Dear TGA Officer:

I am writing in regards to the uniformity requirements in the new TGO 101.

The main point I wish to highlight is that the uniformity requirements for an active ingredient may be difficult to meet if the ingredient concentration is low.

The following example shows a real case that we observed in one of our research projects. The samples were purchased from a supermarket.

This product is in tablet form with the claimed active ingredient concentration at 79ug/g (or 75ug/tablet.)

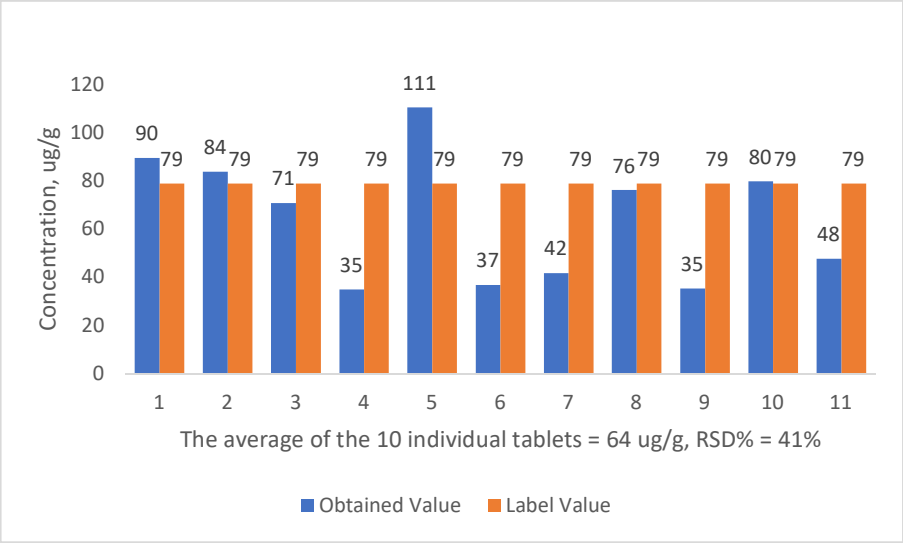

Figure 1. X test results from 10 randomly selected tablets (Same Batch Group 1)

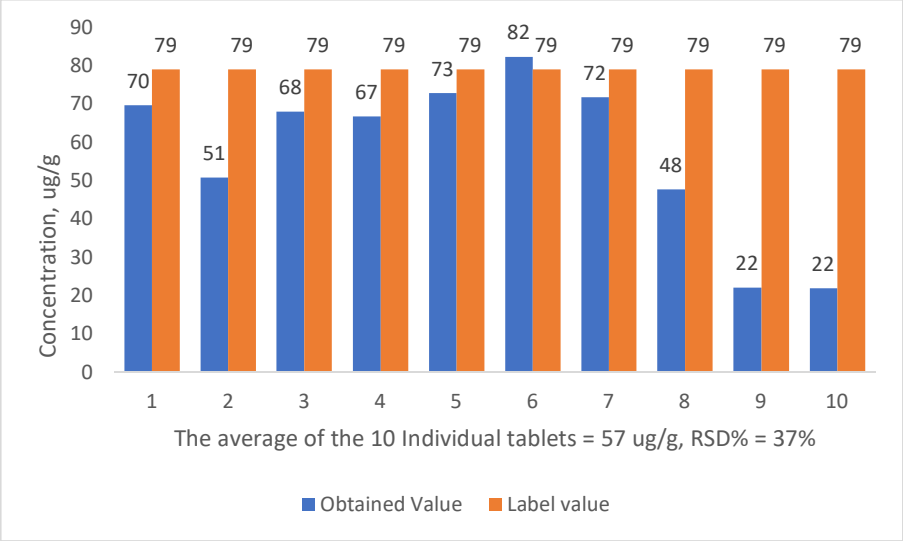

Figure 2. X results from 10 randomly selected tablets (Same Batch Group 2)

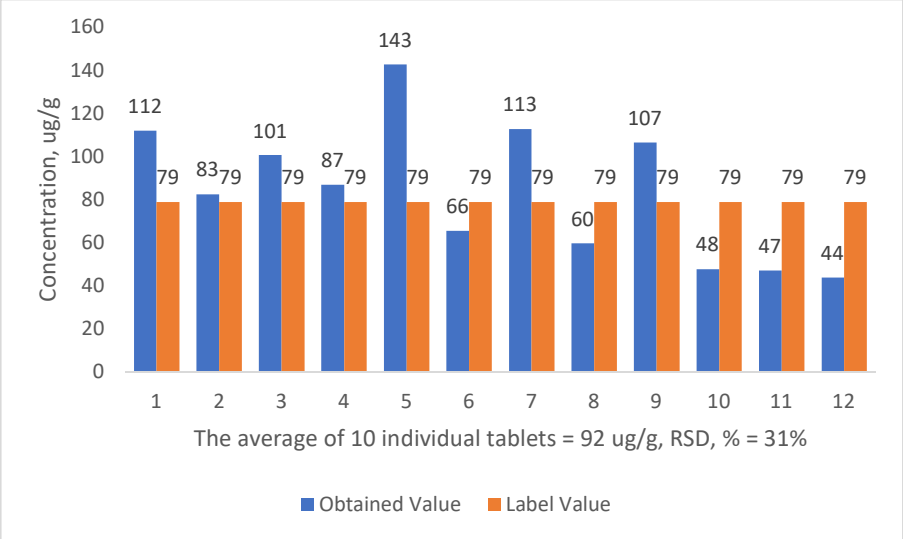

Figure 3. X results from 10 randomly selected tablets (Same Batch Group 3)

We observed very high variations of the test results between each individual tablet. The three groups of the test results all presented an RSD% of over 30%. However, the average result of the 30 tablets was 71 ug/g, which was close to the label value.

To check if the variation was due to the test method, we blended 10 tablets into powder and tested the powder 10 times. The RSD% was reduced significantly to less than 10%.

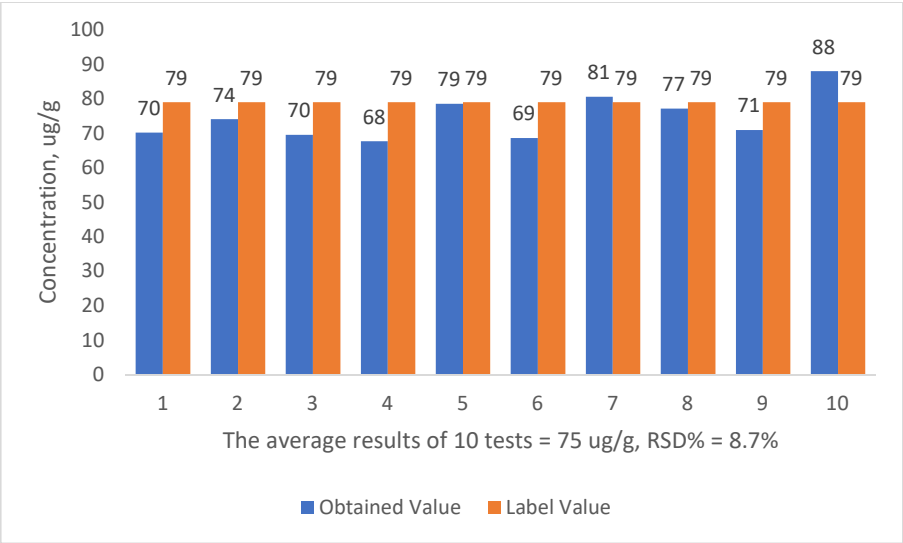

Figure 4. X results from 10 tests of the powder made from 10 tablets

We purchased the same product with a different batch number and carried out the same tests. Although there was an improvement in the uniformity, the RSD% still exceeded 15%.

Given these results, would these products be acceptable under the TGO 101 standards?

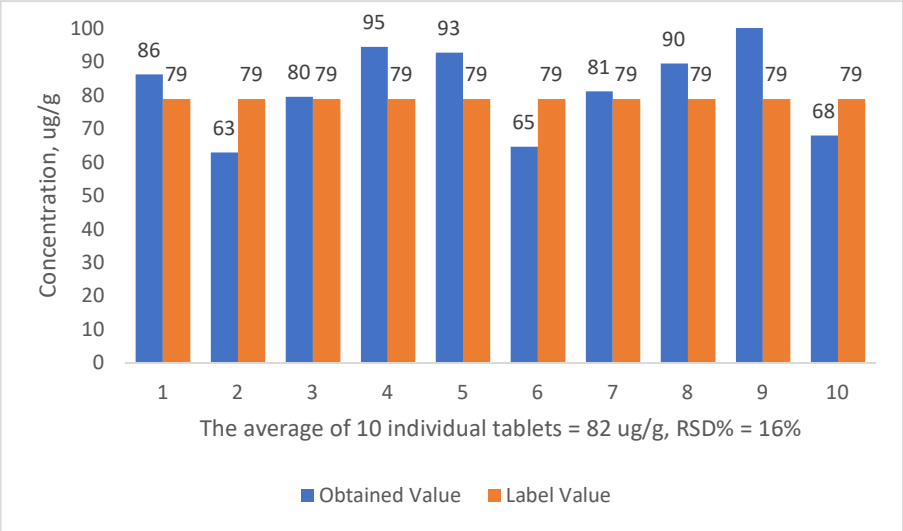

Figure 5. X results from 10 randomly selected tablets (Different Batch)

Summary

- The new TGO 101 (Schedule 1) may be infeasible for manufacturers, especially the requirements for uniformity.
- The uniformity requirements are also presenting challenges for the analytical testing method. Some classical testing methods may have a standard deviation of <2%; however, some new instrument methods have a minimum standard deviation of around 5%.
- The uniformity requirements shall consider the concentration of the active ingredients. It is apparent that low concentration ingredients will be unlikely to meet these requirements
- There are uniformity issues between tablets for some ingredients in the products available to consumers in the market. The above example shows a case at the concentration of around 75ug/g, there are many other ingredients with lower concentrations. They could have similar uniformity issue.

Recommendation

To prove if the new TGO 101 requirements are practical, TGA may consider to conduct a pilot product survey based on the TGO 101 requirements for some products in the market.

Background:

UBO Services Australia Pty Ltd (UBO) provides consultancy services on inorganic testing methods. We also provide onsite testing services using a portable X-Ray Fluorescence (pXRF) analyser.

With the pXRF, we have developed a quick test method (5-10 minutes per sample) to determine the inorganic elements in pharmaceutical products such as zinc, iron, selenium and iodine in

multivitamin tablets. The pXRF can be used as an onsite quick tool for both quality control and uniformity test purposes. Above mentioned issues were observed in the course of the project.

Please don't hesitate to contact me if any further clarification is required.

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