Translational Development of Clinical Diagnostic Platforms

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Abstract

Addressing unmet needs in POC testing (POCT) - A significantly increasing development of, and demand for, POCT is a result of multiple competitive advantages of POCT in analytical measurement and health care services. Several POCT devices have been cleared by the US Food and Drug Administration (FDA) and used in hospital environments, physicians' offices, and even in the home (such as urine dipsticks and glucose meters). A near-patient device that provides rapid test results in the emergency room (ER) or the Intensive Care Unit (ICU) is now a reality for certain test panels, such as cardiac biomarkers, BNP and Troponin I. The speed of obtaining accurate and reliable results can increase clinical effectiveness, lower the cost of care, and improve outcomes for patients. The improved reliability and range of POCT devices further promote the increasing use in community clinics, physician's offices, and the home. The most significant advantage of POCT is the fact that it produces results in minutes instead of hours or days. This is important especially in critical situations such as in the emergency room. Rapid return of results aids the clinician in making crucial treatment decisions on the spot.

Dr. Kent Lewandrowski, MD, a clinical pathologist at Massachusetts General Hospital, published "Three Wishes for POCT Testing: A Compendium of Unmet Needs From the Perspective of Practitioners in the Field" in Journal of Point of Care in 20081. Dr. Lewandrowski's frustration with his own unmet needs in POCT prompted him to question 12 of his colleagues who have an interest in the practice of POCT in their respective institutions. To frame the question more concisely, he asked the question "what are your 3 top wishes for POCT?" Four major unmet needs concluded in this article involved improved devices and reagents, expanding the test menu particularly for molecular pathogen detection, device connectivity and burden imposed by regulations. Special effort has been made to lower the development barriers across various disciplines and to promote the adaptation of POCT technologies in broader clinical fields by establishing an affordable and efficient development platform that provides a verified design library, rapid prototyping, automated assay optimization, and feasibility testing.

Most point-of-care (POC) diagnostics development projects cease development after the clinical testing of prototype point-of-care devices due to the high financial and technical risks of manufacturing for mass commercialization. Therefore the only deliverables and knowledge transfer are through publications, not fabrication. ***A design library of manufacturable POCT components, consumables and systems to be shared with all researchers and developers from academics, government agencies, and industry could be a paradigm shift in translational development of clinical diagnostic platform***. The successful completion of this Apple iPhone App Store-like design library could consolidate the clinical expertise and engineering advancement from industry, academic and government agencies to accelerate the development and commercialization effort. Every registered user can contribute design files of any level (component, consumable, system) according to manufacturing suppliers' design guidelines and specifications. Every design will be verified by the manufacturing suppliers and will be available for other users to readily implement as off-the-shelf parts for their prototype systems. This will significantly accelerate the development effort and reduce the risks of POCT system commercialization and prevent any waste of resources to reinvent the wheel. The POC design library can later be expanded into assay library to partner with assay manufacturer to provide assay kit of any homebrew assay in the library.

Our current integration could significantly shift the paradigm of how POCT technologies and products are developed and commercialized in many aspects. These changes are brought about by integrating scientific, technological and industrial capabilities of POCT technologies, and sharing the manufacturable rapid prototyping infrastructure and design library with researchers and developers in resource-constrained institutions or organizations. Through ongoing clinical feasibility studies with several hospitals, we have (1) benchmarked EK-PCR with a commercial thermal cycler and demonstrate superior amplification efficiency, (2) achieved the limit of detection (LOD) of POC cartridge-based rapid pathogen ID and AST with 1.6E3 CFU/mL without using PCR and 1CFU/mL with PCR, and (3) demonstrated feasibility of on-chip EK bacterial isolation with over 99% recovery rate and over 100-fold assay enhancement.