Response to Discussion Paper on Draft Clinical Evidence Guidelines - Medical devices

About Stellar Consulting
Stellar Consulting is owned by Shelley Tang, previously Head of the TGA’s Conformity Assessment Section and later Acting Head of the Office of Devices Authorisation at TGA, prior to retirement in 2011. Shelley was closely involved in developing both the current regulatory frameworks for medical devices and IVDs, as well as implementing the pre-market regulatory requirements during her 12 years in the device program.

Stellar Consulting provides consulting services in the area of medical device regulation, particularly providing advice and training on the Australian regulatory requirements, and the recommendations of the Global Harmonisation Task Force (GHTF), both in Australia and overseas. The company is regularly contracted by WHO to work in assessing applications for pre-qualification of diagnostics, including auditing of the manufacturer, and in developing regulatory capacity for diagnostics in WHO Member countries. This involves both assessment and strengthening of regulatory capacity and assistance in developing regulatory frameworks appropriate to the resources and needs of the particular country.

Ms Tang is a Subject Matter expert with the World Medical Device Organisation and has developed on-line training modules on medical device regulation for that organisation. She is also an Advisor to Working Group 2 (IVDs) and Working Group 5 (Clinical Evidence) of the Asian Harmonisation Working Party and Project Leader on ISO TC 212 (Clinical laboratory testing and in vitro diagnostic test systems) Working Group 3, developing a standard on Clinical performance studies for in vitro diagnostic medical devices (IVDs) using specimens from human subjects - Good study practice.

Comments
My comments are confined to aspects related to clinical evidence for in vitro diagnostic medical devices (IVDs).

The Introduction to the document states “This document is intended to provide guidance to sponsors and manufacturers of medical devices (including IVDs)...”. However, there is no text specifically relating to IVDs, nor discussion of the differences in clinical evidence requirements between IVDs and other medical devices.
IVDs are used to conduct tests outside of the human body, often in a laboratory, on a specimen derived from the body. They may include tests and related devices, such as test strips and reagents. IVDs rely on specimens – such as blood, tissue or urine – to carry out diagnosis, predictive testing, screening, and monitoring of conditions. These specimens are never reintroduced into the human body, but they do provide valuable information regarding a patient’s health status. IVDs are fundamentally different from other medical devices as they do not come into direct contact with the patient, making their performance and risk characteristics different. Risk based classification systems for IVDs have been developed based on the risk they pose to the general population and the impact of a misdiagnosis on the patient (e.g. incorrect interpretation or a false positive/negative result), not direct harm to the patient arising from the device itself.

The Global Harmonisation Task Force (now superseded by the International Medical Device Regulators’ Forum) recognised the difference in clinical evidence requirements for IVDs and developed a series of guidance documents to address the requirements. The GHTF states “Taking into account the differences between IVD medical devices and other medical devices it was considered necessary to develop a document to specifically address the concepts, principles and terminology for clinical evidence related to IVD medical devices”. This document was followed by others describing the development of clinical evidence for IVDs.

Accordingly, there is now an internationally accepted terminology in relation to clinical evidence for IVDs, and an acknowledgement of the differences in development of that clinical evidence. For instance, the term “clinical investigation” is not used for IVDs – the correct term is “clinical performance study” and “clinical evaluation” is replaced by “clinical performance evaluation”.

In addition, it is accepted that ISO 14155:2011 - Clinical investigation of medical devices for human subjects — Good clinical practice is not relevant to IVDs (in fact it excludes IVDs from its scope). ISO is developing a standard entitled Clinical performance studies for in vitro diagnostic medical devices (IVDs) using specimens from human subjects — Good study practice (ISO TC 212 Working Draft ISO 20916). When published, this will be a parallel standard to ISO 14155.

The current Draft Clinical Evidence Guidelines - Medical devices is causing concern and confusion among IVD manufacturers in relation to the clinical evidence requirements for IVDs. It is recommended that specific discussion of the relevance of the document to IVDs be included. This should not imply that the requirements for clinical evidence for IVDs are less than those for other medical devices, but acknowledge that the process of development of that evidence may differ. Guidance on the TGA’s expectations for clinical evidence for IVDs would also be very useful.

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