

# Weqas INR Programme – An Example of Post Market Vigilance

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## Background

Weqas have provided an INR EQA programme since 2009 and currently has over 2250 participants.

The EQA data for the May 2018 INR distribution showed a much wider variation of results than expected, with a coefficient of variation (CV) of 11.8% for the Roche CoaguChek meters compared with a CV of 2% for the Siemens Xprecia Stride (Figure 1). A CV of 7.6% was observed for the Roche CoaguChek meters for the same material in May 2017 (Figure 2).

## Investigation

Inspection of the data from the CoaguChek indicated a bimodal distribution and the manufacturer was contacted to identify a cause. Roche confirmed that they had recently issued new strips calibrated to the new WHO International Reference Thromboplastin rTF/16 (Figure 3).

Figure 1 All results distribution 0518

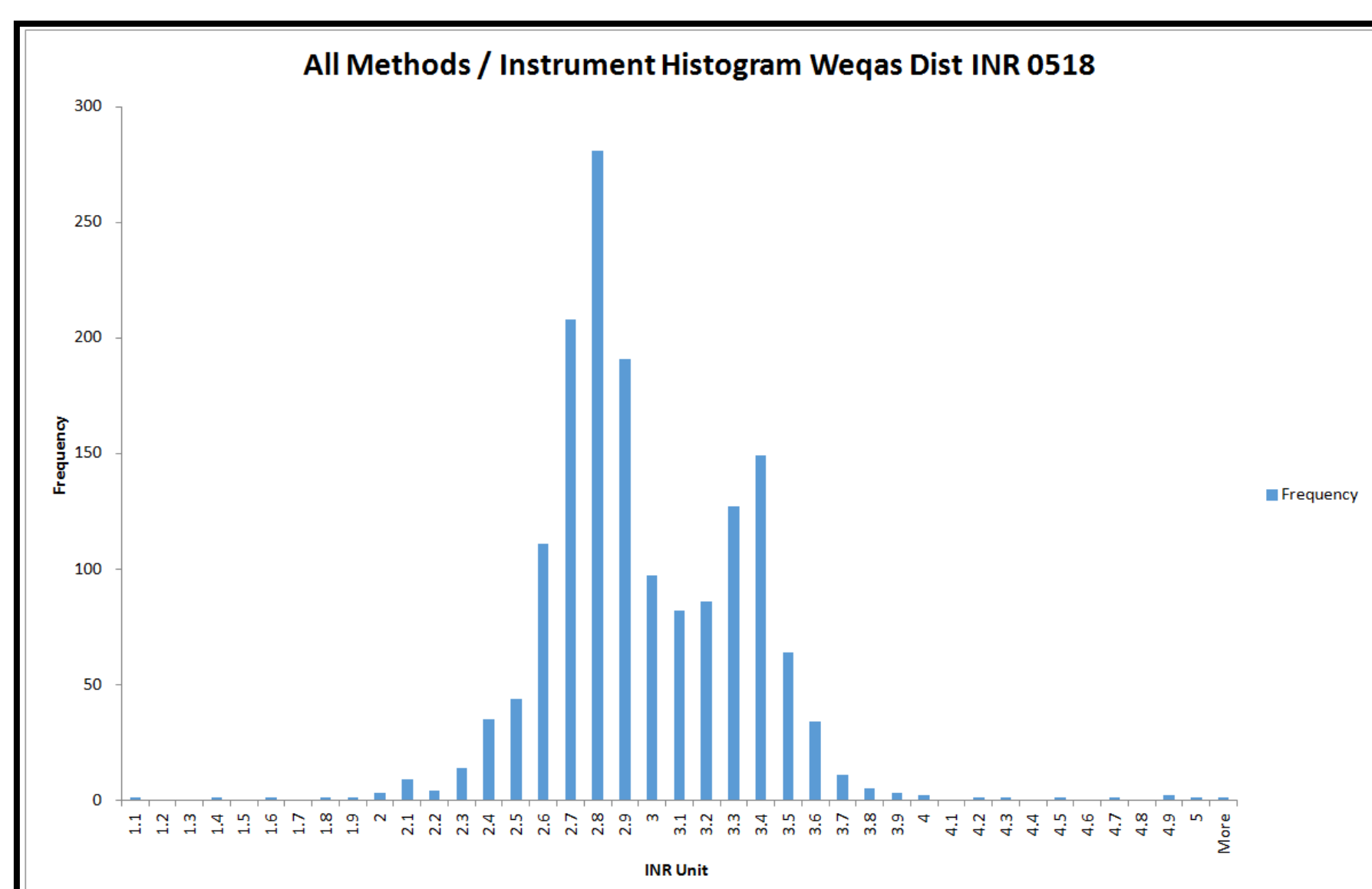
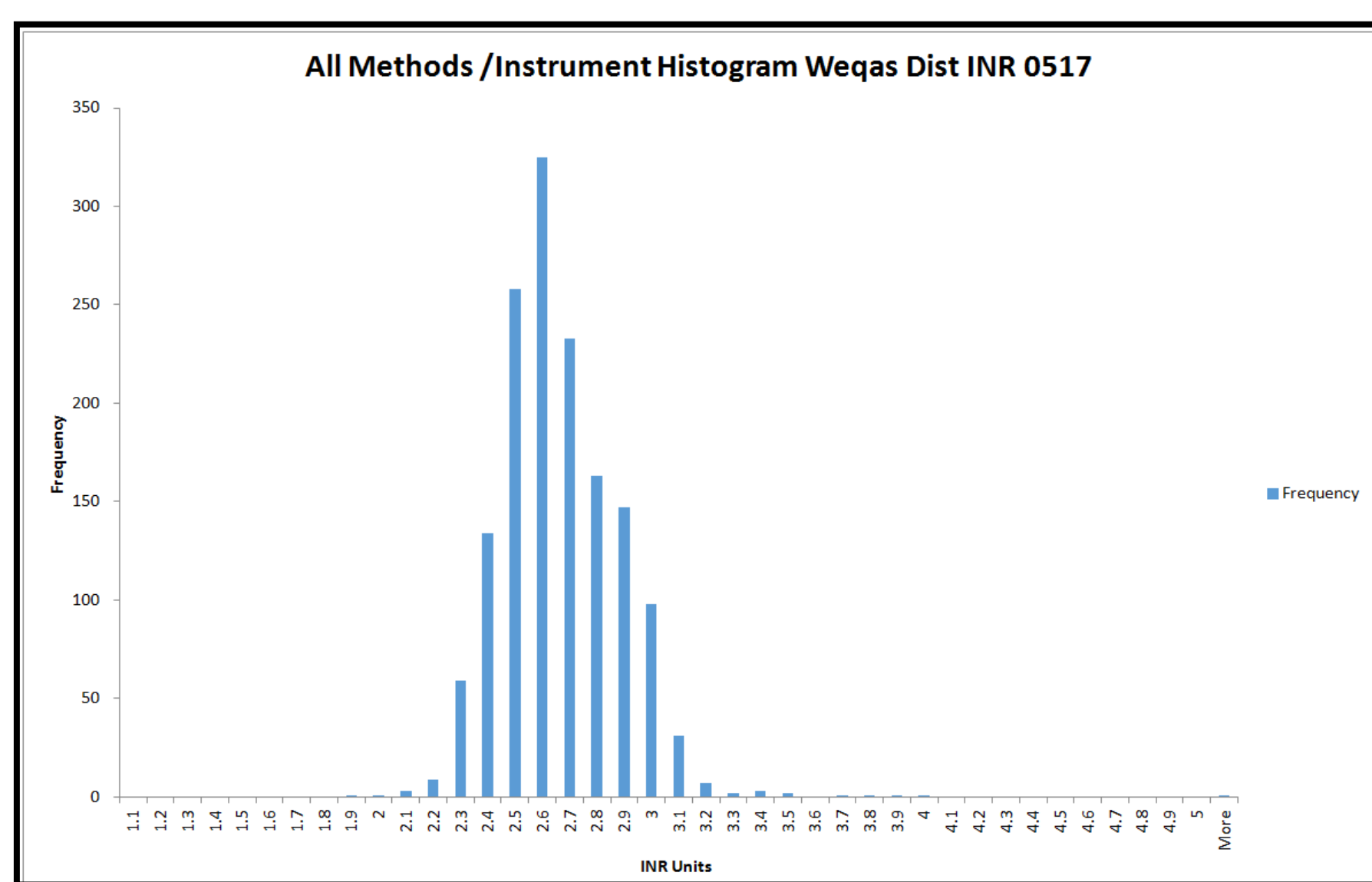
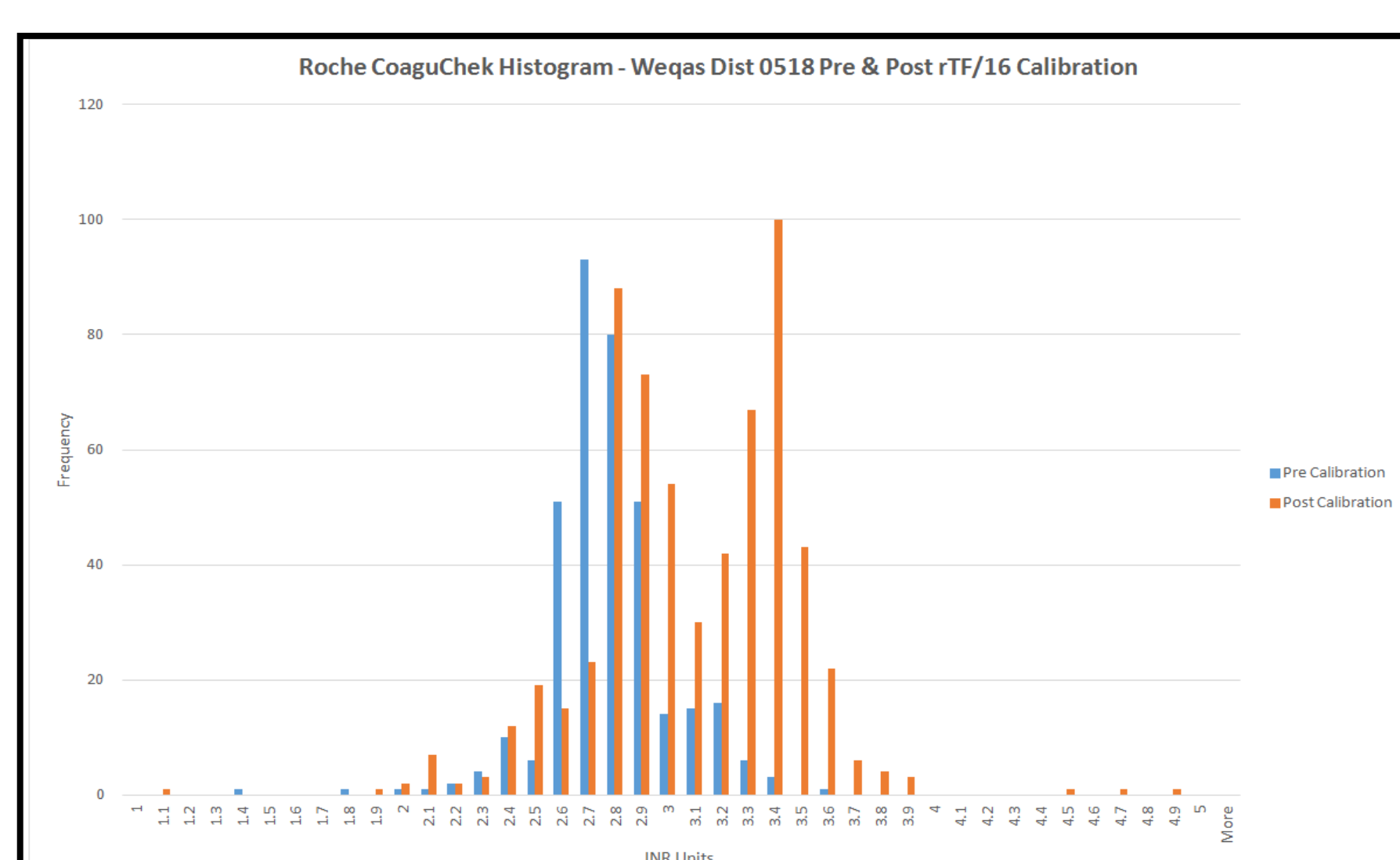


Figure 2 All results distribution 0517



Participants' results were further classified based on strip lot numbers and reviewed in light of the recalibration process, identifying the strips relating to pre and post recalibration results.

Figure 3 Roche CoaguChek results pre and post rTF/16 calibration



## Results

Strips calibrated to WHO reference thromboplastin rTF/09 gave a median of 2.8, which compared well with the results from Distribution 0517 (median 2.8) (Figure 4). However, much higher results and a wider distribution was observed for the rTF/16 calibrated strips. A lot specific bias was also observed, median 2.8 for strip lot numbers prefixed with 286 and 272 (Figures 5 & 6), and median 3.4 for prefix 294 (Figure 7).

Figure 4 Strips calibrated against rTF/09

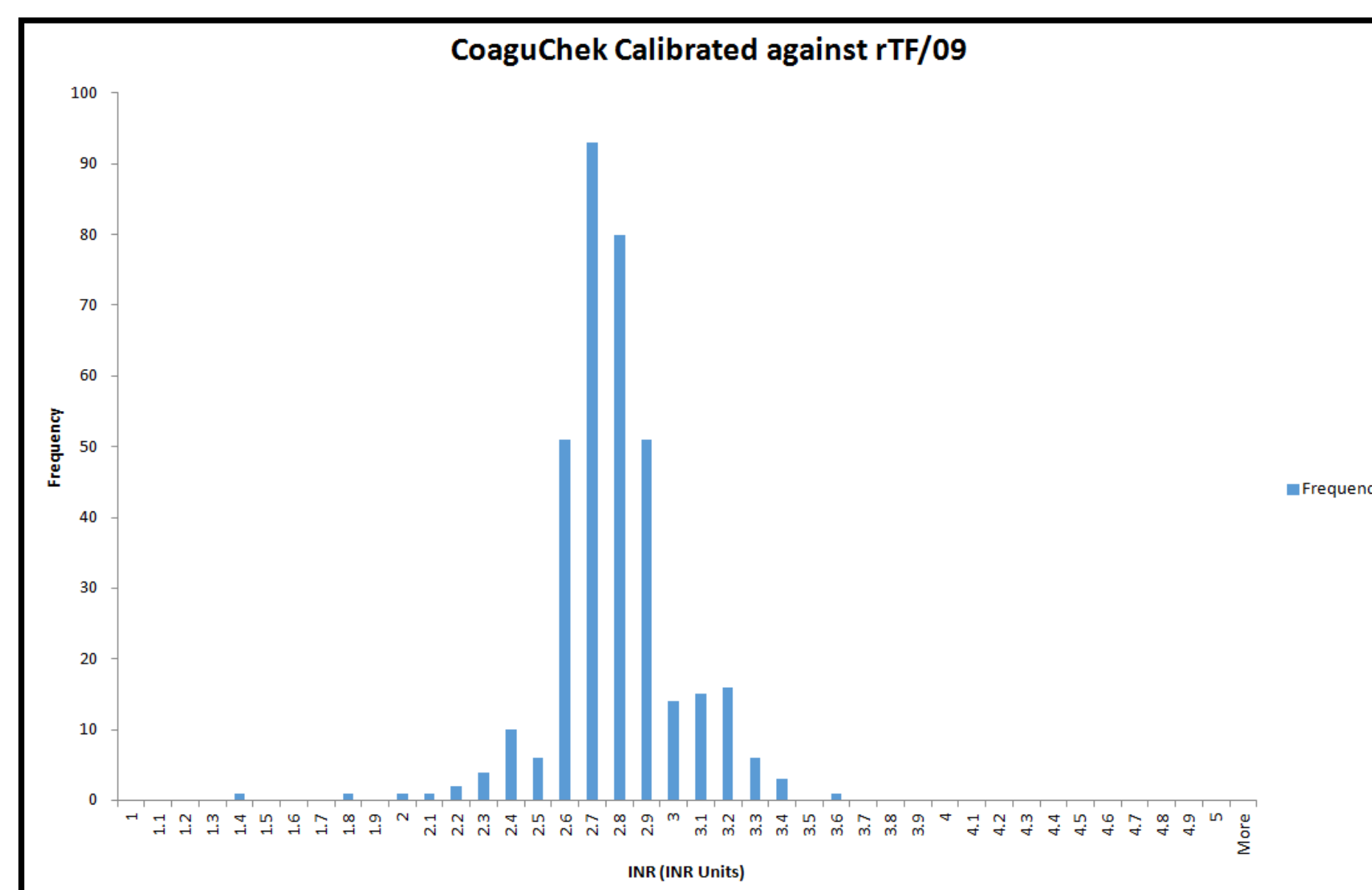


Figure 5 Strips calibrated against rTF/16 with lot numbers prefixed with 272

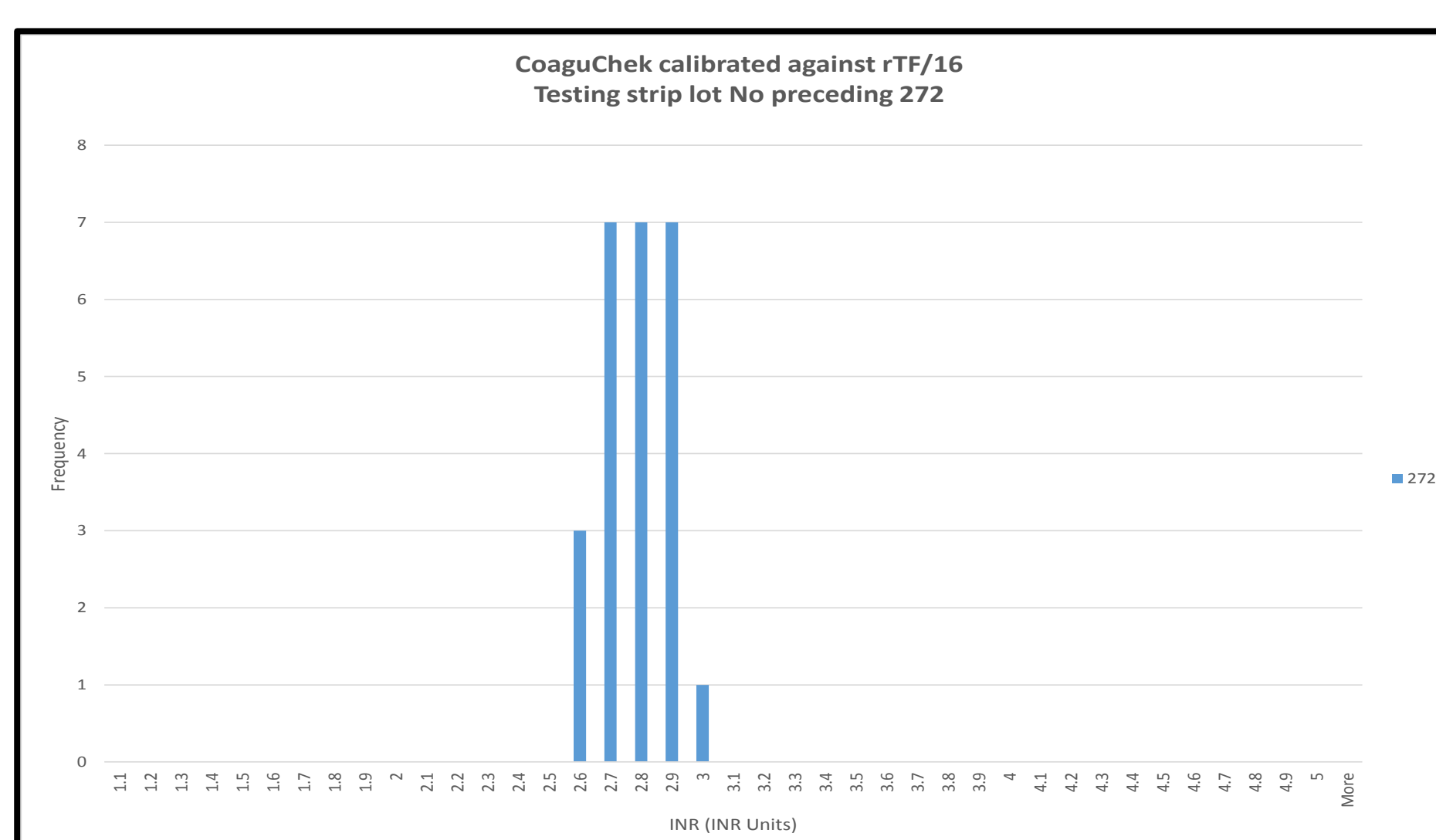


Figure 6 Strips calibrated against rTF/16 with lot numbers prefixed with 286

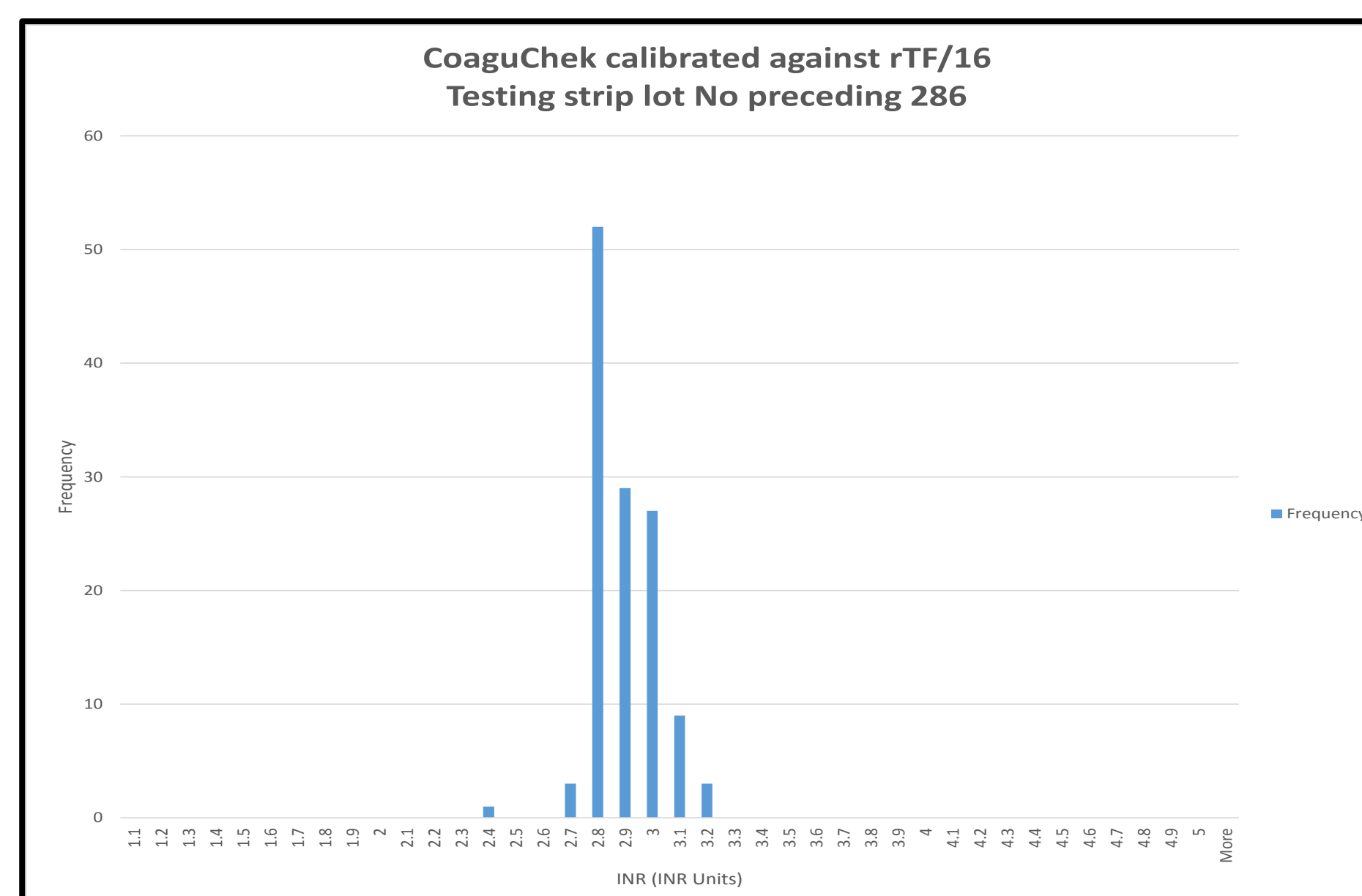
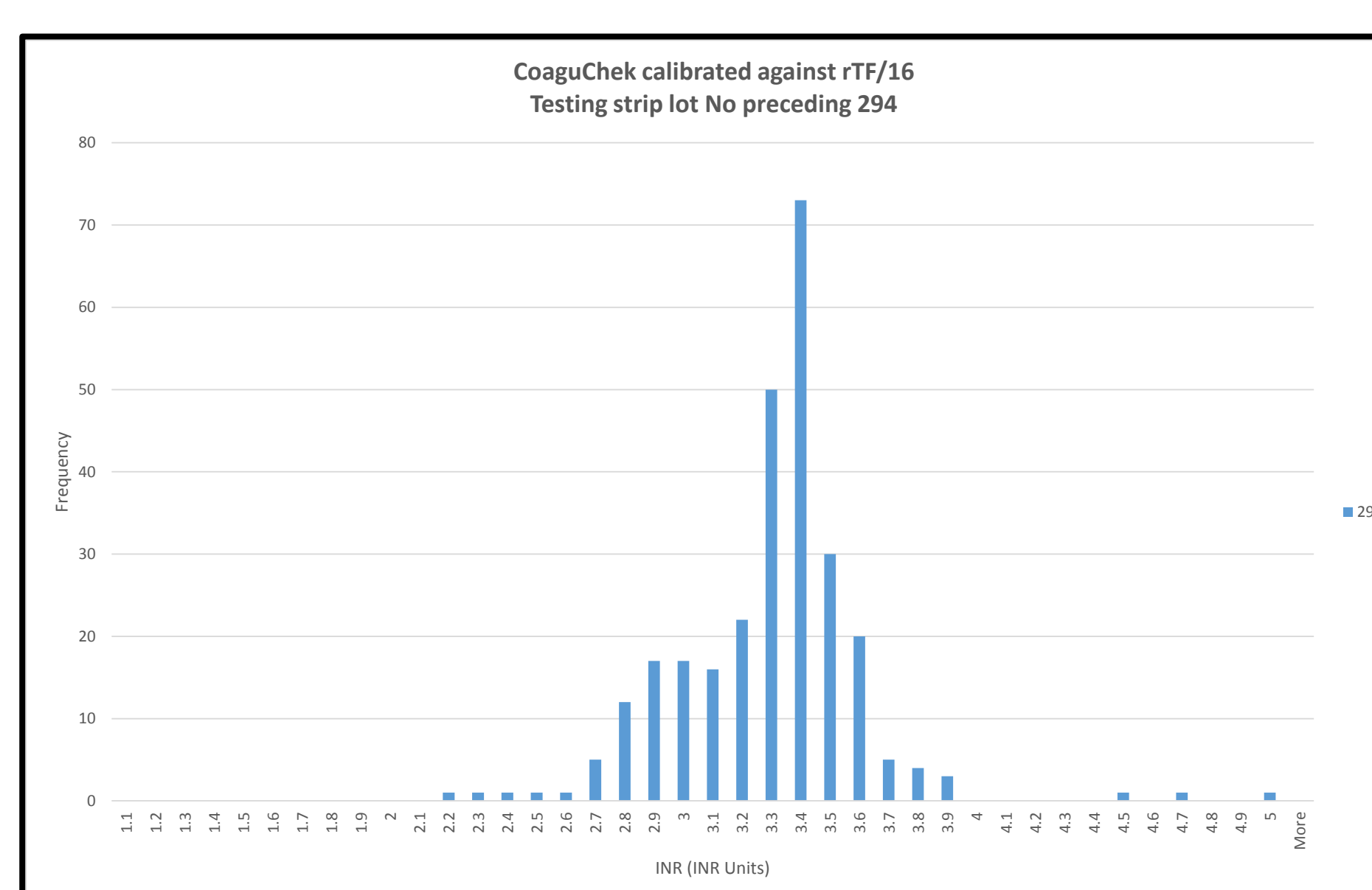


Figure 7 Strips calibrated against rTF/16 with lot numbers prefixed with 294



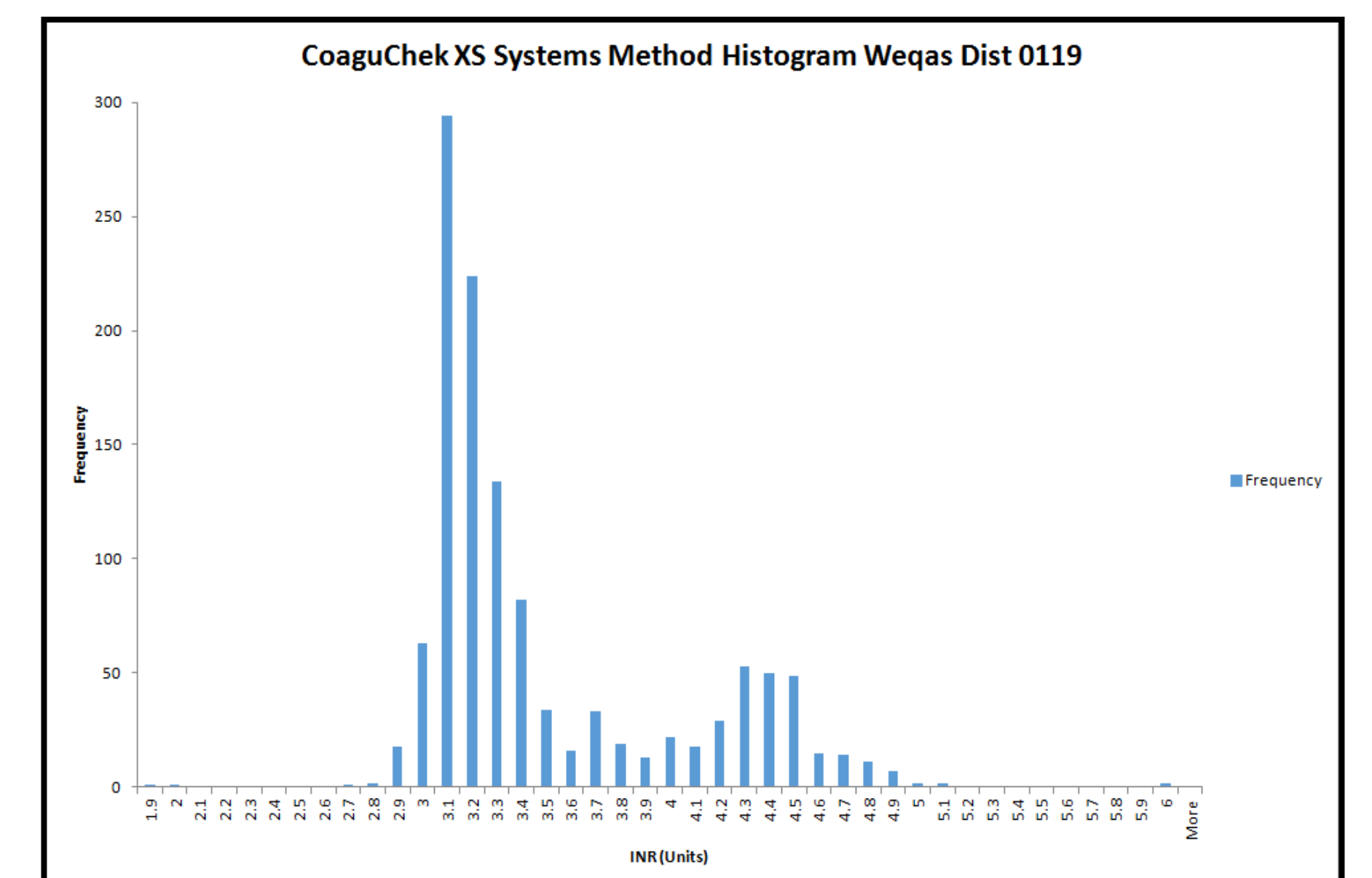
## Discussion

The wider interlaboratory variation was attributed to a change in calibration with a large positive bias observed for lot numbers prefixed 294. Data was supplied to Roche and the MHRA. Roche subsequently issued a field safety notice which stated that the rTF/16 calibration process had resulted in a positive bias and results > 4.5 should be verified with a laboratory. However, our data suggests that for some lot numbers the bias was apparent at a much lower concentration.

## Current Status

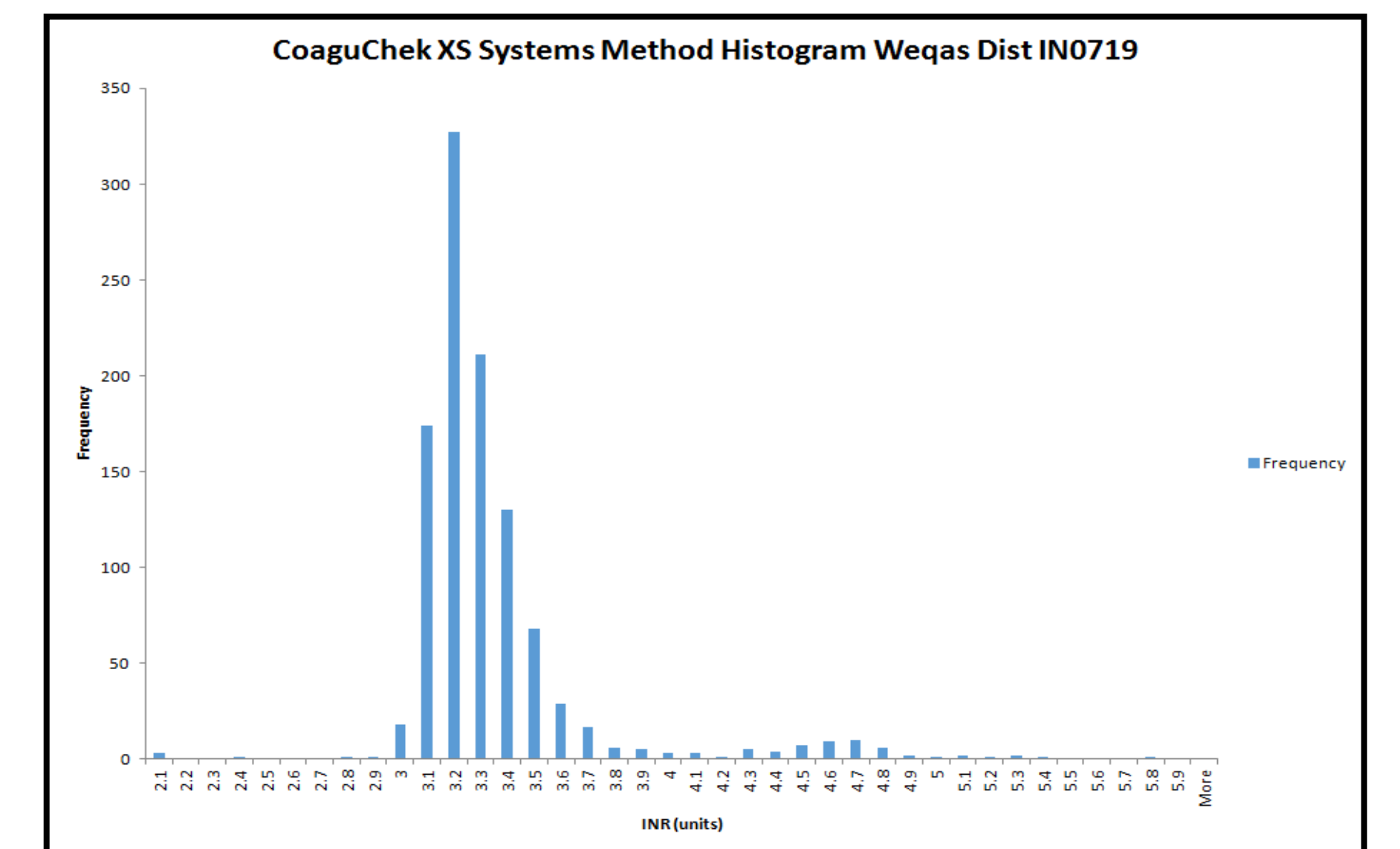
The EQA data for INR distribution 0119, distributed on 22nd January 2019, indicated a bimodal distribution for the Roche CoaguChek XS systems with a CV of 13.7%, median 3.25 (Figure 8). The CoaguChek PRO II systems appeared unaffected.

Figure 8 Distribution 0119



In July 2019, this same sample was distributed once again. A bimodal distribution was observed for the CoaguChek XS systems, however the number of results submitted from participants using strips calibrated against rTF/16 was significantly reduced (Figure 9).

Figure 9 Distribution 0719



Roche have reverted to rTF/09 calibration, with the first of these new strips being available from November 2018. Strip lot numbers higher than 334499xx and Code Key S\_344 have been recalibrated to the rTF/09 WHO Standard. The remaining rTF/16 strips that may still be in circulation currently will be from 272167xx – 334499xx.

## Conclusion

This data highlights the important role of EQA in post market vigilance, and the importance of collaboration with the manufacturers in identifying the causal effect and in addressing the issues.