Herbal Chemical Marker Ranking System (Herb MaRS) criteria for identification of QA/QC in complex herbal medicines

Rank*	Details	Notes
X	There are no bioactivity studies currently available for this compound.	A comprehensive literature search does not reveal evidence to support relevant bioactivity. (Bioactivity studies refer to studies which are designed to determine physiological or pharmacological effects of the relevant compound using *in vitro* and/or *in vivo* models.)
0	Compound's activity is not related to indication of the disease of interest or no pure reference standard is available.	Indication of disease refers to principal indicative symptoms or biological markers of disease.
1	Compound's bioactivity is indirectly related to symptoms of disease *OR* Compound is present in too low a concentration in the herb for it to be screened *OR* Compound's activity is not supported by traditional and therapeutic use of herb	The compound may address a minor or less common symptom of the disease, but not the major clinical presentation. Usually concentration of a constituent in a herbal medicine < 5 µg/g** is generally regarded as too low. Biological activity of the compound is not related to the current use of the herb and/or its traditional use in the context of the formula.
2	Compound has bioactivity related to a symptom (major or minor) of the disease, however there is only 1 good quality*** study to support this action *AND* Compound is present in low concentration (5–50µg/g) in the herb or finished product *AND* Traditional or current use of the herb is consistent with the bioactivity or pharmacological effects of the compound	Minor symptoms include those less clinical troublesome or less common presentations.
3	Compound has bioactivity related to a symptom (major or minor) of the disease, however there is only 1 good quality*** study to support its action *AND* Compound is present in relatively high concentration (> 50 µg/g) in the herb or finished product *AND* Traditional or current use of the herb is consistent with the bioactivity or pharmacological effects of the compound	
4	Compound has high bioactivity related to major symptom(s) of the disease for which there is sufficient evidence to support its activity (≥2 reported good quality*** studies) *AND* Compound is present in relatively high concentration in the herb or finished product *AND* Traditional or current use of the herb is consistent with the bioactivity or pharmacological effects of the compound	
5	Compound may be toxic and needs to be screened to comply to safety limits *OR* *(all the following apply)* Compound has highest bioactivity related to major symptoms of disease for which there is sufficient evidence to support its activity (≥2 reported good quality*** studies) *AND* Compound is present in relatively high concentration in the herb or finished product *AND* Traditional or current use of the herb is consistent with the bioactivity or pharmacological effects of the compound *AND* Compound and/or its metabolites are bioavailable	Potentially toxic compounds are recommended to be monitored if used at 1.5µg/day for genotoxic or carcinogenic impurities[3]

* '5' represents the most suitable analytes for monitoring; '0' represents the least suitable; 'x' means the analyte is currently unsuitable.

** referring to per grams of dried sample

*** Separate scales may be used to determine study quality for both adverse event reports[1] and clinical studies.[2]

[1] Bensoussan A, Myers SP, Drew AK, Whyte IM, Dawson AH. Development of a Chinese herbal medicine toxicology database. *Clin Toxicol* **40**, 159-67 (2002)

[2] The CONSORT Group. *Consort: Transparent Reporting of Trials*. http://www.consort-statement.org/

[3] Food and Drug Administration. Guidance for Industry Genotoxic and Carcinogenic Impurities in Drug Substances and Products: Recommended Approaches, 2008. http://www.fda.gov/downloads/Drugs/.../Guidances/ucm079235.pdf