October 2016

Connecting Insights

Bringing Better Outcomes from Pipeline to Patient Using Data and Analytics
Introduction

The future of medicine rests on data: the evidence that is the basis for the discovery, development and dispensing of prescription products and all other healthcare decisions. Data, and the analysis of that data, informs drug development, portfolio decisions, prescribing behaviors, patient compliance and reimbursement policy in value-based healthcare systems. Mastering the collection and interpretation of data is therefore vital for the vitality and continued global contributions of the biopharmaceutical industry.

This report will explore how connecting disparate streams of data can create a portfolio of evidence—valuable insights that can make the difference in today’s biopharmaceutical marketplace. While these opportunities for connections exist across all disease and therapeutic areas, they may be most acutely needed in the complex and dynamic area of oncology.

This report illustrates a general point using oncology as an example. It makes the case for the process by which a looming crisis in oncology can be averted, by applying the science—and art—of connecting healthcare insights. This report was produced by the QuintilesIMS Institute as a public service without industry or government funding. The contributions to this report of Ian Fisher, Adam Istas, Jason Karas and many others at QuintilesIMS are gratefully acknowledged.

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Executive summary

The past decades have proven the utility of appropriately curated evidence in improving efficiency and efficacy in clinical development and market access, and, perhaps more importantly, in providing actionable insights for the constellation of stakeholders across the healthcare spectrum. The biopharma industry has invested in and benefited from the explosion of data and analytics tools that together comprise the core of the evidence packages that continue to drive drug value, but substantial evidence increasingly resides outside the data collected by biopharmaceutical sponsor companies.

It is when these disparate data streams are applied to clinical interventional and observational research that a new construct for the development and commercialization of the next generation of medicines becomes clearer.

The practice of medicine is often described as both an art and a science. Evidence connects art to science in a continuum that links practice to proof. Evidence is fundamental to the future of medicine and medical technologies—it, too, is an art and a science that must be optimized in today’s value-based healthcare system. Evidence must be strategic. It must be integrated. It must be allocated with the same care as capital. It must connect insights from pipeline to portfolio to population health, and it must be framed by scientific and therapeutic expertise to provide actionable insights for decision-makers.
Recent advances in life sciences

- Genetic information has led to dramatic advances in targeted therapies over the past 20 years
- An explosion in the amount of rich data sources available can complement clinical development decisions
- Cancer treatment is becoming increasingly individualized

Recent transformations in disease treatment

The advancements in biomedical treatment over the past 20 years are staggering. With more than 700 New Active Substances (NAS) discovered, developed and available since 1996, patients and physicians are enjoying a newfound wealth of treatment options – with an additional 225 NASs expected to be launched by 2020 (See Exhibit 1). At the same time, the biopharma industry is taking advantage of a surge of new technologies, access to rich data sources, and advances in scientific discovery related to biomarkers and genomic research, which are changing the playing field for biopharma companies.

Exhibit 1: Global New Active Substances (NAS) Available Since 1996

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>943</td>
<td>718</td>
<td>225</td>
<td>223</td>
<td>388</td>
<td>146</td>
<td>184</td>
<td>225</td>
</tr>
</tbody>
</table>

Note: *denotes estimated values
A better understanding of disease biology across multiple therapeutic areas, combined with an increase in the availability of patient and genetic information derived from increasingly complex data, is moving drug development today toward a more personalized understanding of the patient to help ensure the right medicine gets used at the right time (see Exhibit 2).

**Exhibit 2: Recent Advances in Life Sciences**

These advances are also adding complexity and cost to the drug development lifecycle. Advances in precision medicine support a more precise approach to patient care, but they demand a more sophisticated drug development environment, where teams can manage complex biomarkers across multiple arms of clinical trials, which quickly adapt to shifting protocols and standards of care. This adaptability demands robust technology and data management practices, as well as strong collaborations among sponsors, contract research organizations, and site staff to deliver a robust portfolio of evidence for these products.

**The evolving nature and role of evidence**

The explosion of data brings with it the promise of developing smarter and better research and development systems. Big data—and, more importantly, its effective analysis—enable an unprecedented understanding of the world around us, and make it possible to improve systems and organizations to work more effectively and efficiently.

In healthcare, this deluge of information is a result of the amount of transactional data now collected digitally. Physicians, other healthcare providers, pharmacies, and even patients are moving away from paper-based systems to track health information digitally (see Exhibit 3).

In particular, data in the U.S. is increasingly being captured through Electronic Health Records (EHRs). EHRs are now being used by 76% of non-federal hospitals and more than 78% of office-based physician practices, recording health information in real time on patient health conditions, vital signs, medicine use and lab test results.¹ ²

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¹ ² Connecting Insights: Bringing Better Outcomes from Pipeline to Patient Using Data and Analytics. Report by the QuintilesIMS Institute.
Additionally, data on the 4.3 billion prescriptions now filled each year in the U.S. market, the 1.2 billion visits Americans make to a doctor’s office, and the 629 million patient visits to a hospital (including 460 million outpatient visits) flow from other sources such as billing claims. The non-identified data (data that does not identify the patient), derived from these sources, is now used to support an evidence-based healthcare system in a range of ways to improve patient outcomes and also reduce waste and avoidable costs.

The case of oncology

Nowhere has the advancement of disease treatment and the explosion of available healthcare data been more evident than in oncology. Over the past decade, the field has moved rapidly from a disease defined by tumor location to one focused on individual disease genetic makeup.

Less than 50 years ago, our approach to cancer treatment was brute force – using all-purpose compounds, such as alkylating agents, to attack every kind of tumor, knowing that they would also take their toll on healthy tissue. We then moved into the 1990s when a few compounds in development were aimed at specific molecular targets for particular cancers—such as trastuzumab (Herceptin) used for the treatment of HER2-positive breast cancer. Targeting specific tumor types limited the range of application of these treatments, but it reduced off-tumor effects and decreased the side effects. It marked the beginning of a personalized approach to cancer care. We then learned how to leverage genomic alterations, with treatments like imatinib (Gleevec), which combats Chronic Myelogenous Leukemia (CML), driven by the BCR-ABL fusion, and crizotinib (Xalkori), which provides impressive outcomes in non-small cell lung cancer patients with the EML4-ALK fusion. The discovery of this genomic alteration in lung cancer patients provided an opportunity to develop this agent for a specific sub-population of patients exquisitely dependent on this oncogenic event. Today, targeted agents, immuno-oncology and precision medicine are the priority focus areas for oncology R&D (see Exhibit 4).
Cancer, once a whispered taboo that presumed a “death sentence,” is becoming a chronic treatable disease for a growing number of patients. The recent development of PD-1 checkpoint inhibitor immunotherapies are showing that dramatic cures may be possible.

Today, two-thirds of U.S. cancer patients live at least five years after confirmatory diagnosis, compared to just over half of patients in 1990. As there are currently hundreds of investigational anticancer therapies in development, together accounting for approximately 30% of the research pipeline, it is expected that this trend will continue.

The availability of more treatment options and longer use of cancer medicines due to extensions to life have resulted in a growing level of expenditure on cancer medicines. Globally, total sales of medicines used as oncology therapeutics and for patient supportive care have increased from $90 billion in 2011 to $107 billion in 2015. In the U.S., 11.5% of total drug costs are now accounted for by oncology treatments, up from 10.5% in 2011 (see exhibit 5).
Exhibit 5: Global Oncology and Supportive Care Costs US$Bn

<table>
<thead>
<tr>
<th>Year</th>
<th>U.S.</th>
<th>EU5</th>
<th>Japan</th>
<th>Pharmerging</th>
<th>Rest of World</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td></td>
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<td>2013</td>
<td></td>
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<td></td>
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<tr>
<td>2014</td>
<td></td>
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<td></td>
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<tr>
<td>2015</td>
<td></td>
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</tbody>
</table>

The looming crisis in biopharmaceutical medicine

- Health systems are struggling to respond to the accelerating pace of innovation and information
- Payer evidentiary requirements are threatening returns on investment in innovation
- Smaller target patient populations and more demands for evidence are adding complexity to clinical research

Macro forces impinging on innovation

Scientific advances and growing demand for new medicines are coinciding with constrained healthcare budgets and demands for other social services.

The lingering effects of the global recession continue to be reflected in relatively low macro-economic growth across the developed economies that still account for more than 80% of the market for innovative medicines. Lower GDP growth has constrained public healthcare expenditure budgets, and private insurance markets have also been affected by economic lethargy. At the same time, aging populations with growing chronic healthcare needs, especially related to diabetes, and continued unmet needs in cancer and rare diseases provide upward pressure on healthcare costs.

Health systems are universally challenged by these factors which inevitably impinge on innovation and raise questions about the sustainability of drug expenditure levels and the value of medicines (see Exhibit 6).

Exhibit 6: Pressures on Medical Innovation
These pressures are happening at a time when risks associated with biomedical innovation remain high. For example, almost all of the major research-based biopharmaceutical companies—and several hundred smaller innovative companies—are investing heavily in oncology (see Exhibit 7). Overall, more than 300 companies have R&D pipelines focused exclusively on oncology, with between one and seven late phase therapies aimed at fighting cancer.

Exhibit 7: Companies with Active Late Phase Oncology Pipelines

Growing productivity challenges

As clinical trials proliferate, the number of patients needed for these trials naturally increases as well. At the same time, sponsors are facing constant pressure to be first to market or to differentiate their offering as a way to gain a competitive advantage. In the case of cancer research, this is particularly evident in the immuno-oncology space. In response, early Phase I numbers are being expanded in an effort to more quickly move to Phase III and speed innovative new drugs to market. But this total volume or number of trials that patients need is not matched by disease prevalence and incidence numbers. In many cases, the treatments in development are designed for targeted sup-populations of patients, which shrinks both the recruiting pool and the ultimate market value of a product. This problem is worsened by narrower segmentation of indications using molecular classification of disease; resulting in narrowly defined patient populations. As a result, sponsors are engaging more sites to combat rising screening failure rates (see Exhibit 8).
Biopharma sponsors are having to think more strategically about the cost, time, operational feasibility and productivity of their trials, and seek innovative strategies to improve productivity and adaptability while continuing to meet patient safety and proof of efficacy goals. There appears to be a strong link between site:patient ratio and per-patient cost in oncology, especially for the more selective indications (i.e., lymphoma, leukemias, etc.). The rise of studies in this area portends ever increasing site:patient ratios and growing cost; an issue that is further exacerbated when patient populations are spread across multiple centers. Center dispersion forces the power calculation to “power up” the patients needed in the studies to account for regional or center biases. To the extent that oncology is seen as a bellwether for other therapy areas, and—unless something different is done—a worsening of site:patient ratios can be expected in other major therapeutic areas in the coming years.
Additionally, the collective total cost of development of therapies continues to go up year-over-year. This productivity challenge is made worse when multiple companies develop nearly identical therapies using similar molecules, with similar MOAs, targeted at the same narrowly defined patient subgroups within small indications.

### Closing the Loop on Patient Participation

A recent report from MD Anderson Cancer Center shows a troubling trend in the recruitment of genomic profiled cancer patients to clinical trials. The study, which explores the use of genomic testing to facilitate enrollment into patient-matched clinical trials, found that 789 of 2,000 patients tested (39%) had at least one mutation making them eligible for a clinical trial designed to treat their specific tumor mutation. Yet only 11 percent of those patients went on to participate in these genotype-matched trials at MD Anderson. Multiple reasons for not enrolling were identified by the authors. This finding, and similar results from other academic medical centers, suggests that testing and reporting of genomic profiles with actionable alterations is only the first step in improving patient participation in clinical trials. Additional improvements are needed to fully close the loop from testing to enrollment ranging from data management to site and patient services. Following patient care pathways and outcomes will be critical to enabling these improvements.

### Mounting payer and reimbursement pressures

Scrutiny of value is already intense, especially in European markets where reimbursement decisions by single-payer systems are often guided by established Health Technology Assessment (HTA) tools. In the U.S., notably, new frameworks and approaches to assessing value of innovative medicines, including oncology drugs, are being developed and implemented (see Exhibit 9).

#### Exhibit 9: Oncology-Specific Valuation Assessment Frameworks

<table>
<thead>
<tr>
<th>Traditional Assessments</th>
<th>Newly Developed Value Frameworks</th>
</tr>
</thead>
<tbody>
<tr>
<td>IQWiG Institute for Quality and Efficiency in Health Care</td>
<td>NCCN National Comprehensive Cancer Network®</td>
</tr>
<tr>
<td>HAS Health Action Science</td>
<td>ESMO European Society for Medical Oncology</td>
</tr>
<tr>
<td>NICE National Institute for Health and Care Excellence</td>
<td>ICER Institute for Clinical and Economic Review</td>
</tr>
<tr>
<td>Memorial Sloan-Kettering Cancer Center</td>
<td>American Society of Clinical Oncology</td>
</tr>
</tbody>
</table>

- Developed by payer groups
- Targeted at payers
- Generally ex-US
- Developed by physician and policy groups
- Mixed, some positioned as targeted at payers, physicians or/patients
- Predominantly US-driven frameworks

Source: IMS Global P&MA Conference 2016, June 23-24
Some examples include the American Society of Clinical Oncology’s (ASCO) Value Framework, the National Comprehensive Cancer Network’s (NCCN) Evidence Blocks, and European Society for Medical Oncology’s (ESMO) Magnitude of Clinical Benefit Scale.

The differences between these tools, however, produce surprising variability in results for the same cancer treatments. Although concerning, this variability is not unexpected as we are in the early days of building value frameworks and determining how best to quantify value.

The increased scrutiny of drug prices will likely lead to the use of value-based frameworks as guideposts for drug costs, and major payers have already begun to acknowledge the potential utility of value-based frameworks for coverage decisions. That means biopharma industry leaders may soon need to rely on these frameworks to communicate the value of their products. If each one generates a different value profile, however, it will be difficult to decide which outputs to measure, which evidence to collect, and how best to communicate the value of these products to stakeholders.

Biopharma’s response has been to get the approval, prove the differentiated value of the product in managing the disease subset and seek reimbursement approval.

This has created a problem for payer agencies: they are looking at rising drug costs, even as they attempt to manage the approved populations for the drug to smaller and better defined patient sets, using a growing number of levers at their disposal, including step-tiering, discounts, and pay-for-performance schemes, among others. A recent example of a payer trying to control drug costs is CVS Health Corp.’s decision to exclude three branded oncology products from its standard formulary: imatinib (Gleevec), nilotinib (Tasigna), and enzalutamide (Xtandi). Companies have also entered into innovative agreements with payers, especially in oncology, which seek to minimize payer risk while providing performance-based returns to manufacturers (see Exhibit 10).

**Exhibit 10: Innovative Agreements in Oncology in the European Union, 2006-2014**

<table>
<thead>
<tr>
<th>Total Number of Agreements = 99</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Traditional” Financial-Based Agreements</td>
</tr>
<tr>
<td>Coverage with Evidence Development</td>
</tr>
<tr>
<td>Financial-Based Risk Sharing</td>
</tr>
<tr>
<td>Performance-Based Risk Sharing</td>
</tr>
</tbody>
</table>

Source: IMSIC Innovative Market Access Agreements and Policies Database Q3 2014. Note that database focuses on innovative contracting (CED, finance and performance based risk shares and not traditional finance-based agreements hence the relative frequency shown may not reflect the real life situation).
THE LOOMING CRISIS

Payers are increasingly demanding demonstrable proof of value to support reimbursement for new treatments. Hard data demonstrating improved overall survival, extended treatment free intervals, and/or other endpoints that demonstrate measurable value to the patient, the payer and the healthcare system is expected. When applied to clinical research, these evidentiary demands add increased complexity to the trial process as developers attempt to provide a more robust portfolio of evidence for payers (see Exhibit 11).

**Exhibit 11: Increasing Complexity of Clinical Studies**

<table>
<thead>
<tr>
<th>Design Characteristics</th>
<th>2002</th>
<th>2012</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number ofEndpoints</td>
<td>7</td>
<td>13</td>
<td>86% ↑</td>
</tr>
<tr>
<td>Total Number of Procedures</td>
<td>106</td>
<td>167</td>
<td>58% ↑</td>
</tr>
<tr>
<td>Total Number of Eligibility Criteria</td>
<td>31</td>
<td>50</td>
<td>61% ↑</td>
</tr>
<tr>
<td>Total Number of Countries</td>
<td>11</td>
<td>34</td>
<td>209% ↑</td>
</tr>
<tr>
<td>Total Number of Investigative Sites</td>
<td>124</td>
<td>196</td>
<td>58% ↑</td>
</tr>
<tr>
<td>Total Number of Patients Randomized</td>
<td>729</td>
<td>597</td>
<td>18% ↓</td>
</tr>
</tbody>
</table>


Absent a more strategic approach by developers in their research planning efforts, and collaboration with partners earlier in the development lifecycle to address recruiting challenges and harness new data, technology, and analytics tools to enable a more adaptive and dynamic drug development environment, this confluence of pressures will result in a crisis in biomedical innovation.

**Physician Burden**

Physicians have been particularly impacted by the proliferation of medical, drug and patient information. The number and breadth of treatment guidelines has greatly increased, the number of approved drugs has grown and diagnostics have become more complex. The substantial administrative burden on doctors linked to paperwork, coding and requirements for payer prior authorization has also been well documented. Development and implementation of solutions that benefit providers, patients and payers will require data visibility and management for stakeholder buy-in, performance metrics and value distribution.
Connecting insights to accelerate innovation

- Connecting data and analytics can help to develop a portfolio of evidence needed in today's value-based healthcare system
- New development models will be driven by data from a variety of sources
- Real-world Insights supports clinical development decisions, treatment pathways and adherence strategies

Applying smarter analytics to pooled data sets

The pooling of data sets and capabilities brings new opportunities to produce efficiency and improvement to patient outcomes across the clinical research/healthcare continuum. Smarter analytics applied to these cross-industry data can enable nine solutions—across three streams—that can help enable transformation in drug development and commercialization, thereby averting the potential crisis in biomedical innovation (see Exhibit 12).

Exhibit 12: Connecting Insights to Solutions in Clinical Research and Healthcare

Source: QuintilesIMS Analysis
Transforming clinical research

1. Improving study design via better linkage between indications and target endpoints

Addressing unmet medical needs through clinical trials requires defining potential indications against which the therapeutic agent will be tested. The success or failure of clinical studies is often determined by the choice of precise, useful primary outcome endpoints. For many diseases, the choice of primary endpoint(s) also determines the number of enrollees and the duration of the trial.

Conventional definitions of clinical indications and clinically measurable outcome endpoints result in the use of a gold standard: a commonly used measurement that is broadly agreed upon as a satisfactory indication of patient outcome. Identifying surrogate endpoints that either result from or correlate with the gold standard endpoint, while continuing to address all necessary regulatory and clinical regulations, may enable faster and smaller trials. Clinical validation of surrogate endpoints is required for regulatory acceptance and market access. As a result, validation of surrogate endpoints typically has been done through randomized clinical trials (RCT’s) that are complex, time consuming and expensive, and very few surrogate endpoints have been advanced to general practice despite evidence for clinical utility.

The use of real-world evidence, shared data and large datasets to supplement RCT’s may enable more rapid validation and acceptance of surrogate endpoints. Examples of endpoints that have benefited from this approach include:

- “Minimal Residual Disease” in hematological oncology diseases, including CLL, ALL, CML, AML and multiple myeloma, has been shown to have clinical utility and to correlate with accepted outcomes endpoints. MRD, or forms of molecular monitoring, have become common clinical tools to determine the degree of patient response. For example, as early as 1998, a prospective real-world study demonstrated that MRD correlated with relapse in childhood ALL. However, MRD has not been accepted as a primary endpoint for drug approvals in most indications. The lack of a standardized measurement for MRD has been a major factor, limiting the use of MRD in clinical research. These gaps are now being addressed through collaborative efforts that include use of “big data” and real-world evidence, such as the Black Swan Research Initiative. This initiative has achieved the standardization of a flow cytometry test in the EU and the start of a large real-world study (“iStopMM” – Iceland Screens, Treats, or Prevents Multiple Myeloma) intends to screen all citizens in Iceland over the age of 40. Similar large data-sharing efforts, coupled with smart analytical tools that improve the signal-to-noise problems common to cross-pooling data, are showing promise that MRD can become an accepted approach for not only clinical practice but also clinical research in critical opportunities such as multiple myeloma.

- The use of pathological complete response (pCR) in breast cancer clinical research has been a focus of debate for years. In 2014, the FDA recognized the use of pCR in its guidance “Pathological Complete Response in Neoadjuvant Treatment of High-Risk Early-Stage Breast Cancer: Use as an Endpoint to Support Accelerated Approval”. The guidance was supported by a pooled analysis of more than 13,000 patients. However, the guidance recognized that issues remained with the use of pCR for approval, even while demonstrating evidence for its clinical utility. More recently, multiple observational studies and large analyses of real-world evidence support the clinical utility of pCR outside the clinical-trial environment. While these reports make a compelling case, they do not fully validate pCR as a substitute endpoint for Disease Free Survival (DFS) or Overall Survival (OS), which are the current regulatory gold standards. This leaves open the option for smarter, better designed in silico studies to enable this important endpoint that will surely accelerate clinical research in breast cancer, decreasing study costs and cycle times.
2. Refining targeting of patients based on improvements in inclusion/exclusion criteria and biomarker based segmentation approaches

Biomarker identification has historically been conducted during pre-clinical research on a small scale. The advent of gene expression profiling, genetic analysis and, now, genomic profiling, have pushed target and biomarker discovery from pre-clinical to clinical studies and into clinical practice. Analysis of pooled, metadata sets have led to the identification of multiple drug targets and prognostic biomarkers (see Exhibit 13).

Exhibit 13: TotalAlterations Affecting Protein-Coding Genes in Selected Tumors

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Translocations</th>
<th>Deletions</th>
<th>Amplifications</th>
<th>Indels</th>
<th>SBS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal cancer</td>
<td>40</td>
<td>10</td>
<td>20</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Breast cancer</td>
<td>30</td>
<td>15</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>20</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>10</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

As an example outside oncology, the discovery and recent validation of the CD44 cell surface protein as a potential drug target in Type 2 diabetes was made possible by the analysis of public data sources: 1,175 samples and 130 microarray experiments. In oncology, multiple studies have identified novel oncogenic drivers and potential drug targets using somatic mutation or genomic profiling databases. In addition to genetic and genomic data base analysis, EHR records have the potential to be used to associate drug exposure to patient outcomes to identify novel therapeutic approaches. A recent study linked two large EHRs from Vanderbilt University and The Mayo Clinic to tumor registries to determine that metformin use in diabetes patients was associated with a 22% decreased mortality after cancer diagnosis. This result not only suggests metformin as a potential cancer therapy, but also links response to a specific patient group defined in the EHR. This study is a model for how EHR data linked to other data sources could be used to identify new uses for approved drugs.

While today’s data sets are far larger and more complex than those of decades past, efficient pooling and smart analysis has managed their unwieldy volume and yielded early results. Analytics as a science continues to evolve apace. Developments in data validation and bioinformatics techniques have made it possible to determine correlation between test variables. This can increase the potential for discovery and collaboration, but has also increased the need for standardization to make data-sharing across organizations productive as has been recognized by various industry and oversight groups.
In oncology, stratification approaches have yielded promising results. The probability of success of a clinical trial has been shown to dramatically improve, as biomarker-based stratification approaches are incorporated into a study (see Exhibit 14).

Exhibit 14: Probability of Success in Phase Progression With or Without Selection Biomarkers

![Graph showing probability of success](Source: Biomedtracker from Pharma Intelligence, Informa, Clinical Development Success Rates 2006-2015)

But stratification is not just a tool for improved clinical trial efficiency. Incorporating biomarker-based stratification has an overall benefit in response rate of treatments (see Exhibit 15).

Exhibit 15: Stratification of Patients Drives Improved Responses

Sub-Analysis of variables that correlated independently with higher response rates for:
- Personalized approach vs not personalized
- Hematologic tumors vs for solid tumors
- Chemotherapy-naive patient vs patients who received prior therapy

A separate meta-analysis established that arms testing cytotoxic agents had higher treatment-related death rates than arms testing targeted agents.

Benefit of personalized therapy. (A) Results from the pooled and meta-analysis comparing the personalized strategy versus non-personalized strategy are represented for response rate (RR), progression-free survival (PFS), and overall survival (OS). All P < .001 comparing arms adopting a personalized approach versus a not personalized approach. Six hundred thirty-eight arms had values available for the RR analysis (pooled analysis and meta-analysis; 112 arms were personalized, and 526 were not). For the PFS analysis, 530 arms had values for the pooled analysis (personalized, n = 98; not personalized, n = 444), and 342 arms had median PFS values and their corresponding 95% CIs available for the meta-analysis (personalized, n = 59; not personalized, n = 283). For the OS analysis, 441 arms had values for the pooled analysis (personalized, n = 49; not personalized, n = 392), and 247 arms had median OS values and their corresponding 95% CIs available for the meta-analysis (personalized, n = 21; not personalized, n = 226).
This in turn drives outcomes measures, such as five-year survival rates (see Exhibit 16).

**Exhibit 16: Stratification Example of Patients with Leukemia / Lymphoma**

<table>
<thead>
<tr>
<th>100 years ago</th>
<th>“Disease of the blood”</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 years ago</td>
<td>Leukemia or Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Indolent Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Aggressive Lymphoma</td>
</tr>
<tr>
<td>60 years ago</td>
<td>Chronic Leukemia</td>
</tr>
<tr>
<td></td>
<td>Acute Leukemia</td>
</tr>
<tr>
<td></td>
<td>Preleukemia</td>
</tr>
<tr>
<td>Today</td>
<td></td>
</tr>
</tbody>
</table>

*38 Leukemia types identified:*
- Acute myeloid leukemia (12 types)
- Acute lymphoblastic leukemia (2 types)
- Acute promyelocytic leukemia (2 types)
- Acute monocytic leukemia (2 types)
- Acute erythroid leukemia (2 types)
- Acute megakaryoblastic leukemia
- Acute myelomonocytic leukemia (2 types)
- Chronic myeloid leukemia
- Chronic myeloproliferative disorders (5 types)
- Myelodysplastic syndromes (6 types)
- Mixed myeloproliferative/myelodysplastic syndromes (3 types)

*51 Lymphomas identified:*
- Mature B-cell lymphomas (14 types)
- Mature T-cell lymphomas (15 types)
- Plasma cell neoplasm (3 types)
- Immature (precursor) lymphomas (2 types)
- Hodgkin’s lymphoma (5 types)
- Immunodeficiency associated lymphomas (5 types)
- Other hematolymphoid neoplasms (7 types)

**3. Optimizing site identification and improving site efficiency**

Site related efficiency measures are many, ranging from decreasing non-performing sites to increasing the efficiency and yield of average sites. Applying data and analytics can pull at two and specific levers, increasing patient per site enrollment and minimizing protocol amendments:

*Increasing patient per site enrollment:* As biopharmaceutical companies increasingly pursue therapies to treat new, rare and niche diseases, they are being forced to rethink their clinical operation strategies to ensure timely study completion. Because the condition, patients, and/or investigators are poorly understood, companies are challenged to find sites that will be able to access the right patients, investigators, and infrastructure needed for study success. For these situations, leveraging a patient-driven approach builds upon an understanding of the patient (profile, presentation, location, management, etc.) to inform identification and prioritization of the sites best positioned to find these patients. This approach, based on Patient Driven Site Identification (PDSI), requires a robust range of data, but has demonstrated success in the most challenging conditions.

In a recent case, this approach was applied for a drug targeted to a post-stroke population, which had difficulties recruiting for its Phase Ila study. Secondary and primary data sources were leveraged to locate patient clusters and thus new potential sites, as well as to suggest modifications to the study protocol and investigator guidance to facilitate patient recruitment evaluation while maintaining the overall objectives of the study. The Phase Iib study is ongoing, utilizing guidance from this analysis. Early results show promise: enrollment in the clinical study improved from off- to on-track following application of PDSI techniques (see Exhibit 17).
Minimizing protocol amendments and improving study design: With a 10% probability of securing regulatory approval for a new drug entering Phase I, it is critical that these drugs are given the greatest chance to succeed and that sponsor governance bodies are able to make transparent, evidence-based decisions on how best to invest in, or halt, development across portfolios. Protocol amendments have been identified as one source of avoidable delays, costs and inefficiencies (see Exhibit 18).

Exhibit 18: Impact of Protocol Amendments

57% of all protocols have at least 1 substantial amendment

- 3 month longer study duration per amendment
- $141-535k per Phase II/III protocol
- 45% of all substantial protocol amendments are deemed avoidable
- Lower number of patients relative to plan

Maximizing the value of a clinical asset depends greatly on smart program and trial designs. Transparent processes and methodologies, rapid access to robust data to inform decision-making and combining objective scientific and operational collaboration with sponsor project teams are key attributes of an optimal solution.

The required solution will include iterative assessment of protocol design and evaluation of alternate approaches, using trial performance data from across multiple source records. This data-driven approach to clinical development design and planning provides an understanding of trade-offs of cost, time, risk and value (eNPV) and a comparison of the relative value of alternative scenarios supporting a solid rationale for decision-making.

4. Executing clinical studies more efficiently via risk-based monitoring

The contributions to overall inefficiency and cost of development by clinical trial site monitoring has been well documented and estimates place this cost at 21% of the total cost of clinical trials, making it the single highest cost lever in drug development.\textsuperscript{18}

Data-driven trial execution and risk-based monitoring (RBM) are approaches to pooling data and using rigorous, bespoke analytical methodologies to identify site related risks before they create issues for clinical studies. The approach requires large amounts of longitudinal site, study type, and indication specific data. Models that use big data tools look for risk patterns, particularly for known failure points that follow study start up. Once risks have been identified, this approach lends itself to various risk mitigation strategies, which include deploying resources such as clinical trial monitors where they can be most effective: sites at risk are weighted high with resources and frequency of follow-up; and sites that are weighted low create cost efficiencies by underweighting resource deployment at low risk sites.

RBM as an approach to clinical trial monitoring has been shown to:

- Increase clinical trial efficiency and productivity
- Decrease overall clinical trial monitoring costs by as much as 25%
  - Various studies have documented the value of RBM to an average pharma company. For a top 10 pharma company with total development cost in excess of $5 billion, the savings from RBM are estimated at $250 million. With the competition for and the complexity of oncology clinical trials, with each Phase III study now averaging about $110 million, the cost savings from judicious use of big data via RBM and source/pattern recognition to mitigate risks are even higher.\textsuperscript{19}

Productivity and efficiency benefits from RBM come about from specific drivers. Based on proprietary Quintiles investigator surveys, these drivers include the following:

- Faster data entry (48% of sites comply with 7 day data entry requirement, versus non RBM sites at 8%)
- Reduction in missing pages (45% versus traditional studies)
- 30% reduction in traditional source document verification (SDV) and lower error rates in critical data (75% less than SDV error rates)
- Faster closure rate of corrective action items (47% reduction in time required for closure of corrective action items)
- Focus on and actual reduction of aged queries (>10 days) by as much as 28%
- Improved / timely communications with clinical investigators, resulting in better working relationships with clinical investigators and higher overall satisfaction rates.
Improving patient outcomes

5. Improving standards of care and outcomes analysis to determine optimal care paths

The application of rigorous evidence analysis to real-world treatment patterns, resource utilization and patient outcomes provides actionable insights for healthcare stakeholders. Electronic medical records can be combined with registries, claims data and other sources of evidence to complement clinical research and drive innovative solutions in patient care. These types of observational studies enhance the breadth and depth of our understanding of the disease condition and ultimately can help us develop treatments and strategies for improving patient outcomes worldwide.

For example, the Global Anticoagulant Registry Atrial Fibrillation (GARFIELD AF) is a pioneering real-world prospective registry launched by the Thrombosis Research Institute (TRI) in August 2009 to enhance our understanding of stroke prevention in atrial fibrillation. The goal of The GARFIELD Registry is to use real-world data from more than 1,000 centers, representing all possible care settings around the world, to describe acute and long-term management and outcomes in patient populations representative of everyday clinical practice within each participating country and rolled up for a global perspective. The data are already providing insights into rates of stroke and bleeding complications, as well as other important issues, such as treatment practices, physicians’ compliance with guidelines and patients’ adherence to therapy. In September 2015, registry leaders presented data from the study at the European Society of Cardiology conference, outlining global and local insights and opportunities they provide to improve care for patients around the world.

This type of real-world information is becoming increasingly important as health systems make decisions about which treatments to reimburse, and as clinicians and patients become more interested in localized and personalized data. By following so many patients over several years in this registry, we will be able to see the long-term impact of treatment and how outcomes compare across countries and patient populations. These data will help clinicians better understand how to improve care and outcomes for these patients. It will also inform future clinical research into AF, including where there are unmet medical needs, site selection for trials, inclusion/exclusion criteria, patient engagement opportunities, and where optimal patient populations are most likely to be found.

6. Lifting levels of patient adherence in medication use

Recognition of the importance to health outcomes of patient adherence to recommended medication use is well established and documented. The economic consequences of nonadherence have been estimated to account for 4.6% of global total health expenditure, representing the majority of the world’s total avoidable costs linked to suboptimal medicine use. Stakeholders are contributing to the greater focus placed on medication adherence through actions such as the movement toward outcomes-based contracting, the shift of risk from payer to provider, greater interest in value-based insurance design, and the inclusion of medication adherence measures in health plan assessments by the Centers for Medicare and Medicaid Services.

At the same time, advances in technology and data analytics are enabling new approaches that recognize the diversity of underlying drivers of patient nonadherence, apply predictive analytics to stratify patients based on risk and consequences of nonadherence, utilize a broader range of interventions including low-cost smartphone-based apps, and integrate adherence measures into patient records. Developing and applying analytics based on large and linked datasets are underpinning much of this progress toward improved patient outcomes and lower health system costs through increased medication adherence.

Real-world prescription data linked to mobile app usage can bring important insights on the effectiveness of new mHealth approaches on improving medication adherence in population segments (see Exhibit 19).
7. Reaching physicians and patients with appropriate medicines

Linking real-world data with analytics is bringing insights to understanding patient habits and health journey, their engagement with their own healthcare and healthcare professionals, as well as measuring patient outcomes. It also helps identify those physicians who are likely to have patients who may benefit from new medicines and can help manufacturers bring current and relevant educational information to those prescribers efficiently. As drug development becomes more focused on specialty and precision medicine, tailored drug commercialization approaches are also required.

Recent examples of utilizing real-world insights include:

- Using longitudinal non-identified prescription information to identify treatment pathways and medication adherence for patient segments based on diagnosis, age, gender, managed care coverage and prescription out-of-pocket costs. This enables physician education to be tailored based on how, when and where the medicine was being used. It also provides insight in the patient transition of care from hospital to community care, and ensures prescription medication is maintained post-discharge.

- Sourcing and aggregating EHR data from multiple specialist physician centers to apply predictive analytics to identify patient profiles of those who would normally have to repeat standard-of-care treatments to achieve desired outcomes. This resulted in a risk stratification tool which could be used by physicians to identify patients who would benefit from access to new treatment options that would shorten the time to be effectively treated.

- Creating algorithms based on fit-for-purpose EHR data combined with advanced statistical and machine learning to identify undiagnosed patients with rare diseases. In this case, prevalence is about 1 in 15,000 and the disease is characterized by extremely late diagnosis, impacting quality of life, healthcare resource use and effectiveness of...
therapy. The proof of concept study provided the ability for an algorithm to identify rare disease patients by identifying a “high risk” group who are 300 times more likely to have the disease than those in the general population. This enables education and awareness progress to be more effectively deployed to those physicians and their patients who would benefit from earlier disease diagnosis and treatment.

- Using medical and pharmacy claims data linked to longitudinal prescription data to understand if anti-coagulant therapy selection in the treatment of atrial fibrillation (A-Fib) is optimal across the U.S. based on certain patient risk factors. Through the analysis of EHR data and predictive modeling, it was estimated that approximately 30% of A-Fib patients receiving warfarin would benefit from an alternative therapy that would reduce their future risk of a stroke or bleed event. It was also clear by mapping local treatment variation that primary care physicians were much slower adopters of novel oral anti-coagulants (NOACs) than cardiologists. This led to the prioritization of local prescribers in areas where NOACs were being under-utilized relative to the patient risk profile, and delivered benefits in this patient population (see Exhibit 20).

Exhibit 20: Leveraging EMR Data, Claims and Prescription Data to Reach High-Priority Patients in Local Markets

Source: IMS Health, Q-EMR, July 2016
Driving marketplace value

8. Evaluating medical value and real-world evidence in decision-making

A proliferation of frameworks and assessment approaches now exist around the world to demonstrate therapeutic and economic value in response to increased calls for evidence of the value that new medicines bring to patients and health systems. These new approaches increasingly draw upon information and analysis that goes beyond traditional RCT data. To make access decisions, payer decision-makers are requesting information on how drugs will perform in “uncontrolled” patient populations and many are asking for financial guarantees if drugs do not meet thresholds. Real-world insights generated from real-world patient-level data not collected in conventional randomized controlled trials—including electronic medical records, claims data, mortality data, consumer data, registries, data collected in observational studies and chart reviews—using appropriate scientific and/or commercial analytics, are being used to:

- **Provide more accurate information** on patients and expected outcomes
- **Support RCT findings** over the long term, showing benefit of treatment in real patients
- **Monitor safety data** in a more realistic real-world setting beyond RCTs
- **Support maintenance of adequate price** in price re-assessments by demonstrating clinical value
- **Provide ongoing data** for payers through “coverage with evidence development” – contracts where a rebate or price cut may be required when clinical outcomes are not met (common in Italy, Spain and Sweden)
- **Help expand indicated patient populations** already in early-stage clinical development within EMA’s “adaptive licensing” initiative (pilot launched in March 2014).

Payers in many countries are leveraging real-world insights in making decisions about medicine access at time of launch, ongoing access, price, use and labels (see Exhibit 21).

**Exhibit 21: Real-World Evidence (RWE) Influences Pricing and Market Access**

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CONNECTING INSIGHTS

Real-world insight-driven access agreements are a way for manufacturers to secure access while committing to certain outcomes. While these agreements have become de facto in Europe for premium priced products or bigger budget impact therapy areas, they are in the early stages of development in the U.S. as the value debate intensifies. For example, Harvard Pilgrim Healthcare has recently engaged in three programs that will utilize real-world evidence:

- Using RWE to observe lowering of patients’ low-density lipoproteins to levels observed during clinical trials by tracking the effectiveness of evolocumab (Repatha)
- Using RWE to observe hospitalizations for congestive heart failure by tracking the effectiveness of sacubitril/valsartan (Entresto) in reducing hospitalizations
- Using RWE to evaluate dulaglutide’s (Trulicity) ability to lower HbA1c in diabetic patients

9. Applying post-market data to drive portfolio planning and predict market dynamics

The biopharmaceutical industry is increasingly focused on niche segments such as rare diseases and patient sub-populations. The relative scarcity of precise data in this domain presents challenges when making commercial decisions during asset development. While traditional approaches of market research still have a place in product valuation, they are increasingly falling short when no literature is available, syndicated reports are not specific enough, or representative sampling in bespoke market research becomes challenging.

Inaccurate valuation can have significant strategic repercussions—setting the market potential too high can lead to false confidence in a program’s commercial viability, while setting it too low risks the loss of a valuable business opportunity.

Companies are increasingly addressing these challenges by seeking to leverage real-world data for measuring patient populations in complex settings and using advanced analytics to bridge gaps in data availability. Real-world data can support multiple commercial decisions, including: sizing and segmentation of known indications; identification of undiagnosed and latent patient pools in niche areas; novel identification of patient segments based on risk predictors; and prioritization of indications for asset development. It is particularly valuable in therapy areas where the disease characteristics, setting of care and/or treatment options present particular challenges.

Examples of practical applications of post-market data to drive portfolio planning include:

Product positioning: In this example, analysis of market dynamics and the future market potential via real-world data allowed the biopharma company to size the addressable market, identify market opportunities, and understand the potential place for its new agent in the patient journey.

Prioritizing the tumor universe: In this example (see Exhibit 22), rapid prioritization of tumor segments of interest allowed the pharmaceutical company to focus on two segments with high commercial viability and clinical unmet need, allowing it to focus its resources while reducing burn associated with ancillary tumor programs.

The initial problem faced was a universe of more than 50 tumors and more than 100 clinical sub-segments (e.g., genetic mutations, performance status), and ranged from rare or orphan diseases to those of much higher prevalence. Real-world data was able to reduce bias and more accurately size and compare patient pools across tumors as well as their sub-segments.
Post-market competitive data may also be used to predict market dynamics. RWE is information based on thousands, or even millions, of data points collected in day-to-day clinical practice from a variety of data sources. While RWE is known to complement data from randomized clinical trials, its real potential is in moving decisions away from perceptions and broad extrapolations to the actual facts about patient journeys and outcomes. With innovations in data and technology, RWE is replacing other information sources such as non-behavioral primary market research, standard market reports, consumption/market data purchases, observational studies, and even selected spending on RCTs.

Real-world evidence is delivering deeper insights about patient care, treatment pathways, and drug effectiveness than previously thought possible.

Recent experience shows that companies are leveraging RWE for measuring patient populations in complex settings and using advanced analytics to bridge gaps in data availability. A firm was able to take historical data in a very dynamic marketplace (see Exhibit 23), and use that with predictive modeling to anticipate shifting patterns in drug usage to ensure products will be positioned for maximal utilization in patients with different indications.
Exhibit 23: Tracking Market Dynamics in the Diabetes II Market in Japan

Source: IMS RWD LRx-Japan, MDV Hospital data in Japan
A path forward

- Data is moving across organizational boundaries and must be harnessed and analyzed properly to drive decision-making
- Biopharma must adapt to a more dynamic development environment with an emphasis on creating a portfolio of evidence in support of its products
- Challenges such as transparency and privacy will need to be addressed collaboratively

Putting the pieces together

Many of the challenges addressed in this paper will resonate with health industry leaders, particularly biopharma executives. The issues discussed in the paper, of an industry in peril, that continues to skate on a knife edge of financial uncertainty associated with lowered productivity, rising costs, disparate, complex and seemingly inchoate data, and price and competitive pressures that endanger even its flagship successes such as in oncology, are not new. Much of the guidance and the approaches offered may sound akin to other industry conversations. Even the promise of a portfolio of evidence that links data and analytics to refreshing new solutions may sound familiar to some. The novelty is in the specifics: how can these pieces be put together? What are the tools? What applications need to be developed? And how can our way of working be changed to seek and apply the insights that new evidence can provide?

For us to succeed it is vital for industry leaders to own the task of taking on the less mined frontiers of medical science and break with the development paradigms of the past. The success of this change is predicated upon the ability to connect voluminous amounts of disparate data in meaningful ways:

- Data cannot and must not be a scarce resource. Increasingly, data is moving across organizational boundaries, and a diverse set of actors is making public and private, appropriately de-identified patient data available for analysis and decision-making at the right points in the decision tree.
- Algorithmic approaches are overcoming traditional limitations associated with data such as missing data, or combining data from across multiple studies.
- Best-in-class service providers are changing from supplying point solutions to working with their biopharma clients to work across the value chain, reducing uncertainties associated with decision-making from candidate selection to design and optimization of clinical studies to value added price points.
- Biopharma is beginning to consider an entire portfolio of evidence to better demonstrate the value of new medicines to the broad spectrum of healthcare stakeholders.

The power of evidence, collected as a portfolio, and applied in support of true solutions to compress the value chain is not theoretical. The tools and the process to reach the full potential of this approach exist, as this paper has aimed to demonstrate.
As we look forward, there remain four critical hurdles that need to be overcome to realize the full power of evidence. These include: maintaining data privacy, incorporating dynamic approaches to the application of data, maintaining transparency in data accumulation and application, and collaboration of diverse constituents, with differing interests.

- **Dynamic approach:** The drug development life cycle has gotten increasingly complex, as developers face relentless pressure to be first to market while delivering demonstrable proof of value to regulators, payers, providers and patients. This requires a more dynamic development environment, where projects teams are empowered by data and technology to make faster and better decisions to support patient safety while proving the efficacy of their products.

- **Transparency:** Advances in data access, data analytics and centralized data management tools enable this dynamic drug development environment by giving research teams easy access to multiple data sources and analytics tools to more rapidly mine results to identify trends and respond to patient safety concerns in near real-time. Data transparency allows for faster decision-making and supports more proactive risk management across the trial life-cycle. To make the most of this transparency, researchers need to think about how to better facilitate data networks and develop more effective search tools to support better and more detailed data mining.

- **Data privacy:** Such transparency, which is often enabled by cloud based data storage systems, demands that stakeholders across the healthcare landscape assess data privacy controls to ensure they meet all regulatory requirements and industry best practices. As an industry, we need to continue investing in the development of safe, secure and efficient technology for managing patient data, founded on secure technologies and trust between data owners.

- **Collaboration:** This trust is fostered through collaborations across the constellation of stakeholders. When sponsors work strategically with their partners, they can harness the latest analytics tools, data and technology to develop a more robust portfolio of evidence to support the safety and efficacy of their treatments.

We have seen that properly harnessed data analytics may help drive remarkable progress in diseases such as oncology. However, that progress may lay the seeds of a coming crisis and challenge our ability to make the most of rapidly proliferating data and technologies to balance development and commercialization.
Notes on sources

IMS Market Prognosis is a comprehensive, strategic market forecasting publication that provides insight to decision-makers about the economic and political issues that can affect spending on healthcare globally. It uses econometric modeling from the Economist Intelligence Unit to deliver in-depth analysis at a global, regional and country level about therapy class dynamics, distribution channel changes and brand vs. generic product spending.

IMS LifeCycle™ R&D Focus™ is a global database for evaluating the market for medicines, covering more than 31,000 drugs in R&D and over 8,900 drugs in active development worldwide. It includes information about the commercial, scientific and clinical features of the products, analyst predictions of future performance, and reference information on their regulatory stage globally.

IMS MIDAS™ is a unique data platform for assessing worldwide healthcare markets. It integrates IMS national audits into a globally consistent view of the pharmaceutical market, tracking virtually every product in hundreds of therapeutic classes and providing estimated product volumes, trends and market share through retail and non-retail channels. MIDAS data is updated monthly and retains 12 years of history.

Q-EMR (GE Centricity) database is linked to administrative claims from Truven’s MarketScan database. The database contains EMR records which include clinical information, in conjunction with health care resource use and cost measures from the claims data. Q-EMR draws data from a network of ambulatory-care providers called the Medical Quality Improvement Consortium (MQIC). The MQIC network consists of U.S. provider organizations using the GE Centricity system who have agreed to allow their contributed de-identified patient data to be used for quality reporting and other analytic purposes, with appropriate approval. The MQIC network comprises over 650 member institutions, including over 39,000 providers and over 37 million patient lives.

Quintiles Infosario® is a technology platform that combines analytics, expertise, and proven operational processes into a suite of systems that provide customers with the evidence and insights to make better, earlier decisions in clinical development. Data from multiple sources is integrated and harmonized, providing users with near real time information on their studies and patients. Reporting and analytics provide data visualizations so customers can see “at a glance” discrepancies within their data, and enable them to uncover root causes of issues so actions may be taken swiftly. With near real time data, ongoing transparency, and the suite of tools provided, our customers can easily monitor a study’s progress and make informed decisions to achieve operational excellence and successful clinical outcomes.
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Murray Aitken is Executive Director, QuintilesIMS Institute, which provides policy setters and decision-makers in the global health sector with objective insights into healthcare dynamics. He led the IMS Institute for Healthcare Informatics since its inception in January 2011. Murray previously was Senior Vice President, Healthcare Insight, leading IMS Health’s thought leadership initiatives worldwide. Before that, he served as Senior Vice President, Corporate Strategy, from 2004 to 2007. Murray joined IMS Health in 2001 with responsibility for developing the company’s consulting and services businesses. Prior to IMS Health, Murray had a 14-year career with McKinsey & Company, where he was a leader in the Pharmaceutical and Medical Products practice from 1997 to 2001. Murray writes and speaks regularly on the challenges facing the healthcare industry. He is editor of Health IQ, a publication focused on the value of information in advancing evidence-based healthcare, and also serves on the editorial advisory board of Pharmaceutical Executive. Murray holds a Master of Commerce degree from the University of Auckland in New Zealand, and received an M.B.A. degree with distinction from Harvard University.

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Robin Foldesy  
**Vice President, Strategic Drug Development**

Robin Foldesy is Vice President of Strategic Drug Development at QuintilesIMS, providing leadership, strategic direction and innovative solutions to complex client drug development programs. Robin has more than 30 years’ experience in clinical research and program management with companies such as Johnson & Johnson, GynoPharma Inc, Family Health International and Wyeth. As Vice-President of Project Management at Wyeth, Robin was responsible for the performance of all cross-functional R&D Global Drug Development Teams, project planning, and operational goals for the entire research and development division. Following Wyeth, he served as Vice President of Project Management for the Americas for two years at PRA International. Robin has a Doctoral degree in Physiology from Rutgers University and a Bachelor’s degree in Biology from Lafayette College.

Brad Smith  
**Vice President, Translational Medicine**

Brad Smith is Vice President of Translational Medicine within the Integrated Clinical Services Group at QuintilesIMS. In this position, Brad supports laboratory, clinical and diagnostic strategies for drug development as well as the development of innovative tools for targeted drugs and companion diagnostics. Previously, Brad led corporate development at Cell Signaling Technology, an innovative biotechnology company in the life sciences field. Brad also directed product development and production at Santa Cruz Biotechnology, helping to build that company into one of the largest supplier of research tools for basic research. Brad’s scientific background includes research positions at Stanford University and University of California, San Francisco, focused on cellular signaling mechanisms of disease. He holds a Doctoral degree from Stanford University as well as Master’s and Bachelor’s degrees from University of California, Santa Cruz.
About the QuintilesIMS Institute

The QuintilesIMS Institute leverages collaborative relationships in the public and private sectors to strengthen the vital role of information in advancing healthcare globally. Its mission is to provide key policy setters and decision-makers in the global health sector with unique and transformational insights into healthcare dynamics derived from granular analysis of information.

Fulfilling an essential need within healthcare, the Institute delivers objective, relevant insights and research that accelerate understanding and innovation critical to sound decision-making and improved patient care. With access to QuintilesIMS’s extensive global data assets and analytics, the Institute works in tandem with a broad set of healthcare stakeholders, including government agencies, academic institutions, the life sciences industry and payers, to drive a research agenda dedicated to addressing today’s healthcare challenges.

By collaborating on research of common interest, it builds on a long-standing and extensive tradition of using QuintilesIMS information and expertise to support the advancement of evidence-based healthcare around the world.
Research Agenda

The research agenda for the Institute centers on five areas considered vital to the advancement of healthcare globally:

- The effective use of information by healthcare stakeholders globally to improve health outcomes, reduce costs and increase access to available treatments.
- Optimizing the performance of medical care through better understanding of disease causes, treatment consequences and measures to improve quality and cost of healthcare delivered to patients.
- Understanding the future global role for biopharmaceuticals, the dynamics that shape the market and implications for manufacturers, public and private payers, providers, patients, pharmacists and distributors.
- Researching the role of innovation in health system products, processes and delivery systems, and the business and policy systems that drive innovation.
- Informing and advancing the healthcare agendas in developing nations through information and analysis.

Guiding Principles

The Institute operates from a set of Guiding Principles:

- The advancement of healthcare globally is a vital, continuous process.
- Timely, high-quality and relevant information is critical to sound healthcare decision-making.
- Insights gained from information and analysis should be made widely available to healthcare stakeholders.
- Effective use of information is often complex, requiring unique knowledge and expertise.
- The ongoing innovation and reform in all aspects of healthcare require a dynamic approach to understanding the entire healthcare system.
- Personal health information is confidential and patient privacy must be protected.
- The private sector has a valuable role to play in collaborating with the public sector related to the use of healthcare data.