Water, Water, Everywhere!

Here at Compounder's International Analytical Laboratory we find that the vast majority of the formulations we test are good, having potencies which fall within the required range. Occasionally, however, a potency comes in low and we always test the sample again to see if the number(s) change or if they repeat. If the low potency value repeats there could be several reasons for this and among them is the presence of water or a residual solvent in the active ingredient.

On the Certificate of Analysis which is supplied with the active ingredient, there is a line which provides the % Potency of the compound. Nearly always, this potency is given on the anhydrous basis. This means the powder was dried before it was tested, or the amount of water or residual solvent was determined and its value was subtracted from the weight of the powder before it was assayed and the potency determined. Per the USP, there is a maximum allowed % Water or % Loss on Drying (LOD) for each active ingredient. Usually, this number is less than 1% so might be ignored with little consequence. But for some actives the amount is significant and can seriously lower the potency of the final formulation since some of the powder weight is just water. A few examples of this include:

Azithromycin will have between 4.0 to 5.0% water
Bacitracin can have up to 5.0% LOD
Betamethasone Acetate can contain up to 4% water
Bupivacaine HCl will have between 4.0 and 6.0% water and up to 2% solvent
Ciprofloxacin will have 4.7 and 6.7% water
Clindamycin HCl contains 3.0 to 6.0% Water
Dexamethasone Sodium Phosphate can have up to 16.0% total water and alcohol
Folic Acid will contain up to 8.5% water
Levothyroxine Sodium (T4) can contain as much 11.0% water.
Liothyronine Sodium (T3) can have as much as 4.0% water
There are many more examples, but you get the idea.

When compounding, it is always a good practice to note the % Water or % LOD and to subtract this value from the anhydrous % Potency to determine the actual "as is" potency of the active. In the case of the T4 example above, if the anhydrous potency is 98.3% and the % Water is 9.8%, the actual potency of this powder is 88.5%, so this new value should be used to develop the formulation. Therefore, if the required amount of T4 to make a 1:100 dilution is 1.00gram, then divide the 1.00gram by 0.885 (88.5%) to find that the weight required to achieve the correct concentration, which would be 1.13grams in this case.

Final comments:
We like to suggest that whenever a new batch of active is received, the real "as is" potency should be calculated from the anhydrous % Potency and the % Water or % LOD and written on the front of the container before it is placed in stock. (In fact, even when there is not a significant % water, there might be a lower potency value anyway, such as 95% or 97%). This written potency value would then serve as a reminder as to the actual potency of each ingredient when being used, and the weight adjusted to obtain a more accurate formulation.