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A REBUTTAL TO THE "REPLY"

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At the outset a brief background from a pharmaceutics perspective is presented here. Pharmaceutical industry is one of the most tightly regulated industries. Statistics naturally plays an important role in the implementation of the compendial, regulatory and in-house requirements. The minimal requirement consists of a set of basic statistics, such as mean and standard deviation (SD), associated with each group of sample experimental data intended for submission. However, not only each statistic is individually subjected to a set of compendial, regulatory and in-house specifications, but also the individual observation is required to be within specific range for compliance (e.g. content uniformity). Hence these basic statistics are often referred to as the stand-alone sample (SAS) statistics, meaning that each statistic has to meet its own requirements. In this context, the geometric mean is indeed a SAS statistic. It is meaningful and interpretable directly from its face value. The geometric standard deviation (GSD) as derived in ref(B) is also a (SAS) statistic. It is meaningful and easily interpretable directly from its face value. It has the same sample information and the same interpretation as that of the regular SD. Sometimes, it shares essentially the same magnitude as the regular SD. Besides, it also has essentially the same magnitude as that of the jackknife GSD statistic, GSD(JK). For decades, these geometric statistics have been in practice, particulary, since the

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author of ref(B) was a member of the USP In-Vitro Bioavailability Testing Subcommittee (1970-1975). It has also been accepted fully and freely by the above-mentioned over-sight agencies.

However, GSD, as defined (not derived) in ref(A) is not a SAS statistic. As appropriately mentioned in ref(A), the quantity is indeed a "factor" and as such it should be labeled as, geometric scalar factor (GSF). Note that GSF is not a SAS statistic. It has no resemblance to the SD at all. It is not directly interpretable and it does not contain the same information as that of the SD or the GSD(ref(B)). It would be absolutely meaningless, if the current compendial or regulatory constraints and specifications are applied to the GSF sample magnitude, as a stand-alone quantity. It is absolutely not an "analogue" of the regular SD at all. It would definitely mislead the users who with considerable experience in these statistics routinely use, SD, GM and GSD(ref(B)). For this very reason, it was clearly indicated in ref(B) to positively refrain from using this in practice. Since, in several instances, the misled use of GSF surfaced, a strong message was communicated in ref(B), as a caution to the various users who are quick, ready and eager to accept the numerical face value, just because GSF always provides a value of smaller magnitude than that of the SD or GSD, which is definitely advantageous. Examples of these types are abundant in this industry.

It should be pointed out that, there is no mention in ref(B) about "lognormal" distribution, "Gaussian" distribution or "normal" distribution. It should be remembered that not all asymmetrical distributions are lognormally distributed, and a set of log transformed data from an asymmetrical distribution need not necessarily follow a normal distribution. In practice, (especially in an industrial set up), it would be almost impossible to identify accurately the distribution of each and every set of data generated. If a distributional commitment is made,

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then, in a regulatory environment, one is obliged to properly prove such assertions.

It should be clearly understood that, in ref(B), the topic of log was discussed in the context of a data transformation procedure for stabilizing the variances (homogeneity) of the groups (such as formulations) to be compared and for achieving hopefully some degree of symmetricity in the data.

The expression for GSD given in ref(B) has been achieved by carrying out an explicit derivation of the GSD from the first principles by using two well known statistical procedures, statistical differential method and jackknife statistical method. It was not created by means of a "definition." Whereas, the expression for GSF was indeed created as a "definition" by ref(A). This is the ultimate distinction.

It should be noted here, that GSF was presented as a "proposal" in a letter to the editor under the tacit assumption of a pre-selected distribution of the sample data.

Finally, it should be pointed out that ref(B) has been published in the journal "Drug development and Industrial Pharmacy" and not in "Drug Development and Pharmaceutical Industry," as referenced in the "reply." This is misleading. There is a big difference. This is for the benefit of our readership.

ACKNOWLEDGEMENT

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REFERENCES

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