

# An Acceptance Chart for Medical Laboratories

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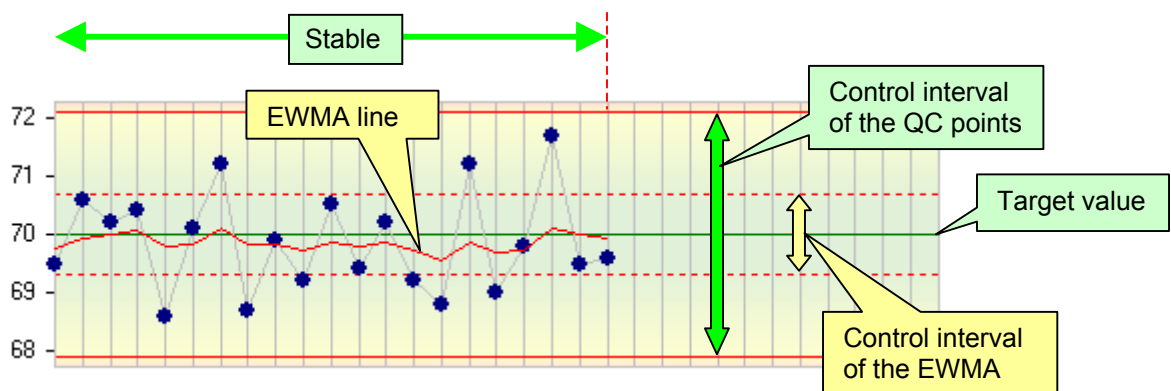
The analytical quality of an assay in clinical chemistry is satisfactory when the deviation of the measured concentration to the true value is not greater than the so-called total allowed error. This wording « allowed error » is widespread but disputable : an error which is allowed is no longer an error ! It is the reason why the software MultiQC borrows from the engineering world the better word « tolerance » which denotes the permissible deviation of an actual property of a product to the par value of this property.

Keeping the whole analytical output within-tolerance should be the chief quality aim of any laboratory. Thus a zero-defect production is achieved. It is very important not to confuse within-tolerance and in-control. They are not the same.

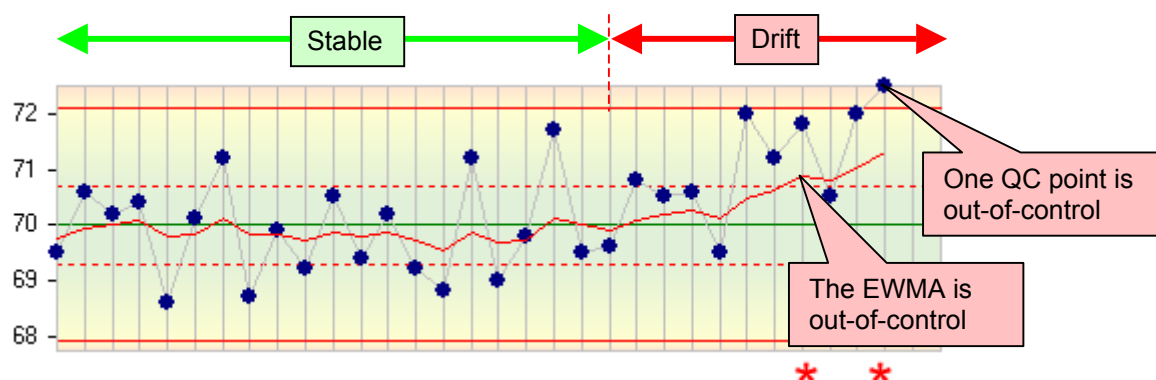
- An in-control process is not necessarily within-tolerance : when the capability index is low, a process may produce out-of-tolerance results even if it is perfectly stable and in-control.
- Conversely when the capability index is high, a process may perform out-of-control and produce however within-tolerance acceptable results.

## Control charts are often too strict

All of the points on the levey-Jennings QC chart below are « in-control ». They are randomly distributed around a mean of 70 and fluctuate within the control interval [68 - 72]. The EWMA line (exponentially weighted moving average) also remains within a narrower control interval [69.4 – 70.6]. The process is performing in a stable fashion.



During the following days, the analytical process drifted upwards for unknown reasons. A first alarm was triggered by the EWMA line when it went across its upper control limit. Three days later, a second alarm was triggered by an out-of-control QC point.

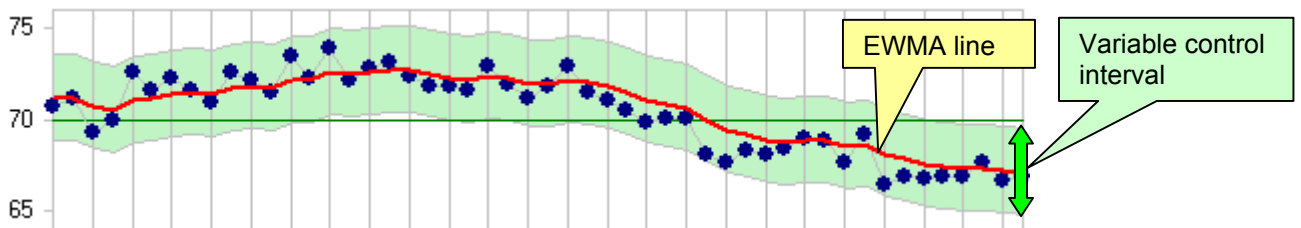


According to the principles of quality control, the analytical process would need an adjustment. However, do not forget that we are in a medical laboratory. The analyte under control is ALT for which a medical tolerance of 8% is generally requested. The observed drift of the QC material ranges to much less than 8%. It has no clinical meaning. The process is obviously acceptable though out-of-control. A corrective action would waste time and money without any benefit for the patient. The level of surveillance provided by the standard Shewhart's chart should be relaxed.

### The acceptance chart

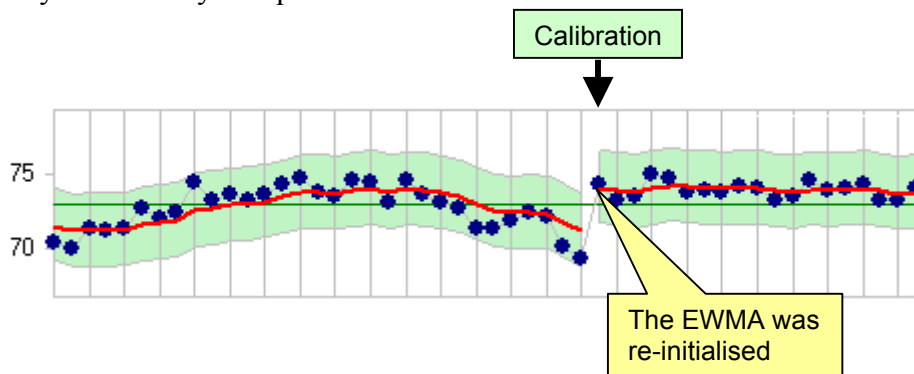
#### 1) A control interval which self-adjusts to slow drifts of the mean

We need a chart that allows analytical drifts to a certain extent. Instead of building the control chart around a fixed target, let us build it around the EWMA (exponentially weighted moving average) with control limits calculated from the short-term standard deviation excluding the long-term variations of the EWMA. The control interval forms a mobile green band on the picture below. Theoretically such a chart would accept any slow drift of the mean because the control interval automatically follows the fluctuations of the moving average.



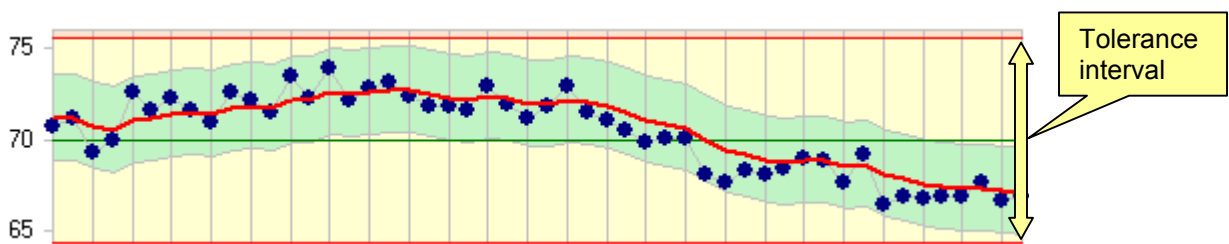
#### 2) A control interval manually re-initialised on intentional shifts

Sudden shifts often occur after routine changes or adjustments of analytical conditions (calibration, new lot, maintenance ...). Due to its inertia, the EWMA would follow the analytical step with a too long delay. It is then necessary to manually re-initialise the EWMA to reset the centre of the control interval to the new shifted average. The gap in the green band below reminds the intentional discontinuity in the analytical process.



#### 3) A fixed tolerance interval

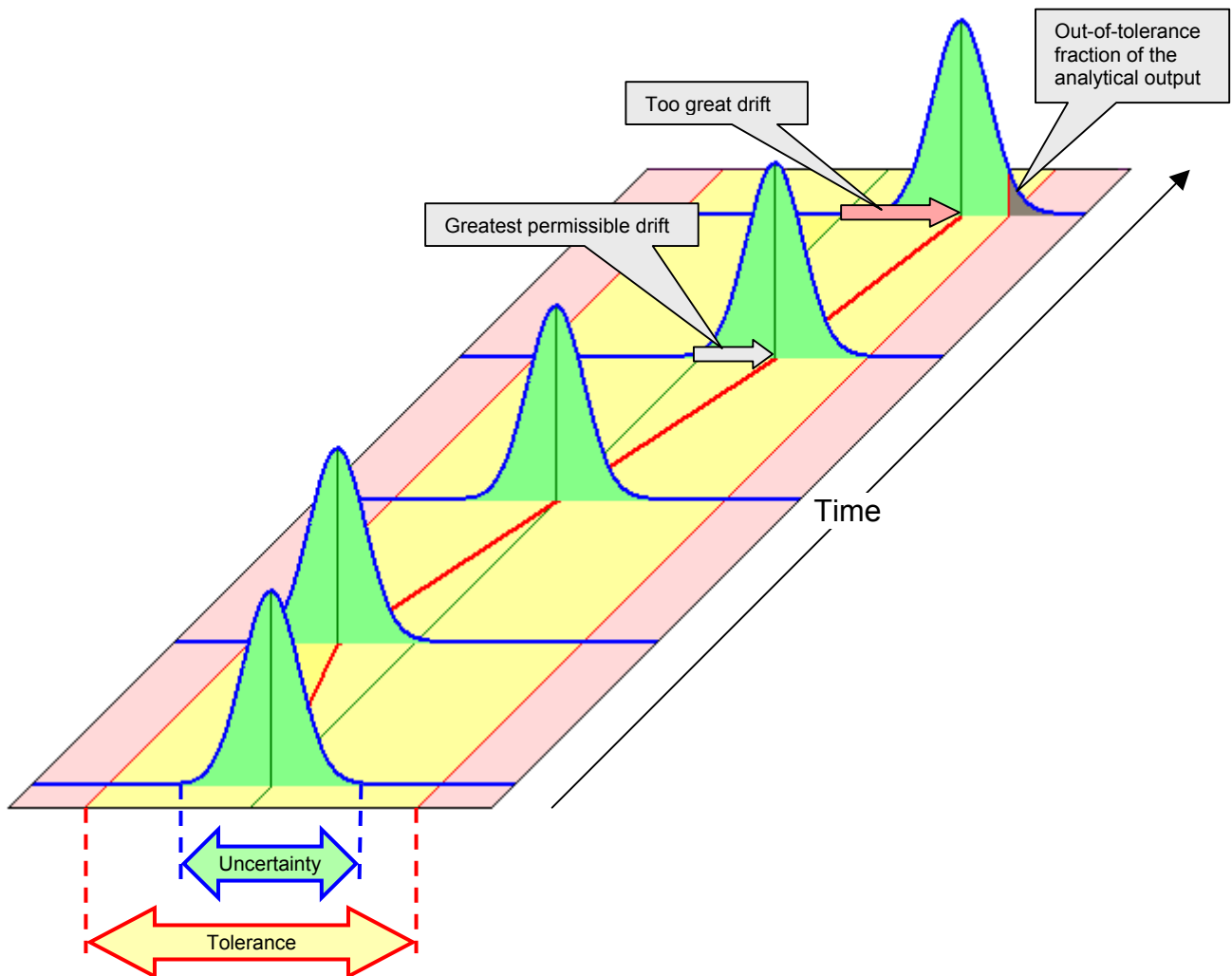
To make the acceptance chart efficient we must set limits to the wandering of the control interval : these are the upper and the lower limits of the tolerance interval.



## Relation to capability index

The green Gauss curve below represents the random distribution of analytical results due to common causes of variation. The span of this distribution is theoretically infinite but conventionally limited to 6 SD and renamed « analytical uncertainty ».

An additional long-term cause of variation may slowly move the green Gauss curve rightwards or leftwards. A zero-defect analytical output is achieved as long as the Gauss curve does not encroach on the left or on the right out-of-tolerance band. It is the reason why the acceptance chart gives up controlling the slow drifts of the mean as long as the uncertainty interval remains nested within the tolerance interval. This is all the easier since the uncertainty is small and the tolerance is large.



The capability index of a method is precisely the ratio of the two intervals we are trying to compare :

$$C_p = \frac{\text{Tolerance}}{\text{Uncertainty}} = \frac{\text{Red Arrow}}{\text{Blue Arrow}}$$

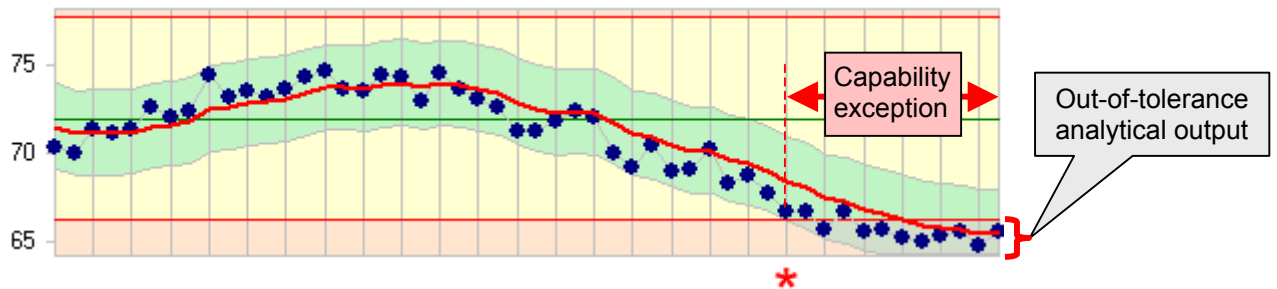
Acceptance charts are only feasible with high capability analytical methods. Several years of practice in a clinical laboratory have shown that  $C_p > 2$  is a good threshold (six-sigma process). Thus about 50% of the analytes in routine clinical chemistry can be controlled by an acceptance chart.

## Working with acceptance charts

Three different situations can be encountered :

1) *Within-tolerance process* : the analytical method is within-tolerance as long as the control interval (the moving green band) remains nested within the tolerance interval (fixed yellow band). The analytical output is thus zero-defect (actually less than 1/740 non-conforming).

2) *Capability exception* : The moving green band encroaches on the lower or on the upper out-of-tolerance red band. A part of the analytical output is out-of-tolerance. This means that the drift of the EWMA is too great in comparison to the capability of the process to ensure a zero-defect production.



3) *Control exception* : One QC point falls out of the mobile green band. In the absence of any intentional shift, this is an out-of-control condition. The process might go on at a pinch if the control interval remains nested within the tolerance interval. However, a special cause of variation occurred and a detailed investigation of the process should be started.

