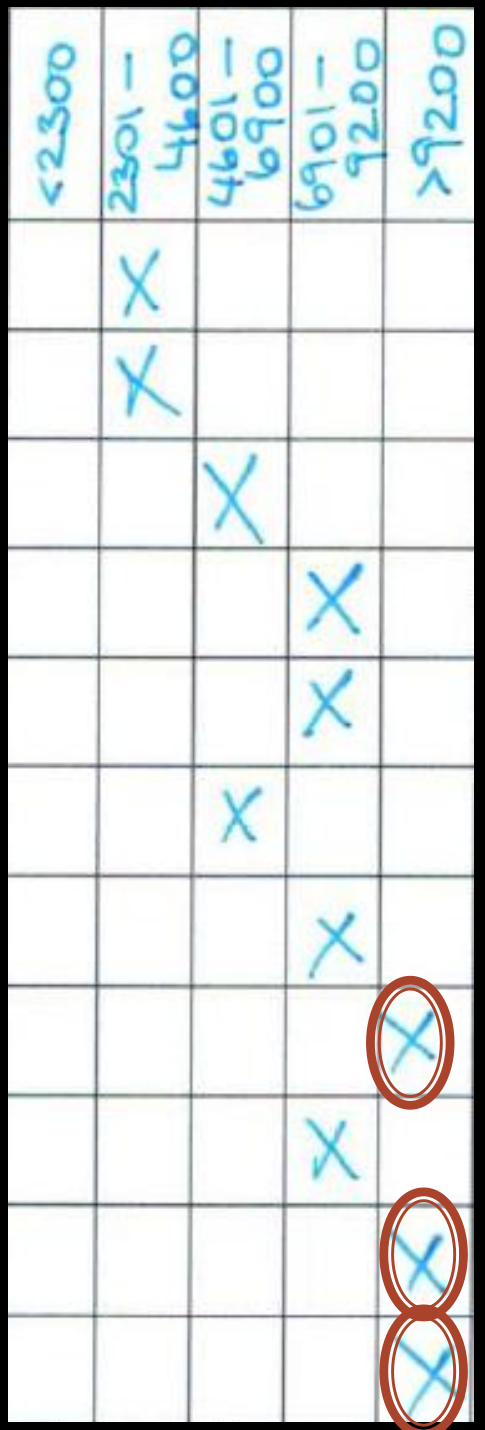
Date	Diluent Batch	Spiral Plate Setting	Media Batch	Initials Date	230 Coun
4/7	Pep 147	50 µL S	PCA 153	JT 4/7	
5/7	Pep 147	50 µL S	PCA 153	JT 5/7	
7/7	Pep 147	50 µL S	PCA 156	MJ 7/7	
8/7	Pep 147	50 µL S	PCA 156	JT 8/7	
11/7	Pep 151	50 µL S	PCA 156	MJ 11/7	
13/7	Pep 151	50 µL S	PCA 156	MJ 13/7	
14/7	PW 157	50 µL S	PC 159	JR 14/7	
15/7	Pep 157	50 µL S	PC 159	RT 15/7	

$_2$ / AnO_2	O_2	Temperature	30°C
ertificate Issue Date	1/7/14	Certificate Expiry Date	15/9/14

Media Batch	Initials Date	2300 - 9200 Count	<2300	2301-4600	4601-6900	6901-9200	>9200	Initials Date
PCA 153	JT 4/7	4700			X			✓ 7/7
PCA 153	JT 5/7	5300			X			✓ 8/7
PCA 156	MJ 7/7	6400			X			✓ 10/7
PCA 156	JT 8/7	41000 ✓ 11/7		X				✓ 11/7
PCA 156	MJ 11/7	2700		X				✓ 14/7
PCA 156	MJ 13/7	4400		X				✓ 17/7 *
PC 159	JR 14/7	5100			X			✓ 17/7 *(lat
159	RT 15/7	2500		X				✓ 18/7

The hi-lo limits are in columns at the top of the page

- It is easy to place an X in the relevant column.
- Over time the columns become the trending data.
- No data transfers, no additional tasks for collating results and analysing them.
- The middle columns are acceptable.
- This example gives us 3 points out of specification.



Are they happy yet?

- Not completely.
- It was very “difficult” to determine the column headings for the limits.
- So now, we have a spreadsheet. The spreadsheet automatically calculates the column headings.

Control Charts

Count obtained	0 to 300	301 to 732	733 to 1165	1166 to 1597	1598 to 2029	2030 to 2461	> 2461	Date / Initials

- In all, using the CRMs means we use much less media for control tests and we can replace several other steps of the testing lab's "normal" QC by using quantified CRMs
- When the test results are plotted directly on the worksheet, there is no additional work – just complete the worksheet as per all tests.

- The day is over more quickly
- We spend less time and money on QA activities, and
- have a greater amount of assurance in the validity of our test