Q&A column, 1/18

Editor: Frederick L. Kiechle, MD, PhD

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Submit a Question

Q. We are in the process of validating the Stago STA Compact Max and Stago STA R Max with cap piercing. The company is stating that the open and closed modes follow the same testing pathway and therefore validation between modes is not necessary. Is this correct?

A. Judging from the limited information provided in the question, we are most likely discussing method verification of manufacturer-provided performance characteristics (CLIA regulation 42 CFR §493.1253) of in vitro diagnostic assays on these Stago instruments, not validating laboratory-developed tests. Although not specific, CLIA leaves it up to the medical director to determine if there is a modification from the FDA-approved methods, which would require a full validation, or if there is technique dependence of the method (most likely not the case).

If the manufacturer has claims on the equivalency between the cap piercing and non-piercing analytic flows and each are part of the same IVD product, and both pathways are being verified at the same time, there is no need, in my opinion, to separately analyze and compare the pathways. If the pathways are being modified after the initial method verification, or if any of the above criteria are not true, then each pathway should be verified and also compared with each other.

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Q. Is PHI (phosphohexose isomerase), also known as GPI (glucose phosphate isomerase), mainly responsible for metastasis and circulating tumor cells?

A. There are no clinical tests based on the *GPI* gene and no prognostic indications that are routinely used in patient care.

Phosphoglucose isomerase (PGI) is encoded by the *GPI* gene. It converts glucose 6-phosphate to fructose 6-phosphate. It is involved in gluconeogenesis, but it is also secreted and has multiple other moonlighting roles. The literature on this dates back to the early 1980s. It was shown that secreted GPI can induce antibody production from peripheral blood mononuclear cells (cytokine-type function). More recently, there is literature showing that secreted PGI (autocrine motility factor) is involved in the epithelial to mesenchyme transition that occurs in carcinomas, giving them more sarcoma-like characteristics with increased potential to metastasize. PGI indirectly blocks *Apaf-1* and *caspase-9* genes interfering with cellular apoptosis pathways and can induce cell proliferation through activation of PI3K/Akt and Erk1/2 pathways. Experiments have shown a role for PGI in the epithelial–mesenchymal transition for many types of carcinomas, but the data seem to be most advanced in experimental breast cancer research.

1. Ahmad A, Aboukameel A, Kong D, et al. Phosphoglucose isomerase/autocrine motility factor mediates epithelial-mesenchymal

transition regulated by miR-200 in breast cancer cells. *Cancer Res.* 2011;71(9):3400–3409.
2. Kho DH, Zhang T, Balan V, et al. Autocrine motility factor modulates EGF-mediated invasion signaling. *Cancer Res.* 2014;74(8):2229–2237.
3. Kho DH, Nangia-Makker P, Balan V, et al. Autocrine motility factor promotes HER2 cleavage and signaling in breast cancer cells. *Cancer Res.* 2013;73(4):1411–1419.
4. Lincet H, Icard P. How do glycolytic enzymes favour cancer cell proliferation by nonmetabolic functions? *Oncogene.* 2015;34(29):3751–3759.
5. Niinaka Y, Harada K, Fujimuro M, et al. Silencing of autocrine motility factor induces mesenchymal-to-epithelial transition and suppression of osteosarcoma pulmonary metastasis. *Cancer Res.* 2010;70(22):9483–9493.
6. Wang L, Hou G, Xue L, Li J, Wei P, Xu P. Autocrine motility factor receptor signaling pathway promotes cell invasion via activation of ROCK-2 in esophageal squamous cell cancer cells. *Cancer Invest.* 2010;28(10):993–1003.

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