Addressing the lack of objective standards for the quality control of Chinese herbal medicines

I experience great trepidation when shopping for herbal products. I know there is no standard for objective quality control. Consequently, the bags and bottles of herbs we find on the consumer market can have an almost limitless composition. At best, the plants contributing material to the composition of the herbal product are all well identified but beyond that all bets are off. In their outline of good manufacturing practices, the FDA emphasizes “identity, purity, strength and composition” as the guiding principles of herbal quality assessment and quality control (FDA, 2009). Unfortunately, these principles are applied at the manufacturers discretion and there is no national standard. In practice this leads to extreme variation in the concentrations of the important active ingredients within these herbal products. This extreme variation is, in my opinion, the biggest obstacle to the efficacious application of Chinese medicinal herbs outside of practitioner skill.

Adventures in quality control – The Artemisia debacle of 2016

In the interest of full disclosure, I am a clinician, QA/QC professional as well as a grower of Chinese herbs domestically (Ross TJ, 2016). I have worn the hats of all the major players in this relationship between growers, brokers, manufacturers, clinicians, retailers and consumers. The
strongest force determining the manner of relation between all of these actors is profit. I would say that safety is also a concern. Unfortunately, efficacy would appear to be an afterthought.

Currently, the Chinese herb Qing Hao/Herba Artemisia annua and its major active constituent Artemisinin have acquired great renown. It is in high demand and at my place of employ as a QA/QC professional we had a huge order for a formula containing *Artemisia annua*. We were having trouble finding any that met our requirement of domestic production. We could only find two large batches of dried *Artemisia annua* from the previous year’s harvest. Both were about 90% stem material by weight. (The World Health Organization recommends that stem be less than 10% of the total weight (WHO, 2006).) Neither showed the presence of any flowers or flower buds.

*Artemisia Annua*, Pacific Botanicals, 2015
Clearly this material did not satisfy the fundamental requirements for the medicinal material Qing Hao as stated in the Chinese Pharmacopoeia (‘‘Harvest in autumn during the time of full bloom, remove the old stem’’) but it was *Artemisia annua* (Chinese Pharmacopoeia Commission, 2010). Additionally, it was free of pesticides, heavy metals and any other adulteration. At the very least it was safe. It could satisfy the basic requirements set forth by the FDA within the current GMP guidelines.

My advice was to separate the stem from the leaf, send the stem back to the growers and demand that portion of the cost be returned. Unfortunately, without using the stem material, production would not have been able to fulfill the order, so the stem material was used along
with the leaf to make the necessary alcohol extracts. A monetary decision trumped concerns about efficacy but this decision was acceptable within the current allowable applications of the FDA’s GMP requirements.

The tests currently required to demonstrate “strength and composition” cannot stop this kind of goal post shifting. Primarily strength and composition is demonstrated by showing conservation of weight to volume ratios which address the amount of herb material present in the product but say nothing about the concentration of active constituents.

There are no national standards for the quality of herb materials used in dietary supplements. Your *Artemisia annua* could be anywhere from about a maximum of 1% artemisinin to a minimum of a 100 or more times less than that. As a clinician, how is one expected to dose materials in a reliable way when the batch to batch differences in the potency of the medicines can be in the 10s, 100s or even higher?

In the case of *Artemisia annua*, we know that the major active constituent is found in the flowers and leaves. The medicinal material should be and has been traditionally limited to the leaves and flowers. It has been shown via modern analytical methods that Artemisinin concentration reaches its peaks around the period of full bloom (Baraldi et al., 2008). So percent flower head would be a decent measure for the quality of the medicinal material derived from *Artemisia annua*. I suggest that controlling for percent flower bud by weight and percent stem material by weight would be adequate. This overcomes the primary objection
from the manufacturers(expense) and provides a time tested method to insure the efficacy of the medicinal material. Ideally we would expand the quality requirements for every herb in a similar way.

**Traditional quality assessment of root medicinals**

Historically, organoleptic methods primarily focusing on the evaluation of plainly obvious macroscopic features has been the main method for the quality control of Chinese medical herb material (Zhao, Liang, & Ping, 2011). The most famous and common Chinese herbs such as Ren Shen/Panax ginseng, Huang Qi/Astragalus membranaceus, Gan Cao/Glycyrrhiza uralensis, Dang Gui/Angelica sinensis and Bai Shao/Paeoniae alba have all traditionally been graded for quality according to diameter and length. Potency has always been associated with higher grade and there is increasing amounts of analytical evidence to support this conclusion (Z. Wang, Wang, & Huang, 2014).

It is important to rank root materials by grade to allow for some basic quality assessment to be made. In general, we see herb brokers moving to cuts that make it increasingly difficult to apply traditional methods of quality assessment that require whole roots or transverse sections. It is my conjecture that this trend is a conscious move to hide the ever shrinking root length, diameter and cultivation length of these important root medicinals. Traditionally the root of Astragalus membranaceus was collected in Inner Mongolia or a nearby arid region after 6 years. Now it is often cultivated in the most incongruous climates and harvested after less
than 1 year. Needless to say, there is a huge difference in the chemical composition of wild crafted 6 year old root when compared to a cultivated 1 year old root (Xin, Ma, Xie, Wang, & Hou, 2015).

Because the great majority of clinicians and consumers in the US have no idea what quality specifications they should look for in medicinal materials, we let material on the market without grading it in any way and a type of false equivalency is established. When the growers realized the market can’t tell the difference between 3, 2 and 1-year-old roots, they started harvesting everything in the first year. (This is a bit of an exaggeration but it is impossible to ignore the steady decline in cultivation length among common medicinals such as Huang Qin/Scutellaria baicalnesis, Dang Shen/Codonopsis pilosula and Huang Qi/Astraglus membranaceus). When we look at the chemical fingerprint of the above mentioned species in the 3rd year as compared to the 1st year, there is no comparison, they are hardly even the same medicinal (Ross TJ, 2014). It is like comparing the mind of a man at 10 to the mind of that man at 30.

We should begin to realize that efficacy is not independent of quality control. When we do not have reproducible qualities within some reasonable limit of precision we cannot expect to have reproducible effects. At the very least, quality requirements need to be expanded to include the traditional macroscopic methods of quality assessment.
For example, Huang Qi/Astragalus membranaceus can be graded for quality according to the following method (金世元, 2010).

- **1st class** is more than 50 cm long, upper and middle portions are more than 1.5 cm in diameter, tip diameter is not less than 0.5 cm
- **2nd class** is more than 40 cm long, upper and middle portions are more than 1 cm in diameter, tip diameter is not less than 0.4 cm
- **3rd class** has variable length, the upper and middle portions are more than 0.7 cm in diameter, tips are not less than 0.3 cm

In addition to these broad criteria there are other more nuanced macroscopic and organoleptic features which must be conserved including –

- Long thick root pieces without a hallowed center
- Pliable, tough
- “Golden cup, silver saucer”
- Powdery, fibrous nature
- “Chrysanthemum flower pattern”
- Bean like flavor

If we look at a raw material specification sheet that is designed to meet the FDA GMP requirements what we would likely find is info on the appearance of the medicinal as whole root, cross-section and powder as well as info on how to accurately differentiate *Astragalus membranaceus* from its common adulterant *Hedysarum polybrys*. What is harder to identify is the material that is informing us on how we might measure and control the quality of this
material. This measure and control is often left to a subjective appreciation of odor and taste and the objective consideration of the amount of extraneous material present (adulteration). This is very different from the traditional notions of quality control described above which could also be expanded to include requirements for growing region, cultivation length, harvest time and processing method.

Ensuring Quality – Education, Regulation, Implementation

What I am pushing for is the reintroduction of the role of pharmacognosy into the practice of Chinese herbal QA/QC. This will require increasing educational demands placed on students and clinicians, an increasing complex regulatory apparatus and the compliance of the herb growers and herbal products manufacturers. This modification to the current practice of QA/QC will require a 3 pronged approach.

1. Creating the broadly accepted QA/QC monographs for each herb by academics and clinicians from the US in conjunction with experts in pharmacognosy from China.

The primary focus will be developing a nuanced and cost effective combination of organoleptic tests, combined with analytical chemical tests when necessary, specific to each individual herb that would allow for the quality control of the medicinal properties of each herb within a range that would ensure clinical efficacy.
2. *Disseminating this information to clinicians, manufacturers and consumers.*

At this point in time, the information required for clinicians, manufacturers and consumers to make expert judgments about the quality of Chinese herb materials is left behind the forbidding wall of Chinese literacy. Moving forward, it will be necessary to translate this material and promote its dissemination to relevant consumers. I would heavily recommend the addition of a single 4 unit class to the core curriculum required for the Master’s degree in East Asian Medicine offered in the US.

3. *Enforcing these standards within the market place by increasing the burden of regulation placed upon herb growers, wholesalers, herbal products manufacturers, and herb retailers*

Inevitably all of the above will only come to fruition if backed up by increased regulations. The FDA policy on the GMP of dietary supplements, at least as it is related to Chinese medicinal herbs must change. We must seriously consider the wisdom of continuing to lump medicinal herbs in with “dietary supplements”. I could see a separation into 2 tiers based on quality regulations. Tier 1 being for “dietary supplements” and requiring only the current set of tests to ensure for identity and lack of adulteration. Tier 2 being for “medicinal herbs” and requiring some set of tests to establish the quality of the medicinal material as being “therapeutic grade”.
The most commonly ignored subject within the discussion about the safe and effective use of Chinese herbal medicines is the question of herb quality. It is not safe for people with legitimate illness to seek care that involves the application of ineffective medicines lacking the necessary constituent concentrations to be therapeutically viable. This frequent failure of clinicians and consumers to get good results with their herbal therapies due to an inability to identify quality medicinals also leads to a diminishing confidence in the efficacy of Chinese medicinal herbs. We must act strongly to prevent any further reduction in the quality of herb material we see on the market by increasing education and regulatory requirements in this area.

"(1) You must select one or more established specifications for identity, purity, strength, composition, and the limits on those types of contamination that may adulterate or that may lead to adulteration of the dietary supplement that, if tested or examined on the finished batches of the dietary supplement, would verify that the production and process control system is producing a dietary supplement that meets all product specifications "


