# On the Button

**Global laboratories have a pivotal role in delivering the changes in information management and data integration the industry depends on to improve and maximise R&D expenditure**

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As the pharmaceutical industry heads toward 2020, it faces acute pressure to innovate, rethink and rejuvenate the drug development paradigm, and significantly shorten drug approval timelines. In 2013, a record number of drugs were approved by the FDA, indicating an improvement in our ability to develop new medicines (1). However, a closer look at the success rates of drugs entering trials shows that only 16% were approved – highlighting the need for further progress and innovation in how we approach clinical research (2).

## Combined Pressures

Traditional approaches to drug discovery and development continue to struggle to deliver new medicines and therapies that will meet the demands of a global population that is living longer and demanding enhanced quality of life. In addition, the potential of targeted personalised drug therapies and treatments places further R&D demands on the industry.

These challenges are not only fiscal in nature, but include pressure on the branded pharmaceuticals market, generic competition, impending loss of major patents, relatively thin pipeline, innovation gaps, government pricing pressure, spiralling development costs, greater regulatory stringency, drug safety concerns and fewer drugs approved. The net result of these combined pressures has seen pharma company earnings significantly squeezed.

## Industry Value

The cost of clinical trials has grown exponentially, without any notable improvement in quality or quantity of medicines developed. According to research from Tufts Center for the Study of Drug Development, the average length of Phase 3 trials increased by 70% between 1995 and 2005, while the typical number of procedures per trial rose by 65%. At the same time, the number of volunteers admitted plunged 21%, with almost a third dropping out before completion.

It is clear that the industry needs a new approach, and one element of this is innovation in clinical, pharmacokinetic and pharmacodynamic (PK/PD) biomarker laboratories – and how this may contribute to more effective use of R&D budgets.

Investigating this subject further, interviews were carried out with a cross-section of industry executives – including clinical operations leaders, therapeutic area experts, outsourcing managers, data managers, independent consultants and technology leaders.

These sought to understand the role of central laboratories, bioanalytical and biomarker services in driving changes within the industry, and how innovation in labs can deliver additional value and cost benefits. Table 1 outlines the trends and opportunities that were identified across all trial phases.

**Table 1:** Trends in drug development and corresponding innovation opportunities

| Phase of research | Trends | Opportunities for labs |
|---|---|---|
| Phase 1 | Increased use of biomarkers<br><br>Multi-country protocols<br><br>More US-based studies<br><br>Increased studies in disease patient populations | Provide integrated, targeted and smarter biomarker data<br><br>Correlate PK/PD data in one single database |
| Phase 2 | More complex studies, more utilisation and usage of FDA End-of-Phase 2A meetings to select the dosing regime and design (3)<br><br>Increased informative dose-response trials and improved dose selection to increase trial success rates<br><br>Reduced study size and exposure to treatment to allow more targeted treatments | Increase utilisation of biomarkers<br><br>Improve integrated lab data to aid these designs<br>Support and aid stratification and dose selection of patients<br><br>Provide faster, more accurate information to decision-making ability of clinical teams |
| Phase 3 and adaptive clinical trials design | Real-time data processing, increased data handling and electronic data capture (EDC)<br><br>Shorter duration merge with Phase 2<br><br>Changed dose or treatment arms as data comes in<br><br>Addition of personalised biomarkers to target subpopulations<br><br>Drop treatment arms based on ongoing results | Provide integrated PK/PD, biomarker lab and clinical data in one real-time database<br><br>Interface with EDC and/or interactive voice response systems to accelerate study progress<br><br>Conduct innovative and personalised biomarker assays to support adaptive study designs |
| Phase 3B/4 | Extended drug safety period<br><br>Risk management approach to improve the safety and efficacy of medicines<br><br>Increased safety surveillance – pharmacovigilance systems becoming increasingly important as regulatory agencies demand more long-term data that proves efficacy, safety and quality | Provide cost-effective, clean, real-time smart data to clinical teams<br><br>Ability to handle large 'mega-trial', long duration studies<br><br>Provide comprehensive and cost-effective total global coverage as naïve populations are utilised |

## Integrated and Smarter Data

The traditional linear approach to drug discovery has previously yielded success. However, in light of the pressures described, it is time for a rethink. We need to place heightened emphasis on basic research into the pathophysiology and mechanism of diseases. This restructuring of the current R&D model will require a fundamental shift in our approaches to information management and integration of data (4).

Future success will be based around a patient-centric research framework where pharma companies, specialist or niche academic institutions, central laboratories, biomarker and PK/PD labs and CROs collaborate seamlessly across previously interdependent domains to collect, process and share data utilising emerging smart, web-based data portals and data clouds. This environment will enable researchers to capture smarter, accurate, real-time data and then – using some of the same web-based applications, smartphones and tablets – make it available, securely and rapidly, to clinicians and researchers (5).

**Table 2:** Integrated laboratory data delivery – innovations and benefits

| Innovation | Benefits |
|---|---|
| Integrated lab services and clinical data | Productivity increase, enhanced speed of decision-making, real-time clean data, reduced database lock times |
| Rapid delivery of data to aid safety and efficacy management | Faster enrolment, shorter screening windows, improved efficiency, time and cost savings |
| Real-time web-based safety and monitoring services | Proactive information for clinicians, enhanced and extended safety and efficacy monitoring, more personal patient-centric data |
| Extended use of biomarkers and integration of data | Enhanced patient stratification, improved safety monitoring accuracy, improved understanding of mechanism of drug action |

The increased use of integrated databases that utilise standardised nomenclatures brings additional opportunities for innovation. As researchers look to improve and

**Table 3:** Innovations in central laboratories and the benefits of a patient-centric approach

| Innovation | Benefits |
|---|---|
| **Patient-centric lab services** | |
| Minimally invasive supplies and blood collection kits | Improved patient experience at site; potential to contribute to enhanced enrolment and patient retention |
| Patient-friendly blood collection protocols | Reduced repeat visits and reduced dropouts due to patient non-compliance |
| On-site web portal for immediate information and data | Improved efficiency and cost savings on supplies at clinical sites |
| **Web portal for study management and ordering lab tests and services** | Reduced kit wastage and better inventory and supplies management<br><br>Improved sample tracking and traceability direct from source back to lab<br><br>Improved study management data, with real-time updates to key patient and study critical data for sites, investigators and clinical teams<br><br>Instant reconciliation with electronic case report form data (possible), results in reduced query rates and faster, cleaner data |

speed up the knowledge-based approach to drug development, they will drive the use of other smart, operational applications such as data analysis systems, clinical trial design, and protocol authoring software. These intelligent systems and data mining tools will be fuelled by centralised clinical database systems.

With analytical and central labs generating up to 80% of the data generated in clinical trials, there is a pivotal role for labs to play in proactively orchestrating and managing this integration (see Table 2).

### Patient Experience

Patient centricity is at the forefront of clinical research excellence and innovation today (6). The pharma industry spends billions of dollars per year recruiting and retaining patients for clinical development programmes. It has been reported that up to 30% of patients recruited for Phase 2-3 fail to complete trials and that the number of volunteers admitted into clinical trials has dropped by one-fifth (7). These figures are a significant concern for the industry, but provide an opportunity for increased productivity.

The role that central labs and PK/PD analytical labs can play in enhancing the patient experience and contributing to patient recruitment, enrolment and retention is often undervalued or completely overlooked. A minimally invasive and patient-friendly experience at each visit, for example, can contribute to recruitment and retention. With central labs involved in excess of 65% of all visits, there is huge scope to make a difference. Table 3 presents a summary and some examples.

### Global Logistics

As globalisation spreads, logistics needs to keep pace with change as it is a significant cost driver. The utilisation

**Table 4:** Examples of logistical innovations and the benefits

| Innovation | Benefits |
|---|---|
| **Packaging and shipping** | |
| Innovative packaging and dry nitrogen shippers to reduce need for dry ice on some studies<br><br>Utilisation of improved lighter packaging to reduce outbound costs | Significant reduction in transport costs; extension of ability to receive and process shorter stability samples for more complex biomarkers and cell-based assays |
| **Integrated courier model to reduce specialist shipments** | |
| Work with large integrator couriers to utilise their global networks in conjunction with local providers | More than 40% savings on specialist courier rates, while achieving same delivery and transit times |

of more complex biomarkers and collection of tissues and biopsies for pharmacogenomics and companion diagnostic investigation places a significant cost burden on R&D budgets.

Logistics costs can be up to 50% or more of complex Phase 2 and 3 trials, making it a target for potential savings. As sample analysis represents as much as 80% of all clinical study data, sample transport and management is a crucial cost driver. Examples of innovations and the potential benefits in logistics are outlined in Table 4.

## Making Innovation Count

Currently, the focus in the pharma industry is to reduce costs and maximise R&D spend on clinical research. While this direct approach delivers results and has value, it focuses solely on driving down unit costs and service fees – it is only one part of the potential savings that could be achieved.

Constant downward pressure on price alone can often stifle the opportunity or negate the ability for innovation. It can mask the true value of what can be achieved when pharma companies work in a true collaborative partnership with central lab and PK/PD biomarker providers.

The following two real-life case studies demonstrate how some of the innovations outlined in this article have yielded significant actual efficiencies on complex projects.

### Phase 3 Global Hepatic Disease Trial

In this trial, global enrolment was planned, with more than 40% of patients located in China. The protocol design required a stratified approach to patients. Essential specific and uniform classification and diagnosis of the stage of liver disease was key enrolment criteria.

As biopsy samples cannot be transported out of China, digital pathology and integration of global data was suggested to allow centralised reading. This resulted in enrolment goals being met, while achieving significant cost savings by minimising delays.

### Developing a New Leukaemia Treatment

In a separate study, a novel treatment for leukaemia required a stratified approach to patient selection. The mechanism of action of the drug required trial patients to be in a specific stage of the disease. This would be confirmed by differential diagnosis using flow cytometery, immunohistochemical staining and bone marrow pathology.

The approach used was to combine the global biomarker data from regional specialist labs, and then integrate the data and present it to a central expert panel to allow standardised confirmation that patients met enrolment criteria. The trial achieved faster, targeted enrolment and reduced overall study duration, helping to shorten the drug development time and bring broad cost savings.

## New Landscape

The drug development landscape will undergo significant change over the next five to ten years, with innovations made by central and PK/PD biomarker labs playing a critical role in improving and maximising R&D expenditure.

As the industry reshapes, we should also not underestimate the value of expert and informed scientific and technical experience. Innovation is essential, but so too is experience and knowledge to ensure that new smart systems and services are applied effectively and efficiently in the highly regulated field of clinical research.


**References**

1. FDA new molecular entity approvals for 2012, 28 January 2013. Visit: www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm336115.htm
2. Large pharma success rate for drugs entering clinical trials in 1993-2004: 16%, Tufts Center for the Study of Drug Development Impact Report 11(4), 2009
3. Guidance for Industry End-of-Phase 2A meetings prepared by the FDA, 2009
4. Pharma 2020: The vision, PricewaterhouseCoopers, 2007. Visit: www.pwc.com/hri
5. Research Rewired: Merging care and research information to improve knowledge discovery, PricewaterhouseCoopers, 2008. Visit: www.pwc.com/hri
6. Getz K, A critical need to support patient centricity in clinical research, Tufts Center for the Study of Drug Development, 2014
7. Growing protocol design complexity stresses investigators, volunteers, Tufts Center for the Study of Drug Development Impact Report 10(1), January/February 2008


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