An Industry Call to Action: A CONVERGENCE MODEL DRIVEN BY REAL WORLD INTELLIGENCE

As payers escalate measures to contain costs, providers adjust to new models such as the Affordable Care Act, and patients assume more financial responsibilities for their care, manufacturers are being forced to generate more complex and comprehensive bodies of real world evidence (RWE) about drugs' effectiveness and value.

Given the industry's R&D productivity challenge and an overall risk-averse regulatory environment, maintaining a consistent focus on optimizing value across the product lifecycle has become critical to manufacturers' survival.

These dynamics represent an opportunity to develop a novel best-in-class operating model that not only responds to stakeholders' rising evidentiary demands, but also moves beyond traditional norms to transform R&D productivity.

With the proliferation of data and demands for more transparency, a critical focus must be how RWE can be utilized by all external stakeholders to inform decision-making in early development.

While the use of RWE is not novel, the industry can push the envelope of current business practices by being more proactive about bringing insights from a broader range of stakeholders into early clinical development. To do so, manufacturers need to take the lead to establish connectivity between the disciplines that analyze RWE, and, in particular, bridge the silos of clinical and commercial groups throughout the product lifecycle. Convergent teams can creatively and innovatively deliver value by mapping key decisions against RWE from electronic health records (EHRs), observational research, mHealth devices, data from patient communities, and emergent predictive big data initiatives. This strategy facilitates deeper payer and patient-centric insights into optimal target indications, opportunities to improve care management, product feature profiles that align to potentially non-obvious patient populations, and viable protocol designs or recruitment strategies.

INDUSTRY, PAYERS, AND PATIENTS MUST PARTNER TOGETHER TO OPERATIONALIZE REAL WORLD EVIDENCE AS INTELLIGENCE TO INFORM PRODUCT INNOVATION.

The informed application of RWE to key decisions is an advance we call "Real World Intelligence." A new best-in-class operating model must employ real world intelligence to demonstrate improved comparative efficacy and cost effectiveness to payers and rapidly innovate differentiated products. Two additional strategies support the feasibility of this new operating model: patient-centric innovation — which can deliver transformative gains in the operational efficiency of studies — and vigilance for emergent technologies — which are pivotal for generating real world intelligence and forging stronger connections with stakeholders.

We believe this new model, based on real world intelligence, patient-centric innovation, and emergent technologies will open a number of key opportunities:

R&D Driven by Real World Intelligence

Velocity of innovation. The efficiency at which novel therapeutics reach patients in need can be improved through real world intelligence's application to triage R&D resources, augment potential regulatory approaches, enrich endpoint strategies, and proactively manage safety risks.

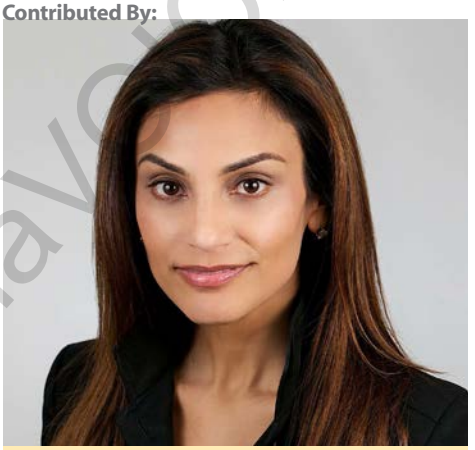
Post-marketing groups possess a trove of RWE on customers' behaviors, preferences, existing treatment pathways, and disease and economic burdens that are today used only for more narrowly defined, post-approval purposes. Under the new model, RWE is interpreted for clinical teams to align product development with specific unmet patient needs and hidden value opportunities. Insights reach R&D that ordinarily take years; beta-blockers, for example, found expanded use to control hypertension only after retrospective analysis of four decades of use in heart attack patients.

In more resource-constrained portfolios, real world intelligence also can inform continuous asset valuation and support more robust investment criteria. One biopharma reported that simulations based on RWE and early clinical efficacy signals confirmed that while a compound would be safe, efficacious, and viable at launch, other portfolio assets could generate greater returns on the same capital. Resources were thus redirected.

Regulatory strategies can be augmented, too. In a precedent-setting case last year, RWE of patient risk preferences influenced the FDA's approval of EnteroMedics' weight loss implant. After the device missed its weight loss endpoint in its pivotal trial, the FDA considered evidence that a subset of eligible patients were willing to accept the risks of the device in exchange for prolonged weight loss, thus supporting approval and a targeted label.

The utility of a study's endpoints can also be enriched to more clearly demonstrate efficacy and effectiveness. Some established endpoints, such as the six-minute walk test (6MWT), do not reflect a treatment's benefits in terms that matter to patients. For example, a sedentary patient may value a therapeutic that simply improves his or her ability to move between rooms. This patient-relevant outcome may be more sensitively demonstrated by augmenting the 6MWT with a validated wearable

Contributed By:



RAMITA TANDON
Executive VP Commercialisation and Outcomes
ICON plc

activity tracker, making the endpoints more meaningful.

Safety is another major application for real world intelligence. Adverse outcomes in randomized clinical trials can be subject to reporting bias, misattribution, and divergent perspectives between patients and clinicians. Structured RWE collection of adverse outcomes from patients, cloud-connected devices, and PRO-enabled online communities can augment clinically-reported safety information, mitigate potential biases, and increase regulators' confidence in a drug's safety profile. Furthermore, cloud-connected devices can accelerate detection of adverse event signals and expedite emergency care for patients. For example, a study with congestive heart failure patients could benefit by using a web-enabled scale to detect rapid weight gain and alert clinicians.

Accelerate true time-to-market. An estimated two-thirds of drugs fail to meet revenue expectations in their first year. Arrival at regulatory approval with limited evidence of real-world cost effectiveness and a suboptimal prioritization of payer targets will delay market access, restrain early revenue potential, and concede control of a product's value story.

An R&D model enhanced by real world intelligence ensures momentum to market. Early insights, the nuances of a drug's value to relevant stakeholders, and the potential future scenarios that may influence stakeholders at launch can enable manufacturers to collect the appropriate evidence package at the right time and through the most efficient strategies. Furthermore, as formulary decision-making begins more than a year in advance, a strong a priori communication strategy is critical to success.

Patient-Centric Innovation

As payers, healthcare providers, and regulatory bodies demand RWE at larger scales, an intensified focus on the patient will be required to adapt development programs efficiently.

Evidence strategy. Adopting the concept of a Health Technology Assessment (HTA) toolkit can empower manufacturers to approach rising evidentiary requirements with confidence. The HTA toolkit represents a global value dossier of all information needed through all phases of market access and submission, including existing evidence that can effectively and efficiently direct further research. The toolkit addresses scenarios that may impact RWE requirements, including: the evidence gaps that will exist for the fragmented array of payers who will gate access in each region, the possibility of being on or off a treatment pathway at launch, or the prospect of different outcomes in populations excluded from prior RCTs. A targeted RWE generation program, publication strategy, and KOL engagement plan developed from and incorporated within the HTA toolkit will determine future success.

Enrollment challenges. The large size and global nature of the post marketing programs, often necessary to demonstrate cost effectiveness to diverse payers, often present severe recruitment challenges, particularly due to deviations from enrollment estimates reported by sites during feasibility. Accuracy can be significantly enhanced through a direct-to-patient strategy using EHRs. Live EHR data allows tabulation and verification of patients who match enrollment criteria and visit a site with sufficient frequency. An ICON pilot program with IBM Watson Clinical Trial Matching employs this approach and uses cognitive computing to parse physicians' notes. Furthermore, IBM Watson Clinical Trial Matching has the capability to alert physicians of all patients who may be eligible. CRO-owned site networks also enable EHR-driven feasibility analysis and structures to ensure accurate feasibility estimates.

Easing the burden of trial participation. Appreciation of patients as partners in clinical research, rather than as subjects to be acquired and studied, is driving an evolution in patient engagement.

At the most superficial level, communication strategies such as disseminating trial results with lay summaries can help to acknowledge and thank trial participants for their contributions to the advancement of medicine. Lay summaries can also support patients, caregivers, and communities who research health information online.

The partnership perspective also improves enrollment success — that is, to ensure enrollment of not just enough patients, but the right patients. Emerging electronic informed consent platforms not only mitigate errors in the consent process, but also allow delivery of educational material to patients that employs comprehension-enhancing video and multimedia educational tools. Some platforms enable patients to also view these materials outside of the clinical setting. With this additional time, patients can better prepare questions for their doctors and further examine a trial's visit-by-visit requirements.

During a trial, attrition risks can be ameliorated through mHealth technologies that reduce the impact of a trial on a patient's normal routine. Electronic clinical outcomes assessment instruments can enable patients to report outcomes without clinic visits, for broader collection of RWE that can be instantly leveraged for R&D. Asthma Health, an inspired mobile app for at-home data collection by the Icahn School of Medicine, not only tracks patients' health and treatment responses, but also encourages habitual use by alerting them to local asthma triggers.

Emergent Technologies

A fundamental differentiator for best-in-class status will be continuous vigilance for new technologies that gate the relevancy, scale, and efficiency of RWE generation, utilization, and communication. No single organization can innovate the breadth of technologies required, from social media platforms for patient recruitment and informed consent to validated actigraphy wearables that independently monitor specific patient behaviors to big data analytics that consolidate and parse EMRs for enhanced recruitment or adaptive risk-based monitoring. Manufacturers, and their partners, will need to monitor and capitalize on innovations from external organizations, including companies not traditionally associated with drug development, such as Apple and IBM.

An Industry Call to Action — Initiate Reform

The changing commercialization environment is a call to action for the industry to rethink the traditional R&D approach. Industry, payers, and patients must partner together to operationalize real world evidence as intelligence to inform product innovation. For both emergent and established companies, the R&D path can be simplified and enhanced by strengthening the connections between independent R&D and medical affairs organizations. Ultimately, the industry must rethink how to accelerate products to the clinic and attune them to patients' most pressing needs. PV