Future best practices in oncology development

Critical aspects of co-developing and launching an oncology drug and companion diagnostic (CDx)

Brad Smith, PhD, Vice President, Center for Integrated Drug Development, Quintiles
Joshua Ransom, PhD, Principal Consultant, Global Market Access, Quintiles; Associate Director, Genetics, Biotech, and Emerging Medical Technology Institute, National Association of Managed Care Physicians
Daryl Spinner, PhD, MBA, Principal Consultant, Global Market Access, Quintiles
Eric Faulkner, MPH, Director, Global Market Access, Quintiles; Assistant Professor, Institute for Pharmacogenomics and Individualized Therapy, University of North Carolina at Chapel Hill; Executive Director, Genomics, Biotech and Emerging Medical Technology Institute, National Association of Managed Care Physicians
Executive summary

The promise of drugs targeting defined disease mechanisms and patient populations based upon the successes of drugs such as Herceptin and Xalkori has directly greatly redirected biopharma development strategies. However, the success of these efforts requires the development, approval and adoption of CDx to identify patients who will benefit. The biopharma and diagnostic (Dx) industries are currently learning how to best address that reality in the context of the regulatory, commercial and clinical systems in place in various global markets. This review describes the challenges facing the industries and stakeholders and possible approaches or solutions. The challenges range from technical, such as choice of platform, to health technology assessment (HTAs) and strategies to obtain reimbursement. Rapidly emerging technologies or models, such as next-generation sequencing or direct to consumer genetic testing, may suggest the need to rapidly recognize and address challenges as opportunities rather than barriers. Various biopharma companies are looking to address the broader issues of misalignment of development timelines and value distribution between the therapeutic (Rx) and diagnostic developers by bringing CDx development or management in house. We have yet to see the results of these alternative models. Therefore, it is important to consider a range of approaches and solutions. Many of these are discussed in this paper, including the identification of stakeholders, tools for driving uptake and reimbursement, and strategies for building organizations that can take advantage of these approaches. The ultimate success of personalized or precision medicine to improve drug development productivity will require standardization of these approaches consistent with regulatory and HTA standards.
# Table of contents

- Executive summary 2
- Introduction 4
- Challenges of co-developing and launching an oncology drug and CDx 5
  - Scientific challenges in drug and Dx co-development 5
  - Technology challenges in drug and Dx co-development 5
  - Business challenges in drug and Dx co-development 7
  - Key considerations for the regional regulatory pathways 8
  - Commercial challenges in drug and Dx co-development 9
    - Pressure for change influences innovation uptake 9
    - "Gears" of the system and shifts in incentives 9
    - Additional trends, considerations, and implications 10
- Solutions to the challenges 11
  - Critical success factors for CDx development and molecular test execution 11
    - Ensure evidence plans appropriately integrate the CDx 12
    - Understand the landscape plus the test clinical and funding flows 12
    - Understand reimbursement and pricing channels 13
    - Ensure that plans meet multiple stakeholder needs 13
    - Build an internal model for personalized medicine (PM) success 14
    - Adapt market access and commercial force to optimize PM success 15
    - Consider pricing and access expectations versus market realities 15
    - Planning for curve balls and future market dynamics 16
- Towards standards for PM 16
- PM and CDx value requirements 17
- Conclusion 18
- References 19
- About the authors 21
Introduction

In February 2012, Parkinson et al. published an influential article in the journal *Clinical Cancer Research*, entitled “Making personalized cancer medicine a reality: challenges and opportunities in the development of biomarkers and companion diagnostics.” In the paper’s introduction the authors commented:

“More than a decade of clinical experience with biologically targeted cancer therapeutics has both revealed their great potential and exposed the inadequacies of historical pathology-based classification systems as a basis for treatment selection. Studies have repeatedly shown the biologic heterogeneity of patients who have been categorized within classically defined disease entities. It is now generally acknowledged that improved biologic profiling of individual patients is needed in order to better link patients with biologically relevant targeted therapies.”

CDx are enabling the identification of patients best suited to receive, or not to receive, specific drugs. Hence the co-development and launch of an oncology drug and an associated CDx is increasingly important for the success of targeted cancer therapy. This is particularly true in a global market environment struggling to manage the economic realities of health care expenditures, where PMs can play a pivotal role in improving the quality and potentially cost-effectiveness of oncology care. As both payers and providers increasingly focus on value and care optimization, PM is one stratagem in the armamentarium of health care reform.

There are now several examples of the United States Food and Drug Administration (FDA) approving drugs in the oncology Rx area in conjunction with an FDA-approved CDx test. Crizotinib and vemurafenib were so approved in 2011. Crizotinib was approved to treat patients with late-stage (locally advanced or metastatic), non-small cell lung cancers who express the abnormal variant anaplastic lymphoma kinase (ALK) gene. Vemurafenib is indicated for patients with melanoma with a certain abnormal variant of the BRAF gene, BRAFV600E. Both obtained accelerated approval and demonstrated impressive efficacy in patients.

More recently, at the end of May 2013, dabrafenib and trametinib were approved. Dabrafenib is indicated as a single-agent oral treatment (Tx) for unresectable melanoma or metastatic melanoma in adult patients with BRAFV600E mutations. Trametinib is indicated as a single-agent oral Tx for unresectable or metastatic melanoma in adult patients with BRAFV600E or BRAFV600K mutations. Approximately 50 percent of patients with metastatic melanoma have a BRAF abnormal variant. The BRAFV600E mutation accounts for approximately 85 percent of all BRAFV600E abnormal variants in metastatic melanoma, and the BRAFV600K abnormal variant makes up approximately 10 percent of all BRAFV600 mutations in metastatic melanoma.

According to the FDA, these abnormal variants must be detected by an FDA-approved test, such as THxID™-BRAF (a CDx assay from bioMérieux S.A.). These approvals suggest that the pace of dual approvals may be increasing, placing greater focus on integrating CDx development into the development of oncology Rx. Further, it has been estimated that 56% of the current oncology drug pipelines are associated with one or more biomarkers and may emerge as co-developed technologies, increasing the potential for substantial output of PMs in the next 5-7 years.

Understanding key strategic priorities in the planning of the development, launch, and commercialization of an oncology drug and an associated CDx test has therefore become very important. Evidence generation for both the drug and the CDx must be maximized to improve the chances of gaining regulatory approval. Furthermore, key trends in the healthcare industry influencing the direction and uptake of oncology CDx as the standard of care also must be identified to optimize market access of PM drugs and their CDx in global markets.
Challenges of co-developing and launching an oncology drug and CDx

There are multiple challenges in co-developing a drug and CDx, including scientific, technical, regulatory and commercial challenges. Additionally, challenges do not stop at the point at which the drug and Dx receive regulatory approval: launching the products must receive careful attention, and trends impacting market access and commercial potential of the products, including optimization of test use, must be analyzed and integrated into development and commercial plans.

Scientific challenges in drug and Dx co-development

Three considerations of particular importance are the degree to which the biology of the disease or condition of clinical concern is understood, the quality of the related Dx test, and the degree to which the test result can be tied to definitive decisions around Tx selection. Success is much more likely if there is a good understanding of the biology of the disease and the drug’s mechanism of action (MOA) to inform the choice of marker and test specifications. A test must also have good analytic performance and meet the regulatory requirements for in vitro diagnostic devices (IVDs) or laboratory developed tests (LDTs). Additionally, for provider and payer acceptance, the role and value of the test in selecting patients for a specific Tx must be clear and actionable. Lack of any one of these components often will result in failure.

Technology challenges in drug and Dx co-development

A CDx must not add to the risk of the drug due to poor performance or faulty technology. The technology must also help drive adoption and commercial success. These technology strategy decisions fall into four categories, as shown in Table 1. Within each category there are issues and questions that need to be addressed. For example, one needs to determine whether single analytes or multiplex testing strategies are to be employed. Advantages and disadvantages, including costs and risks, need to be balanced in terms of development and potential market access.

<table>
<thead>
<tr>
<th>Category</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology Selection</td>
<td>• Dominant technologies versus emerging technologies. Should single analytes or multiplex testing strategies be employed? What are the risks and costs? • With regard to performance, how do sensitivity and specificity parameters compare? To what degree are false negatives and false positives avoided? • What is the degree of the technology’s robustness, and what are the training and QC requirements? • What is the platform’s availability in target geographies, and has it been validated? • Are there clinical pathway or economic considerations that would influence willingness to test or use the target test?</td>
</tr>
<tr>
<td>Category</td>
<td>Issues</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>
| Partnership & Licensing Strategy | • What is the current status of kit/reagent licensing? If not yet licensed, what steps need to be taken to achieve this?  
• What type of partner is best? Assessments of technical capabilities, platform breadth and validation, clinical experience, goals, commercial scope, and necessary support.  
• What will be the nature of the relationship’s structure and terms? Items to be considered include: visibility, control, and governance; incentives alignment and pricing; and funding and risk-sharing.  
• Is the test technology proprietary and are there freedoms to operation concerns? Is LDT or LDT-to-IVD a viable path? What is the risk/cost of using a single lab development and commercialization model?  
• Are there intellectual property considerations associated with the target test and/or test provider partner? How would this influence uptake in key markets? |
| Logistics Requirements          | • What are the plans for testing channels; sample access and handling; platform availability; awareness, education, and training; and patient, payer, and provider journeys? |
| Approval & Adoption Hurdles     | • Assessments of regulatory landscapes in various geographical regions will be required, which will impact the development strategies that are planned.  
• Assessment of reimbursement environments across geographical regions will also be required. Factors of importance include, but are not limited to, stakeholder analysis (for Rx and CDx), evidence-based medicine (EBM) value platform, implications of centralized region-based testing approaches, and pricing and reimbursement (P&R) strategy.  
  • Who are the primary decision makers for test reimbursement – e.g., national, regional, local payers, or providers?  
  • Will HTA of the Rx and CDx occur through the same body or separate bodies?  
  • What HTA criteria will be employed in evaluating the test? Does this vary between CDx and standalone Dx?  
  • Are specific codes required for reimbursement or does the target test type fit into existing test coding systems?  
  • Do funding sources for CDx exist in the target markets? Who pays for testing? Will test subsidization by the manufacturer be required for test use and/or optimization? If so, what are the options (e.g., voucher or grant systems)?  
  • Will the balance of percentage of potential responders versus test cost be a problem for payers or physicians?  
  • How familiar or comfortable are providers with testing in the target indication? To what extent is education of physicians, laboratory personnel, and patient necessary to support adoption?  
  • Do providers have processes (e.g., stepwise testing in the case of multiple biomarkers, pathways or guidelines) that must be taken into account?  
  • Are there challenges obtaining enough material to test? Is tissue storage required?  
  • Are there patient educational needs or cost considerations (e.g., out of pocket requirements) that must be taken into account to optimize testing and appropriate targeted drug selection? |
Clearly, the choice of test approach, technology and platform, including operational and regulatory considerations, is a complex process that requires planning and preparation. The performance issues that remain with traditional or routine methods, such as immunohistochemistry (IHC), present challenges that may eventually be addressed with new approaches or technologies. There is a wealth of options available for moving toward Dx use in the near future in the immunoassay and genomic fields (including epigenetics) while mass-spectrometry based proteomics, metabolomics and glycomics also hold great promise. The evolution of ALK testing in non-small cell lung carcinoma (NSCLC) from fluorescence *in situ* hybridization (FISH) to IHC to polymerase chain reaction and possibly sequencing is illustrative of how quickly technologies and practices may change. The current, less than universal, level of adoption and technical acceptance of the test and the recent launch of competing tests, including an IHC test, indicate that the story has yet to be completed for the Xalkori CDx and ALK testing in NSCLC.

**Business challenges in drug and Dx co-development**

Consider next the challenge of new collaborations or business partnerships. Whenever new stakeholders are introduced into a process, healthcare or otherwise, considerations concerning incentives and commitment arise. A key question becomes: To what extent will everyone contribute to the overall success of the Rx/Dx combination? Unfortunately, there are currently several misalignments of drug and CDx development timelines. These have broad implications for planning, budget, and operations in the biopharmaceutical industry. One fundamental misalignment is in the development timelines of a Dx test compared to when the Dx partner is first brought into the Rx program. This misalignment is highlighted in Figure 1. As shown in the figure, this misalignment could result in a CDx not being ready to support the launch of a drug. The case study of Xalkori is illustrative of a success story in meeting this timeline. However, it is not clear how reproducible or ultimately successful that example is for the industry. Pricing of the first CDx kit is another important factor in the strategy to drive drug adoption. The Xalkori example also illustrates that test price may impact adoption of the test and the emergence of cheaper LDT alternatives.

**Figure 1 Misalignment of drug and CDx development timelines**

As new stakeholders are introduced, a key question becomes: To what extent will everyone contribute to the overall success of the Rx/Dx combination?

**Case study: Xalkori**

The clinical development for Xalkori represents a success story in terms of developing a CDx test in time for Rx approval. The impact on the clinical development program is captured by metrics shown in Table 2. The stated decrease in trial cost may be significantly underestimated as it is based upon an assumed standard cost per patient. These figures demonstrate that targeting of a drug to a highly responsive patient subpopulation using a selection test may decrease trial cost by over 150%, decrease trial size by three times and shorten development time by three years. The simultaneous launch of Xalkori and the Abbott ALK FISH test may have benefited from a preexisting FISH assay approved in a different indication but does represent a very aggressive timeline for approval of a Dx.
Table 2 Clinical development of Xalkori

<table>
<thead>
<tr>
<th></th>
<th>Relative clinical trial development costs (Percentage: based upon a standard cost per patient)</th>
<th>Total clinical trial enrollment (participants)</th>
<th>Phase I initiation to New Drug Application (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Xalkori</strong></td>
<td>100%</td>
<td>960</td>
<td>1.8*</td>
</tr>
<tr>
<td><strong>Iressa</strong></td>
<td>146%</td>
<td>2850</td>
<td>7.0</td>
</tr>
<tr>
<td><strong>Tarceva</strong></td>
<td>154%</td>
<td>3110</td>
<td>5.3</td>
</tr>
</tbody>
</table>

a: only phase 2 trial results for FDA approval. EMA approval included interim phase 3 trial results

An additional and more fundamental challenge that exists for the new Rx/Dx developers is a misalignment of drug and CDx risks and rewards, which are not shared equally between biopharmaceutical and Dx manufacturers. The biopharma drug developer’s business model has high risks and high rewards. The timelines are tight, budgets and investments are large, and there is a great potential for lost revenues if there are delays in development. For the Dx/IVD manufacturer, there is low risk and low reward. There is less room for investment and loss, lower requirements for time to market, and pricing driven by reimbursement. The question therefore becomes: How does one reward CDx development and share risk? The rapid development of the Xalkori CDx, based upon a pre-existing Dx test, is illustrative of a success story in meeting this timeline. However, an important question to consider is: Was the value created through the Dx adequately distributed or was it primarily a risk borne by the drug company?

The IVD manufacturer may view PM from a variety of assumptions including the four listed in Table 3. However, these premises are meeting evolving realities, a few of which are also included in the table. These viewpoints may help inform a solution for incentivizing CDx development.

Table 3 Common assumptions of PM: the IVD manufacturer’s perspective

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Evolving realities</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM strategies can reduce the time and cost associated with test development.</td>
<td>Depends on the rarity of the marker, requirements for comparative effectiveness, and uncertainty of new Tx.</td>
</tr>
<tr>
<td>PM strategies reduce risk of reimbursement rejection of the test via a more targeted efficacy/safety story and reduced budget impact.</td>
<td>Not always. It depends on the balance of efficacy/safety vs. costs, strength of linkage of test to Tx, and the unmet medical need.</td>
</tr>
<tr>
<td>PM is a true differentiator for an IVD test in the emerging global marketplace as payers place increasing pressure on innovative technologies.</td>
<td>This is true assuming that outcomes are superior to existing alternatives although ease of developing “me too” assays eliminates the pricing differentiation for most current payers.</td>
</tr>
<tr>
<td>PM can increase the rapidity of market uptake of the IVD by increasing certainty of Tx response, which is valued by payers, physicians, and patients.</td>
<td>Not always. It depends on “familiarity” with testing, degree of payer management in the respective Rx area, and logistic considerations for indications with multiple biomarkers/testing panels.</td>
</tr>
</tbody>
</table>
There is not currently a single solution for how CDx development will be supported, although various models are being explored by biopharma. Innovative models based upon patient profiling for multiple markers and drugs are being explored by both biopharma and Dx companies (across clinical trials and even in clinical practice). However, new business or commercial models may be significantly negatively impacted by P&R.

**Key considerations for regional regulatory pathways**

A review of the regulatory considerations and challenges impacting CDx development would require another full review beyond the scope of this article. The importance of being familiar with guidance documents including the FDA Draft Guidance Document of July 2011 cannot be overstated. It is essential to know the type of regulatory approval required for the device [e.g., pre-market approval (PMA) or pre-market notification 510(k)] given the significant differences in risk, costs, timelines, and level of evidence required. As in many other situations, it is best to assume a model of “early and often” communication with the agency.

It is also important to know the differences between approval pathways for Tx and CDx and the region-specific requirements. In the United States, the CDx path will typically be with Center for Devices and Radiological Health (CDRH) or the Center for Biologics Evaluation and Research (CBER). Scenario planning for the IVD kit and possibly a PMA-approved LDT path should be conducted.

**Commercial challenges in drug and Dx co-development**

There are a number of common commercial problems faced by CDx manufacturers or companies entering the PM field as summarized in Table 4.

<table>
<thead>
<tr>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Ensuring evidence plans contain sufficient information about the CDx;</td>
</tr>
<tr>
<td>2. Understanding the landscape plus the test clinical and funding flows (across disease, drug, and testing markets);</td>
</tr>
<tr>
<td>3. Understanding Dx reimbursement and pricing channels;</td>
</tr>
<tr>
<td>4. Ensuring that development and commercial plans address multi-stakeholder needs;</td>
</tr>
<tr>
<td>5. Ensuring that the internal development and launch model is “built for success;”</td>
</tr>
<tr>
<td>6. Adapting market access and commercial field force for success;</td>
</tr>
<tr>
<td>7. Pricing and access expectations take into account market realities;</td>
</tr>
<tr>
<td>8. Planning for “curve balls” and future market dynamics.</td>
</tr>
</tbody>
</table>

The common problems are leading to a number of key trends impacting the development and access for CDx or PM products. These trends include:

**Pressure for change influences innovation uptake**

Pressure for change is influencing innovation uptake. Considerations include unsustainable spending, cost control pressures, quality improvement pressures, the need for continuity/standardization, recognized inefficiencies in delivery, the drive to identify appropriate subpopulations/focus Tx, and the meeting of patient choice and affordability. In addition, there is an emerging expectation in certain markets for biomarkers and CDx to be the default approach. These considerations have led in many markets to a variety of health reform changes, including cost control/economic management schemes, insurance structure changes/redesign, coding system reform, HTA/EBM process development and refinement, and restructuring of delivery systems. Among some of the most common developments that raise key questions for PM are comparative effectiveness research, value-based payments, conditional coverage schemes, and pay for performance/risk sharing approaches. In some markets such as the United States, policies that shift risk to providers, including the accountable care organizations (ACOs) and other steps towards similar financial-at-risk models may also need to be taken into consideration.
“Gears” of the system and shifts in incentives
In the new economic environment, companies must create real value for their products to differentiate themselves from existing products and satisfy the ever-changing needs of stakeholders. A question of interest is: As the architectural landscape shifts, where does PM fit in? Determining the answer requires consideration of the players, ‘gears’ of the system, and the ‘oil’ that keeps it all moving. As noted earlier, players include payers, hospitals, physicians, manufacturers, and laboratories. In this context, the term ‘gears’ refers to operational processes and mechanisms, funding flows and financial incentive structures, decision processes, and policy. The ‘oil’ that keeps it all moving refers to considerations such as mission and motivators, including business goals and incentives, standards and criteria, and ‘feedback loops’ and interconnectivity among stakeholders.

While emphasis on PM is increasing, particularly in disease areas such as oncology, specific policies and drivers that would induce or inhibit uptake of PM are currently very heterogeneous across markets like Australia, the United Kingdom, and the United States, having advanced specific decision criteria, and others such as Germany that have had limited specific interest in PM. Increasing requirements for comparative evidence and “real world” evidence raise important questions around expectations and methods for comparing “personalized” therapies to technologies historically targeted at broader populations. These regional conditions are important variables in determining strategies for drug and Dx co-development.

Additional trends, considerations and implications
There are several additional trends to be cognizant of, listed shortly, all of which may vary by geography. The regulatory landscape for LDT, IVD, and CDx is changing rapidly, and manufacturers (and indeed other stakeholders) need to remain aware of new developments from regulatory agencies. As noted previously, an in depth discussion of regulatory considerations is beyond the scope of this review. However, it is important to note two future developments impacting CDx strategies. In the United States, potential FDA oversight of LDT’s and Clinical Laboratory Improvement Amendments (CLIA) laboratories remains a significant concern potentially discouraging investment in early test development and innovation but also promising to improve test consistency and reporting. In the European Union, proposed “fit-for-purpose” medical device regulations are expected to begin to be implemented starting in 2014, potentially greatly altering the regulatory requirements for CDx. Changes in CDx coding and payment need to be monitored. For example, there is a shift in focus toward value; however, this has not caught up with CDx on the payment side. There is a near-term proliferation of more complex Dx, which are perhaps better, faster, and cheaper than currently available products, though many global reimbursement and regulatory mechanisms have not anticipated this shift towards evaluation of multiple biomarkers and vanguard products will face significant uncertainty in terms of approval reimbursement processes and outcomes. Both payers and physicians will require significant education to broadly uptake massive multiplex testing. There is also movement towards more prescriptive EBM clinical pathways and coverage with evidence development: progress has been slow here, but the potential is considerable.

HTAs, health systems, healthcare providers and networks are now influential stakeholders. For example, the National Institute for Health and Care Excellence (NICE) rejected Pfizer’s crizotinib, and, following a rejection of Zaltrap (ziv-aflibercept injection for intravenous infusion), a drug indicated for co-therapy in metastatic colorectal cancer, including the high profile rejection by Memorial Sloan-Kettering Cancer Center, Sanofi halved the drug’s price. There are various rationales for stakeholders rejecting Tx. They may consider that there are evidence gaps in value story (e.g., biomarker epidemiology, linkage between test information and Tx use, and difficulty in interpreting the results of a test) and/or that the price of the drug outweighs its perceived benefits (i.e., there is insufficient cost-effectiveness). They also consider the presence of safety risks, whether there is sufficient differentiation from alternative Tx, and whether there is a lack of comparative effectiveness data or an insufficient impact on unmet need(s).
In March 2012 the United Health Group released a document entitled “Personalized Medicine: Trends and Prospects for the New Science of Genetic Testing and Molecular Diagnostics.” It identified key issues for the appropriate integration of PM, each of which has various implications for the health system:

- Protect, support, inform patients; decision support;
- Develop an evidence base to determine which tests work;
- Encourage tests proven to work (including revised payment systems and clinical pathways);
- Monitor care through coding and utilization reporting;
- Ensure lab tests are performed safely and accurately (improve accreditation standards);
- Educate providers; keep them up to date, including their awareness of Tx guidelines.

These guidelines define the healthcare environment in which drug and Dx co-development must succeed.

**Solutions to the challenges**

Having outlined some broad challenges in the co-development and launch of a drug and Dx, and in the ensuing practice of PM, it is important to discuss potential success factors and solutions. These will be outlined below.

**Critical success factors for CDx development and molecular test execution**

The critical success factors for CDx development and molecular test execution fall into a few general categories, including sample access, test performance, Dx kit development, regulatory approval, commercialization and reimbursement. The list presented in Table 5 highlights these factors as well as lists a few additional aspects.

**Table 5 Critical success factors for PM and CDx**

<table>
<thead>
<tr>
<th>Critical success factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sufficient test performance balanced and optimized to support the Rx;</td>
</tr>
<tr>
<td>• Defined Responder population size;</td>
</tr>
<tr>
<td>• Evidence linking test to Tx options;</td>
</tr>
<tr>
<td>• Greater certainty of Tx response for “biomarker positive;”</td>
</tr>
<tr>
<td>• Reduced budget impact vs. “broad” Tx;</td>
</tr>
<tr>
<td>• Reduced “wastage” of resource;</td>
</tr>
<tr>
<td>• Cost-effectiveness &amp; budget impact vs. alternatives;</td>
</tr>
<tr>
<td>• Appropriate Dx partnering and knowledge of lab acceptance requirements;</td>
</tr>
<tr>
<td>• Ensuring testing strategy maps to logistics capabilities</td>
</tr>
<tr>
<td>• Harmonize regulatory &amp; reimbursement reviews</td>
</tr>
<tr>
<td>• Knowledge of Dx stakeholder acceptance requirements to ensure broad test availability and timely results;</td>
</tr>
<tr>
<td>• Planning and active lifecycle management taking into account Rx and Dx competitive landscape (e.g., multiple tests in an indication with limited sample)</td>
</tr>
</tbody>
</table>

The key consideration for sample access is the availability of suitable, high quality samples while maintaining trial feasibility. Important factors are the trial’s protocol and laboratory manual, which will determine participant and sample requirements, and sample acquisition, which will be impacted by site selection, set up, training, and monitoring. The overall test menu and specimen management will determine sample availability.
With regard to test performance, the most important consideration is: Will the test results be actionable, i.e., be robust for clinical decision-making? A critical first step is technical and scientific evaluation to determine feasibility. Technical validation must then be performed to CLIA/regulatory standards. The quality of the data is optimized by quality systems, lab harmonization, and quality assurance (QA) procedures.

The availability of a Dx kit, if needed, has to be addressed at the right time in the drug development cycle. Engaging the Dx partner early in the process enables design control, regulatory compliance, and early commercial planning. This means that the test and clinical plan must not only be feasible for the sponsor but also for the Dx partner.

Coordination between the sponsor, the Dx company, and contract research organization or development vendors is extremely beneficial, accelerating test development, approval, and commercialization. Furthermore, as the PM portfolio expands, companies should evaluate the portfolio of Dx partnerships in order to account for potential synergies by streamlining processes, systems, and resources across all the alliances.

While obtaining marketing approval remains necessary, it is no longer sufficient: it is vital to consider how to make the test commercially successful. Misalignment of timelines is common, and hence early planning, resourcing, and budgeting is required. Additionally, all of these strategies can vary by region, clinical situation, and commercial landscape. Health economics, reimbursement, freedom to operate, and commercial due diligence should define the appropriate label, protocol, and launch plan.

As health systems adapt to changing pressures it is important to build an evidence toolkit to address new health trends. Components included in this toolkit are listed in Table 6.

Table 6 Health trends evidence toolkit (for both Rx and Dx)

<table>
<thead>
<tr>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Stakeholder research;</td>
</tr>
<tr>
<td>• Randomized controlled trials, practical clinical trials, observational studies, and registries;</td>
</tr>
<tr>
<td>• Claims and electronic medical record data;</td>
</tr>
<tr>
<td>• Budget impact model;</td>
</tr>
<tr>
<td>• Lab budget impact and economic model;</td>
</tr>
<tr>
<td>• Value message testing;</td>
</tr>
<tr>
<td>• Value dossier;</td>
</tr>
<tr>
<td>• Cost-effectiveness model;</td>
</tr>
<tr>
<td>• Time-in-motion studies.</td>
</tr>
</tbody>
</table>

The following discussion focuses upon how to translate these success factors and tools into successful CDx plans.

1. Ensure evidence plans appropriately integrate the CDx

Evidence requirements for PM are changing at a fast pace as requirements in many markets evolve rapidly, and hence the nature and utility of the CDx need special considerations. Payers, for example, are likely to ask various questions to determine the value of a CDx. A principle question concerns whether the test results are actionable. No amount of accurate test information is useful in this context if it cannot be acted upon to improve patient management and health. Once this primary concern has been successfully answered, payers will want to know the accuracy of the test (the false positive and false negative rates), whether test interpretation is clear, how many tests must be paid for before one treatable patient or adverse event is identified, and how much more effective Tx is in the responder population compared with standard of care Tx. Additional questions of interest include the proper comparison strategy for PM when others...
do not exist for the indication and the impact of avoiding wastage. Final question of interest is how and to what extent should ancillary procedures like biopsies factor into discussions and decisions and the Rx manufacturer’s portfolio mix between therapies with and without CDx.

When addressing these questions, the following considerations should be borne in mind. First, it is important to understand which questions are most important to both the market and to stakeholders. Second, the economic evaluation of PM is still evolving and is highly variable among markets. Third, prepare for the most sophisticated PM markets, which are currently Australia and the UK. Fourth, keep your “ear to the ground” because this space is moving quickly. Markets with growing requirements for high levels of evidence include Brazil, South Korea and Japan.

2. Understand the landscape plus the test clinical and funding flows

Various pitfalls in this area can be identified. There can be a lack of understanding of which stakeholders drive CDx use and associated funding decisions, and where pressure points fall in this process. The cascade of decision makers involved in test selection and use can vary markedly by disease area and market. Lack of understanding of the impact of procedures such as biopsy and spinal fluid taps on access may result in suboptimal test uptake. Inappropriate understanding of what lab directors need to see to support adoption decisions and the interplay of hospital administrators can be problematic, as can inappropriate market preparation for sample storage/availability and availability of target testing platforms. In addition, consideration of whether the target testing approach is at risk for insufficient funding should be considered on a market-by-market basis. Awareness of these factors can greatly improve the chances of a successful test.

A range of mitigation strategies is available. Sponsors need to take a “deeper dive” into market research that goes beyond conventional drug scenarios to address the additional layers of complexity associated with PM via proper planning. The test access and commercial plan should be aligned to anticipate and proactively address PM considerations and pressure points. In some cases, test subsidies by the manufacturer may be required to support test uptake (e.g., leveraging voucher or grant approaches) and manufacturers should understand the implications of removal of testing subsidies (e.g., recent withdrawal of funding for epidermal growth factor receptor testing had limited impact in the United Kingdom, while it resulted in a plummet in testing rates in Canada). Coordination between central and local affiliate functions across the product lifecycle is needed. Novel commercial personnel that help support test uptake by providers and laboratories may be needed to optimize commercial potential and navigate around unexpected testing bottlenecks or roadblocks.

The rapidity of change in the PM/CDx landscape means that emphasis on appropriate aspects of development should start early (in Phase II trials for the drug), and the strategy employed should be able to facilitate and accept rapid changes. Therefore, the adequacy of staff training for both development and commercial teams must be ensured. Provider and patient market education/preparation may also be required to ensure a fertile launch landscape.

3. Understand reimbursement and pricing channels

While drug manufacturers understand drug reimbursement processes, navigating reimbursement for CDx remains a steep and complex learning curve. Various considerations include the determination of the key decision maker for CDx and how and where drugs and Dx tests flow through different HTA and reimbursement channels. It is important to determine when and where the flow through these channels is the same for the combination of drug and Dx as it is for a drug alone (e.g., in France and Australia the companion test and drug will flow through different channels with different criteria whereas in other markets the test and drug will be evaluated together). For drug manufacturers to know whether or not their CDx strategies are sufficient, it is important to determine what clinical and economic evidence is critical in each of the markets where entry is desirable. Test coding and payment rate setting must also be taken into account as this may range from complex national processes to facility-level “value judgment” decisions, unlike drugs which are virtually always evaluated at a national level.
Certain implications follow from these lines of questioning. First, it is necessary to ensure that development plans “cover the bases” by understanding the pathway through HTA and reimbursement for CDx in each market. Second, it is important to avoid evidence “landmines” that are unique to CDx, hence avoiding potential one- to four-year delays in launch because insufficient emphasis was placed on the Dx. If the CDx is not reimbursed, this can have a devastating effect on companion Tx access. Third, drug P&R is typically a top-down process, whereas Dx is a bottom-up process, though regional and some national-level processes exist (e.g., national level coding, HTA, and test fee schedule setting). Adaptations to market access plans are thus required that go beyond conventional drug scenarios and increase the complexity of access optimization. Some markets may provide test subsidies either through direct support or block grants.

4. Ensure that plans meet multiple stakeholder needs
PM and CDx introduces new stakeholders with different information needs and decision drivers. Inclusion of these stakeholders in planning is critical for CDx success. As noted previously, there are various key stakeholders, including the oncologist, hospital administration, and the sample procurer, patient, and payer.

With regard to laboratory acceptance, it will need to be determined whether testing platforms and laboratory contracts are in place, or whether additional platforms will need to be purchased and contracts put in place for a new CDx. Potential disruption to existing operations and workflows would need to be evaluated, and whether the lab would conduct the test in-house or outsource to a reference lab would need to be decided upon. Factors to be considered include the economics associated with running the new CDx in terms of cost, sample flow, and staff requirements; the available of sufficient tissue to support testing; and provisions for storing samples. Whether or not the hospital would support a “loss leader” test if there were sufficient cost offset related to Tx use is also important.

Given the higher risk of product failure and/or payer decision drivers, it is advisable to consider early payer engagement to clarify evidence plans. Multiple HTA and payer advisory bodies (e.g., NICE, The Canadian Agency for Drugs and Technologies in Health, Centers of Medicare and Medicaid Services) have formal and informal means of obtaining feedback on evidence plans. Targeted early engagement can help mitigate the risks of rejection and identify areas for “gap” filling and prioritizing the value story. These meetings may also be opportunities to sound out new clinical trial approaches (e.g., adaptive designs, pragmatic clinical trials), real-world evidence requirements (if any), and novel patient management approaches.

5. Build an internal model for PM success
Various important questions must be addressed when building an internal model for PM success. A key consideration is the composition and role of the PM team within the organization. Subsequent considerations include salient organization and processes, support and strategic advising, lifecycle data capture and reconciliation, optimal integration with internal stakeholder groups (e.g., functional area and brand teams), degree of interface across clinical and commercial activities, and optimal alignment of local and central functions to ensure that “no box goes unchecked” that could jeopardize access. The level of complexity of a PM internal function should align with pipeline and disease area focus across the portfolio. In the case of oncology products, PM is an essential consideration.

Organizations are adopting new business models for PM and CDx’s. So far, however, these models are highly variable and reflect different levels of commitment to this paradigm. Several model types are shown in Table 7. A fully dedicated team for portfolio-wide PM may emerge in the near future at select biopharma companies depending on the return on investment for what often are termed centers of excellence.
Table 7 Model types and their pros and cons

<table>
<thead>
<tr>
<th>Model type</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM Center of Excellence</td>
<td>• Dedicated focus on best practices + asset support.</td>
<td>• Resource intensive.</td>
</tr>
<tr>
<td></td>
<td>• Enables coordination among business units.</td>
<td>• May not take into account other MA trends like comparative</td>
</tr>
<tr>
<td></td>
<td>• Most effective if some budget has been allocated.</td>
<td>effectiveness research (CER), value-based reimbursement, risk</td>
</tr>
<tr>
<td></td>
<td>• Leverages collective knowledge.</td>
<td>sharing.</td>
</tr>
<tr>
<td>Matrix-based/SWAT team</td>
<td>• Focused on asset development.</td>
<td>• Does not enable best practices.</td>
</tr>
<tr>
<td></td>
<td>• Enables coordination among business units.</td>
<td>• Often funded by brand teams.</td>
</tr>
<tr>
<td></td>
<td>• Does not enable best practices.</td>
<td>• Limited internal authority/</td>
</tr>
<tr>
<td></td>
<td>• Limited resource requirements.</td>
<td>responsibility.</td>
</tr>
<tr>
<td>Independent (internal) advisor</td>
<td>• Limited resource requirements.</td>
<td>• Does not actively engage business units.</td>
</tr>
<tr>
<td></td>
<td>• Does not actively engage business units.</td>
<td>• May not have sufficient geographic scope and organizational</td>
</tr>
<tr>
<td></td>
<td>• May not have sufficient geographic scope and organizational “buy in.”</td>
<td>“buy in.”</td>
</tr>
<tr>
<td></td>
<td>• Limited influence.</td>
<td>• Limited influence.</td>
</tr>
<tr>
<td>Watch-n-wait</td>
<td>• Limited resource requirements.</td>
<td>• Reactive not proactive.</td>
</tr>
<tr>
<td></td>
<td>• Deployed only on assets where absolutely necessary/ market driven.</td>
<td>• May slip “behind the times.”</td>
</tr>
<tr>
<td></td>
<td>• May miss differentiation opportunities.</td>
<td></td>
</tr>
</tbody>
</table>

6. Adapt market access and commercial force to optimize PM success

As system incentives change and the number of relevant stakeholders for PM and CDx increases, market access and commercial models must adapt in tandem. Sponsors need to consider not only the risks of adapting access and commercial models, but also the risks of not adapting them. They must determine what information concerning the Dx is critical and who needs access to it. The must also determine the location of key pressure/influence points for PM market access, how key stakeholders different from the conventional drug-alone model, the right incentives and steps to take, and which processes, tools, and data resources will optimize success for PM.

The commercial success of a therapeutic with a companion diagnostic is integrally linked to the uptake and use of the diagnostic. Therefore, ensuring the success of the companion diagnostic is becoming increasingly important. To this end, some manufacturers are deploying new expert commercial staff to focus on provider and laboratory test utilization and optimize uptake. This is, at present, occurring separately, but would also align with broader commercial restructuring efforts occurring in the pharmaceutical industry to address a) a more complex, EBM sales environment, b) need to go beyond the provider and integrate payer facing roles, and c) to respond to a more granular, decentralized and locally focused environment in some markets. Development of commercial metrics that link improved test use to selection of the targeted Tx is also an important consideration. A review of the various aspects of test uptake follows.
Start early to understand the current and evolving PM market:

- Patient and test journey
- Funding flow for testing
- P&R scenarios
- Stakeholder perspectives on test:
  - Adoption and use
  - Pricing and reimbursement
  - Evidence scenarios and needs
  - Areas of challenge
- Testing logistics and tissue sampling requirements
- Develop Dx market prior to launch (e.g., for some markets this may require supporting foundations, advocacy groups, and facilitation with key opinion leaders)
- Consider multi-channel models that assist with preparing and coordinating the market around the CDx (e.g., Dx Navigator)
- Evaluate partnership resource allocation to support PM Rx given resourcing expectations and capabilities gaps (e.g., market access function area) at Dx manufacturers

7. Consider pricing and access expectations versus market realities

As a growing number of PMs enter the market, manufacturers, payers and providers are beginning to gain experience and refine expectations in this space. The extent to which the value of a identifying a Tx responder (and thus shrinking the target population) has in the past 18-24 months begun to shift towards expectations that the PM will offer significantly improved outcomes to justify anticipated price premiums. The next 5-7 years may reflect a significant realignment of expectations and “rules of the road” for PM and test the “premises of PM” mentioned earlier. This realignment must include the CDx manufacturers, large reference laboratories and reimbursement D handsome reimbursement policies as well.

As noted earlier, clinical development for Xalkori was significantly cheaper, faster and involved fewer patients compared to similar oncology drugs. However, it was also initially rejected by the NICE and the Institute for Quality and Efficiency in Healthcare (IQWiG), bringing into question personalized business models. NICE’s core rationale focuses on: insufficient cost-effectiveness (£181K/quality-adjusted life year [QALY]); the absence of CER data; progression free survival was not in mixed Tx analysis; and questions concerning Quality of Life assumptions. Those for IQWiG were the absence of sufficient CER evidence versus best supportive care, and methodological issues making interpretation difficult. These decisions also test the premise of PM and may challenge manufacturer investment in this space. If pricing opportunities do not align with smaller indications or at least more secure market positions, manufacturers may “back off of the throttle” in some key PM areas such as oncology.

These occurrences illuminate the need for sponsors to identify when expedited clearance may be a market access risk, the degree of efficacy that is currently “differentiated,” whether there is a pricing threshold for PM (specifically in the oncology Rx area), how pricing thresholds shift depending upon cost per patient and overall budget impact to find PM responders, and the implications for their PM business model.

Start early to understand the drug and the test used to address the following considerations:

- HTA evidence requirements
- Payer requirements
- Potential alternative approaches to evidence generation
- P&R scenarios
- Resource allocation geography to account for test subsidies from Rx manufacturers expected by payers

If pricing opportunities do not align with more secure market positions, manufacturers may “back off of the throttle” in some key PM areas such as oncology.
8. Planning for curve balls and future market dynamics
A variety of additional factors, including technological, clinical- and value-based, and economic, complicate development, launch, and market access planning for PMs need to be considered. It is critical to understand timeliness, impact potential, and influence on return of investment of potential curveballs. Examples of factors that may limit CDx success range from the lack of clinical pathways, reimbursement and guidelines for testing using next generation sequencing to a lack of cost effectiveness data for cell-based cancer vaccines. One historical example is that, upon the launch of Vectibix (panitumumab) as a PM for colorectal cancer, payer projections for the use of biomarker testing for Erbitux (cetuximab) resulted in new United States commercial payer policies requiring biomarker testing as a prior authorization condition within 8-12 months.17 Often these curve balls may be foreseen and prepared for. For example, biomarker development plans should include a path to an IVD if there is a possibility of a CDx test. In setting up internal PM functions, the PM team should work with functional area heads and local access leads to “horizon scan” for such curveballs, assess their likelihood of impact, and prioritize response accordingly. Ideally this can be accomplished as a routine component of evaluating commercial risks early in the clinical development program to ensure that key development potholes can be avoided.

Towards standards for PM
It is important to consider how to build the right yardstick for stakeholders, and how value components flow into addressing requirements for each of them. Various groups are beginning to discuss such standards for the field. Table 8 lists the relevant questions to ask to establish the right standards for PM developed by the Pharmaceutical Benefits Advisory Committee (PBAC) and the Medical Services Advisory Committee (MSAC).

Table 8 Sample questions that represent the multiple dimensions in PM

<table>
<thead>
<tr>
<th>PBAC/ MSAC Guidance on Assessing Codependent Technologies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimensions</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Role of biomarker</td>
</tr>
<tr>
<td>Test performance</td>
</tr>
<tr>
<td>Epidemiology</td>
</tr>
<tr>
<td>Comparative effectiveness</td>
</tr>
</tbody>
</table>
PBAC/ MSAC Guidance on Assessing Codependent Technologies

<table>
<thead>
<tr>
<th>Dimensions</th>
<th>Relevant questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient management</td>
<td>Is there direct evidence of prognostic impact associated with different biomarker status?</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Does the direct evidence provided show a clinically important and statistically significant impact on patient-relevant health outcomes?</td>
</tr>
<tr>
<td></td>
<td>Is there linked evidence available of the test’s impact on patient health outcomes?</td>
</tr>
<tr>
<td>Cost effectiveness</td>
<td>Was the positive predictive value (PPV) of the test calculated and included in the model?</td>
</tr>
<tr>
<td></td>
<td>Was the incidence of drug-related adverse events for true positives and false positives included?</td>
</tr>
</tbody>
</table>

PM and CDx value requirements

As noted earlier, PM and CDx value requirements can differ by geographic region. Drug therapies that incorporate the use of a biomarker for Tx selection have been accepted in most – but certainly not all – markets, making it clear that PM and CDx strategies by themselves are not a guarantee of success. For example, lapatinib has been accepted by certain organizations in various countries (the PBAC in Australia; the Haute Autorité de Santé (HAS) in France; Medicare and private payers in the United States) but not by NICE and Scottish Medicines Consortium in the United Kingdom.

Conclusion

Several principles guide the development of oncology CDx in an R&D setting dependent upon regulatory, commercial and technical conditions. The overall priority is that the Dx must add value and not risk to a sponsor’s drug(s) in the marketplace. While the stand-alone business value of Dx is currently limited compared with new drugs, biopharma strategies to improve drug development productivity are increasingly utilizing CDx. Second, the range of assay-driven technologies and paths to commercialization require multiple, and often novel, partnerships that must be carefully evaluated and maintained. Third, the Dx registration process is regulatory-driven and defined by current guidance and rules. Any successful CDx program must take into account these three principles. This review discusses the various aspects of the first two principles including challenges and solutions. The regulatory aspects of CDx development, testing and commercialization represent one of the most significant concerns facing biopharma and IVD manufacturers and should be addressed with regulatory experts in close communication with the appropriate regulatory agencies. Perhaps a most encouraging observation for the oncology field is the much greater level of communication and cooperation that is now occurring across the Tx, Dx and healthcare communities to bring these novel drugs and tests to patients. New CDx approaches such as patient genomic profiling and standardization of test platforms and reporting of results promises much greater test adoption, quality of testing and impact on patient outcomes.
References


References


About the authors

Brad Smith, PhD
Vice President, Center for Integrated Drug Development, Quintiles

Brad Smith currently is a Vice President of Translational Medicine within the Integrated Clinical Services Group at Quintiles. 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. In this position, he focused on new diagnostic and clinical partnerships and markets. His previous positions at Cell Signaling Technology include management of research and clinical technology development departments and laboratories. Previous to Cell Signaling Technology, Brad 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 and Master’s and Bachelor’s degrees from University of California, Santa Cruz.

Joshua Ransom, PhD
Principal Consultant, Global Market Access, Quintiles; Associate Director, Genetics, Biotech, and Emerging Medical Technology Institute, National Association of Managed Care Physicians

Joshua Ransom is a Principal Consultant in Quintiles’ Global Commercial & Market Access Strategy practice serving leading pharmaceutical, biotechnology, medical device, and life sciences companies focusing on commercial innovation and market access strategies for personalized medicines and emerging medical technologies. Josh also co-directs the Genetics, Biotech, and Emerging Medical Technology Institute within the National Association of Managed Care Physicians, an association of payers and manufacturers.

Prior to joining Quintiles, Josh was a Senior Associate with McKinsey & Company in their New Jersey office with a focus on innovation strategy and commercial strategy redesign. Josh holds a Ph.D. in Biomedical Sciences and Genetics from the University of Texas Southwestern Medical Center at Dallas in the lab of Deepak Srivastava, a B.S. in Biochemistry and a B.A. in Chemistry, both from North Carolina State University. While pursuing the Ph.D., Josh also performed research at the University of California, San Francisco / J David Gladstone Institutes. Josh has been published on the topics of clinical evidence development, value-based reimbursement, human genetics, heart development, and signal transduction in top journals such as Nature, Cell, and JBC.
About the authors

Daryl Spinner, PhD, MBA
Principal Consultant, Global Market Access, Quintiles
Daryl advises pharmaceutical, biotechnology, medical device, diagnostic and other healthcare clients on global pricing and reimbursement, market access, health economics and outcomes research strategy, health technology assessment (HTA), commercial planning, market forecasting and product valuation. His expertise in oncology includes personalized medicine and companion diagnostics, medical devices, and cellular and regenerative therapies. Daryl served on the Academy of Managed Care Pharmacy (AMCP) Formulary Submission Format Addenda Writing and Review Work Group to update the dossier format for personalized medicines and companion diagnostics, and is currently on the leadership committee of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Medical Devices and Diagnostics Special Interest Working Group focused on companion diagnostics.

Prior to joining Quintiles, Daryl was a consulting Associate Director with RTI Health Solutions. He previously spent 14 years conducting research, most recently as Research Group Leader and Lab Director at the New York State Institute for Basic Research directing programs focused on R&D of neurological disease diagnostics and therapeutics, including Alzheimer’s, Creutzfeldt-Jakob disease (CJD), and autism. Daryl received an MBA in Finance and Health Sector Management from Duke University’s Fuqua School of Business, a Ph.D. in Molecular and Cellular Pharmacology, and an honors degree in Chemistry from the State University of New York at Stony Brook.
About the authors

Eric Faulkner, MPH
Director, Global Market Access, Quintiles; Assistant Professor, Institute for Pharmacogenomics and Individualized Therapy, University of North Carolina at Chapel Hill; Executive Director, Genomics, Biotech and Emerging Medical Technology Institute, National Association of Managed Care Physicians

Eric C. Faulkner, MPH brings 17 years of experience of focus on health technology assessment, product reimbursement and commercialization, health care management, and health policy analysis for medical devices, diagnostics, and biopharmaceuticals. His prior project work has included global market strategy analysis, qualitative and quantitative research, evidence-based practice and policy, design of clinical trials to meet third-party decision requirements, life sciences portfolio due diligence, and decision support. Eric has also has led health policy assessments, including CMS’s Coverage with Evidence Development (CED) and Clinical Trial Policy, value-based purchasing, competitive bidding, cost-effectiveness, comparative effectiveness, and pharmacogenomics for life sciences manufacturers, industry and medical professional associations, and government agencies, including HHS, NIH, FDA, CDC, and ASPE.

Eric is a recognized global thought leader in personalized medicine, biopharmaceutical, medical and emerging technology market access. He has recently served as an expert advisor to the Personalized Medicine Subcommittee of the President’s Council of Advisors on Science and Technology and as an invited expert for standards setting with the Austrian government. Eric has led multiple platform setting and business transformation strategies and implementation plans for personalized medicines focusing on value communication, pricing and reimbursement, market access and commercial applications. He serves on the Leadership Committee of the HTA Special Interest Group, including the working groups on Pharmaceuticals and for Medical Devices and Diagnostics and formerly as the Chair of ISPOR’s Personalized Medicine Special Interest Group.