DISCUSSION PAPER

The Cancer Policy Environment, Barriers to Faster Oncology Innovation, and Strategies for Moving Forward

Discussion Paper prepared for the Patient Access to Cancer care Excellence (PACE) Global Council meeting on November 9, 2012, in New York City.

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Created by Lilly Oncology as a global collaboration spanning diverse sectors, PACE stands for Patient Access to Cancer care Excellence.

Progress against cancer is by nature stepwise, but with the insights and tools of today's science, it does **not** *need to be slow.*

PACE exists to encourage public policies and health care decisions that speed the development of new medicines, assure cancer treatments respond to the needs and qualities of individual patients, and improve patient access to the most effective cancer medicines.

Together and with each step, we can build momentum towards cures.

PACE Mission Statement

Health policy *refers to decisions, plans, and actions that are undertaken to achieve specific health care goals within a society.*

An explicit health policy can achieve several things: it ***defines a vision for the future*** *which in turn helps to* ***establish targets and points of reference for the short and medium term****.*

It ***outlines priorities*** *and the expected roles of different groups; and it* ***builds consensus and informs people****.*

World Health Organization definition of "Health Policy"

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Aim

This discussion paper provides PACE Global Council participants with a collection of resources in preparation for the first Council meeting on November 9, 2012, in New York City, with the goal of identifying policy changes that can help to accelerate the development and uptake of new cancer drugs.

Background and Scope

PACE pursues three "pillars" of activity. The first centers on a long-term policy agenda to bring regulatory and Health Technology Assessment (HTA) policies more in line with the scientific and medical realities of cancer, and to speed patient access to new medicines. The second seeks to increase the involvement of patients and patient groups in clinical trials and in HTA decision making. The third emphasizes the education of policymakers and opinion leaders on the nature of oncology innovation and the prospects for improved cancer care.

PACE aims to make a difference in a policy field that is wide-ranging, from scientific and logistic issues to ethical questions and health economics. A review of the literature on this subject cannot possibly be comprehensive. Although this review did not exclude insights on the holistic treatment of cancer, it did not explicitly examine forms of treatment outside of chemotherapy, such as surgery and radiotherapy. Furthermore, because PACE is focused on cancer innovation and the uptake of innovation usually happens first in developed countries, the content of this review focuses primarily on issues common to developed countries and must regrettably defer consideration of the many challenges to cancer treatment in developing nations.[1]

This discussion paper is meant to provide a rough map of the cancer policy terrain and to encourage readers to focus on common challenges regardless of geography, culture, or profession. Preliminary work was undertaken, in consultation with Lilly staff, to examine key organizations and initiatives already active in public policy related to cancer (see **Appendix 1** for a summary of the key organizations and initiatives identified). Additional insights were solicited from PACE Global Council participants, who were asked to (1) list the most important one or two barriers to the more rapid progress of cancer innovation and/or the clearer establishment of value, which need to be overcome; (2) identify organizations or initiatives already working to overcome these barriers; and (3) suggest actions or initiatives essential to overcoming these barriers in the next five years.

The paper begins with a brief description of the policy context, followed by a summary of prominent barriers encountered today in the development of innovative cancer care and treatments, several suggested concrete steps forward, and a selective overview of

[1] See, for example: Boseley S. Cancer fight stalls amid push for profits, doctors say: Newer drugs fall short of hopes and cost too much, say experts who pledge to improve care in poorer countries. *The Guardian* (October 28, 2012). http://www.guardian.co.uk/society/2012/oct/28/targeted-cancer-drugs-expectations-experts.

ongoing initiatives and resulting strategies and actions. It concludes by summarizing ideas for clinical trial reform, an issue that connects many of the more prominent barriers and initiatives highlighted throughout the review. The list of acronyms is included as **Appendix 2**.

Policy Context

The National Cancer Act of 1971, a U.S. federal law, signified the beginning of what has come to be known as the "War on Cancer." The long-term goal of this action was to eradicate cancer, while more concrete and short-term goals included increasing resources for research and prioritizing efforts against cancer.

Almost 40 years later, cancer is recognized as a global health crisis, with nearly 12.7 million new cases in 2008, about 44 percent of which occurred in more developed regions.[2] Cancer is a leading cause of death worldwide, responsible for 7.6 million deaths (13 percent of all deaths) in 2008.[3] Approximately 29 percent of cancer deaths in 2008 occurred in more developed regions,[4] and 30 percent of cancer deaths are due to the five leading behavioral and dietary risks (high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, alcohol use) and thus are considered preventable.[5] By 2030, 21 million new cancer cases are expected, representing an increase of 68 percent from 2008, and deaths from cancer worldwide are projected to be 13.1 million.[6]

Cancer mortality rates have decreased since the 1970s, although not at a pace that satisfies many physicians, researchers, or patients. The War on Cancer turned out to be much more difficult and protracted than expected. Researchers have come to realize that cancer is not one single disease and that patients respond even to advanced treatments in highly individualized ways based on their genetic profiles and disease stages. Recent advances in genomic technologies have provided researchers with unprecedented abilities to characterize tumors at the DNA level. Unfortunately, results from these studies suggest that there is not only large heterogeneity between tumors in different patients, but also heterogeneity of tumor cells within the same patient.[7]

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[2] Ferlay J, Shin HR, Bray F, Forman D, Mathers C, and Parkin DM. GLOBOCAN 2008 v2.0: Cancer Incidence and Mortality Worldwide. IARC CancerBase No. 10. Lyon, France: International Agency for Research on Cancer; 2010. http://globocan.iarc.fr (accessed August 5, 2013).

[3] Bray F, Ren JS, Masuyer E, and Ferlay J. Estimates of global cancer prevalence for 27 sites in the adult population in 2008. Int J Cancer July 3, 2012). doi: 10.1002/ijc.27711. [Epub ahead of print], as reported in World Health Organization Cancer Fact Sheet no. 297, February 2012, http://www.who.int/mediacentre/factsheets/fs297/en/index.html (accessed August 5, 2013).

[4] Ferlay et al., GLOBOCAN 2008.

[5] World Health Organization Cancer Fact Sheet no. 297, February 2012. http://www.who.int/mediacentre/factsheets/fs297/en/index.html (accessed August 5, 2013).

[6] Ferlay et al., GLOBOCAN 2008.

[7] Gerlinger M, Rowan AJ, Horswell S, Larkin J, Endesfelder D, Gronroos E, Martinez P, et al. Intratumor heterogeneity and branched evolution revealed by multiregion sequencing. *New England Journal of Medicine* 366, no. 10 (2012):883–892.

In addition to inherent biological complexities of the disease, a number of other barriers including those related to translational medicine, the drug approval process, and early detection have conspired to thwart progress in defeating cancer.

The World Cancer Declaration

In 2008, the Union for International Cancer Control (UICC) drafted the World Cancer Declaration to bring attention to the ongoing and increasing cancer crisis and reduce the global cancer burden by 2020. It describes 11 key targets supported by a worldwide community and calls on decision makers to support key actions required for a cancer-free world. As of 2012, nearly 520,000 cancer advocates have signed the declaration.

Personalized Medicine and Targeted Therapies

The realization that each tumor is unique and that each patient carries a different kind of tumor demands a paradigm shift in treatment approaches. New treatments must be tailored to fit the unique profile of each patient. Classification of cancers is shifting from an organ-based to a molecular defect-based categorization.

The new treatment approaches are accompanied by a large set of new requirements regarding clinical trial design, ethical and legal issues, health technology assessment, and health economics. Health policies must be revised in order to align with the new reality. However, this change is happening only slowly.

It can be helpful to see the relative growth in the numbers of publications per year in the area of targeted therapy, specifically related to cancer, in the health policy space over time. **Figure 1** shows results from a bibliometric survey based on publications found in PubMed over the past 20 years.

The search term "targeted therapy" was queried alone or in combination with "oncology OR cancer." The green line shows a dramatic increase over the past 20 years of publications on targeted therapies. The purple line, which shows the results when combining this search with "oncology OR cancer," illustrates that about half of the targeted therapy publications indicate that they are specifically related to cancer. Results were similar when conducting this analysis on "personalized medicine" with or without restricting the search to "oncology or cancer" (data not shown).

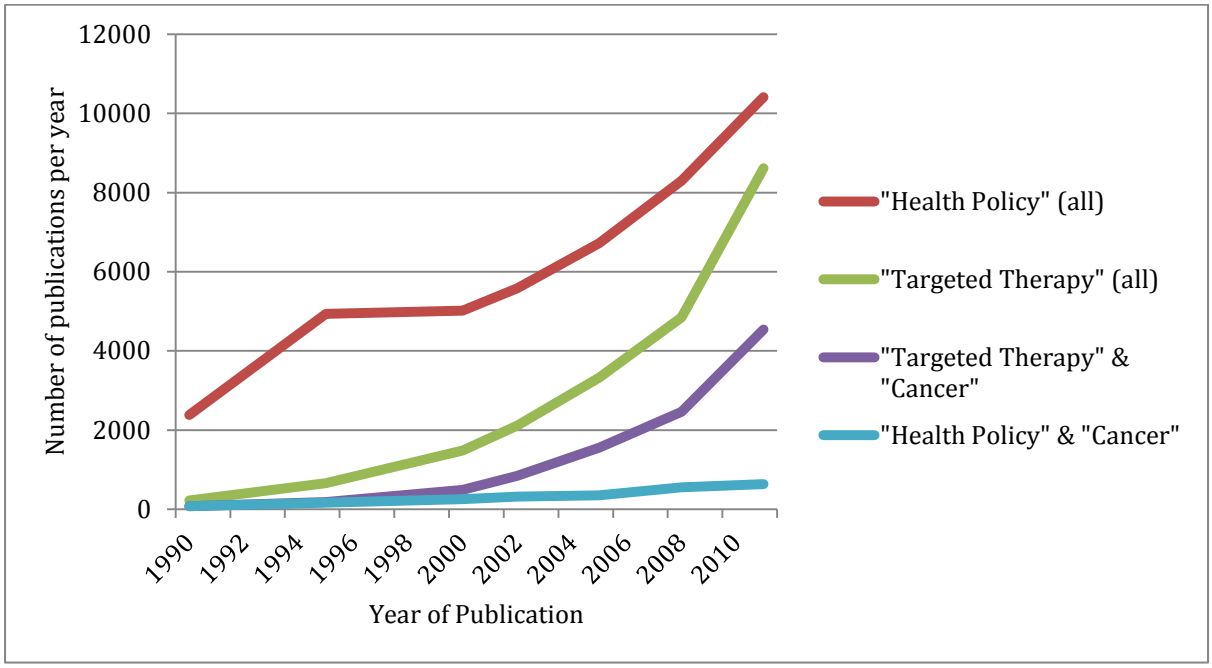
The red line illustrates a dramatic increase during the same time period in publications on "health policy" (similar results were obtained with the term "policy" alone). However, the blue line indicates that references to "cancer/oncology" ("cancer policy" and/or "oncopolicy" gave similar results) are not highly represented among these health policy publications.

There does not appear to be a simple explanation for the dramatic increase in health policy publications outside of cancer; publications related to other noncommunicable diseases (such as cardiovascular disease, diabetes) or infectious diseases also comprise only a modest subset of the total.

Thus, although there has been an increase in health policy papers during the past 20 years, this increase does not seem commensurate with the demand that the new

challenges in targeted therapies and personalized medicine have created in the cancer field.

Figure 1. Targeted Therapies and Health Policy – a Bibliometric Survey Based on PubMed



In many areas, this literature review found the policy reform needs in the field of cancer to be very closely aligned with challenges encountered for other diseases. Many of the organizations and initiatives identified herein do not restrict their efforts to any single disease entity and, most of the time, reform will likely be achieved fastest when stakeholders act across diagnostic boundaries to reach common goals.

In the realm of targeted therapies and personalized medicine, however, cancer appears to assume an extraordinary driving role that may imply a unique responsibility and mandate to take a leading position in policy reform.

The war on cancer simply cannot succeed based on policies established before the new insights on cancer. A continuing overhaul of laws, regulations, and programs governing the research, development, regulation, evaluation, and uptake of cancer treatments today is vital.

In order to create new policies, there needs to be agreement on common goals for improvements of the status quo. In order to arrive at these goals, it is helpful to first carry out an assessment regarding the most prominent barriers to the development of innovative cancer care and treatments.

Barriers to the Development and Uptake of New Cancer Drugs

A summary of previously identified barriers was developed by mining the literature, news feeds, websites, and publications by organizations and initiatives dedicated to improving cancer care (see **Appendix 1** for list of key organizations examined). Additional barriers to the development of innovative cancer care and treatments were mentioned by PACE Global Council participants.

The summary results are presented in **Table 1**, with abridged references to identified barriers. Some of the entries in this table embody several individual barriers, each with its own set of possible solutions. To help make the list easier to digest, the barriers are clustered into broad categories as follows:

- ***Leadership*** – This category includes the need for strategic leadership that sustains momentum created by current and new initiatives, achieves the proper balance of risk and reward to encourage transformative research and novel approaches, and ensures uniform access to new treatments and technologies.
- ***Scientific*** – These barriers include the challenges associated with unanswered basic scientific questions that stem from the complexity of the disease, its different forms, and its constant evolution; heterogeneity in pathophysiology and treatment effects; lack of consensus on surrogate endpoints; unnecessary duplication of effort and missed opportunities for collaboration; and unmet need for cancer health professional expertise.
- ***Technical*** – These barriers include limitations to the tools and resources needed for vital cancer research, including valid and well-defined biomarkers to predict prognosis and treatment response, sufficient quantities of high-quality biospecimens and associated data, development of effective companion diagnostics, and post-approval data collection.
- ***Logistic*** – This category includes the need for faster, smarter, and more flexible clinical trial designs; better communication with and education of consumers to encourage greater participation in clinical trials by patients; and more efficient infrastructures to ensure that all patients receive the best available treatment.
- ***Economic*** – These barriers center on the high cost of clinical trials; the need for proper financial incentives to encourage desired behaviors by patients, physicians, and drug companies that benefit society; the lack of agreement regarding what constitutes "value" in a new treatment; and the relative cost of a specific drug in the context of the entire cancer care pathway.
- ***Legal*** – These barriers include differences in assessment approaches across countries, privacy and country-specific laws that inhibit research, and lack of consistent regulatory agency guidance where needed.
- ***Cultural*** – These barriers include different values (and thus priorities) across cultures, organizations, and countries, placed for example on the importance of the patient perspective, the types of cancer care emphasized, equal access to new treatments, and the encouragement of innovation.

Table 1. Barriers to the Development and Uptake of New Cancer Drugs

Category	Subcategory	Title/ Description of the Barrier	Organizations* (examples)	Council Participant(s)
Leadership	Strategy	Lack of strategic leadership for cancer innovation, i.e., no comprehensive plan, coordination, mapping, bridging	C-Change, C-Path, FasterCures, PMC	❇
	Risk/Reward	Risk-averse funding entities, effectively discouraging transformative research		❇
	Risk/Reward	Pharma companies risk-averse in picking up ideas on novel approaches, either from scientists directly or from biotech start-ups	FasterCures	❇
	Governance	Lack of efforts at the national and international level to ensure uniform uptake of existing treatments and technologies (aka "post code lottery")	NCRI, RCF	
Scientific	Complexity	"Cancer" not a single disease but hundreds of diseases undergoing constant evolution	ASCO	
	Complexity	Heterogeneity in pathophysiology and treatment effects, and challenge of identifying molecular targets/pathways with limited adverse effects		
	Outcome Measures	Lack of consensus on surrogate endpoints		
	Expectations	Failure to understand the natural incremental and cumulative nature of oncology developments		❇
	Collaboration	Competitive grant mechanisms inhibit collaborative efforts	ASCO	
	Collaboration	Widespread duplication of efforts	ASCO, EUnetHTA, ICH, INAHTA, PMC	
	Care	The demand for cancer services is projected to exceed the current supply and/or expertise of cancer health professionals	C-Change, ECPC	❇
Technical	Biomarkers	Lack of valid and well-defined biomarkers to predict prognosis and treatment response, and lack of accompanying regulatory agency guidance	ASCO, Oncotyrol	

Table 1. Barriers to the Development and Uptake of New Cancer Drugs (Cont'd)

Category	Subcategory	Title/ Description of the Barrier	Organizations* (examples)	Council Participant(s)
	Biospecimens	Lack of sufficient quantities of high-quality, optimally preserved tissue on which to do vital research	FasterCures	❇
	Data	No widely used system to make Electronic Health Records (EHRs) available for research	ASCO	
	Data	Lack of rapid assessment of response rates and duration of response in the clinic		❇
	Data	Lack of comparative effectiveness trials for approved medications		❇
	Diagnostics	Challenges in developing effective companion diagnostics including assessment, regulation, reimbursement, etc.	ASCO	❇
	Context	Lack of understanding of drug therapies within the entire process of cancer care		❇
Logistic	Clinical Trials	Clinical trials take too long and focus too much on survival	ASCO, GPC	❇
	Clinical Trials	Need faster, smarter, more flexible clinical trial designs	ASCO, GPC	❇
	Clinical Trials	Decisions on products via clinical trial mechanisms are too slow; need to accelerate accrual and timeline for go/no go decisions	IOM	❇
	Communication	Many patients are completely unaware of opportunities to take part in clinical trials	ASCO, EURORDIS	
	Collaboration	The needs of biotech start-up/spin-off companies, which make important contributions to drug and assay development, are neglected	C-Path, IMI	
	HTA	Working internationally, companies are required to develop multiple dossiers and employ multiple analytical approaches	EUnetHTA, FasterCures, GPC, HTAi	
	Infrastructure	Patients may not receive the best available treatment unless referred to a "center of excellence"	PCRI	❇
	Education	Patients and physicians lack sufficient knowledge about personal medicine and targeted therapies	EAPM	

Table 1. Barriers to the Development and Uptake of New Cancer Drugs (Cont'd)

Category	Subcategory	Title/ Description of the Barrier	Organizations* (examples)	Council Participant(s)
	Patient Access	Phase 3 trial requirements are too stringent and restrict patient access to potential treatment options	EAPM, GPC, IOM, PhRMA, Project FDA	❇
Economic	Clinical Trials	Clinical trials are too expensive		❇
	Clinical Trials	Patients not financially incentivized to participate in clinical trials	FasterCures	❇
	Collaboration	Physicians in local clinics no longer willing/able to absorb the costs of running cooperative group trials		❇
	Collaboration	Essentially no financial incentives exist for drug companies to test combination therapies	ASCO	
	Value	Lack of consensus around what constitutes "value" in a new treatment	ASCO, HTAi	❇ ❇ ❇ ❇
	Value	Unaffordable cost of new drugs; lack of transparency about how the price of a drug is calculated		❇
	Value	Failure to understand the whole cost of a cancer care pathway and the relative cost of a specific drug		❇
	HTA	Different economic measures are applied in different countries, leading to inconsistent results	EUnetHTA, OECD	
Legal	Clinical Trials	Lack (or inconsistency) of regulatory agency guidance on biomarkers and endpoints for clinical trials	ASCO	
	Collaboration	Complex rules for clinical trials make it difficult to collaborate on combination treatments		
	HTA	Assessment methods vary widely between countries, making it difficult for companies to act across borders	EPF	❇
	Privacy	Laws such as the Health Insurance Portability and Accountability Act (HIPAA) protect privacy but inhibit research.	C-Change	
Cultural	Value	Prevention, early detection, and palliative care are valued differently in different countries and by different organizations	C-Change	

Table 1. Barriers to the Development and Uptake of New Cancer Drugs (Cont'd)

Category	Subcategory	Title/ Description of the Barrier	Organizations* (examples)	Council Participant(s)
	Patient Perspective	Patient needs and preferences ignored	EPF	❊ ❊ ❊
	Patient Perspective	Paternalistic/hierarchical doctor-patient relationship fails to value patient/citizen involvement in treatment decisions		❊
	Disparities	There is discordance between the development of efficacious prevention and treatment options established through cancer research and the delivery of this care to all population groups	Brookings, C-Change, CRCHD	
	Attitudes	Governments do not sufficiently value innovation or foster a "can do" culture		❊

* See **Appendix 1** for a brief description of key organizations and their goals/approach and links to major initiatives.

Concrete Steps Forward – PACE Global Council Input

PACE aims to seek consensus among the Council participants on a small set of policy-reform goals achievable in the next three to five years that would have a positive impact on the development and uptake of innovative cancer drugs. The point of this exercise is not to suggest that PACE or the Council participants would achieve these goals in and of themselves. Instead, the power of a set of consensus goals would be (a) to demonstrate that significant cross-sector agreement exists; (b) to provide a rudimentary roadmap to opinion leaders and the public as a basis for debate and action; and (c) to clarify priorities for PACE and its partners on how they could help to advance these goals even if they cannot achieve them alone.

Table 2 presents a compilation of the potential solutions offered by PACE Global Council participants to overcome a number of identified barriers in the next five years. These suggestions are organized where possible using the categorization presented in **Table 1**.

The primary reason for the existence of some identified barriers appears to be simple inertia or lack of resources. However, a few barriers are associated with no clear agreement about the best way forward. For example, the absence of active patient involvement in setting research priorities might be seen by some stakeholders as a barrier because they value the unique perspective offered by patient advocates, while others might prefer to limit the influence of patient advocates because they see such input as uninformed with respect to the scientific evidence.

Table 2. Potential Solutions Identified by Council Participants

Barrier Category	Subcategory	Potential Solution(s)	Council Participant(s)
Leadership	Strategy	▪ Create multi-stakeholder forum including patients/citizens and develop concrete policy proposal ▪ Promote dialogue between clinicians, public health entities, patient associations, and companies to get a better sense of priorities	❇ ❇
	Risk/Reward	▪ Learn from NCI's Provocative Questions Initiative ▪ Establish fund for "high-risk" pilot projects ▪ Encourage serendipitous studies ▪ Ban research funding to investigators aged 30+	❇
Scientific	Value	▪ Support research to define the "utility" for patients of treatments that can be built into or supplement cost-effectiveness calculations	❇ ❇
	Care	▪ Develop information that is more health care system based (better understanding of drugs within the process of care)	❇
Technical	Data	▪ Require mandatory clinical data reporting or release of tumor registry data ▪ Utilize databases (such as that at UnitedHealthcare) and registries that potentially allow for observational comparative effectiveness evaluations ▪ Increase number of comparative studies and subgroup analyses ▪ Learn from ASCO rapid learning system	❇ ❇
Logistic	Clinical Trials	▪ Better establish research networks based on defined "centers of excellence" to make recruitment into clinical trials much easier for which the numbers of patients are small ▪ Develop nimble incubators for go/no go decisions on therapeutic targets and drug development ▪ Properly incentivize physicians to enroll patients in trials and reimburse doctors/clinics for their efforts ▪ Properly incentivize patients to participate in trials	❇ ❇
Economic	Value	▪ Increase international collaboration among stakeholders to define value and innovation ▪ Increase cross-training among decision makers at different levels of health care	❇ ❇ ❇ ❇ ❇ ❇

Table 2. Potential Solutions Identified by Council Participants (Cont'd)

Barrier Category	Subcategory	Potential Solution(s)	Council Participant(s)
		(to better understand each other's criteria for valuing innovations) ▪ Involve patients' perspectives in cost/efficacy equation ▪ Improve understanding of the costs of different elements of the whole patient "journey" from first symptom, through referral to specialist care, treatment, and survivorship, to terminal and palliative care; develop modeling devices to assess the impact of interventions at various stages to facilitate the cost-benefit analyses of new technologies by funders ▪ Establish an independent nonpartisan "Institute of Regulatory Pharmaceutical Science" that provides quantitative estimates of the full costs and benefits of proposed reforms but also considers nonfinancial costs and benefits ▪ Call on journal editors to encourage reporting of patient-reported outcomes	
Legal	Clinical Trials	▪ Develop more accommodating regulatory pathways that can keep pace with advances in cancer innovation and the expectations of patients	❇
Cultural	Patient Perspective	▪ Increase the "shared treatment decision making" of the patient with his/her doctor ▪ Improve monitoring (audit) of the local-regional uptake of new technologies to expose gaps (empowers charities and patient groups where to press for better standards)	❇ ❇
	Patient Engagement	▪ Introduce procedures/tools for patient engagement ▪ Provide information, reports, and research results on patient/citizen early involvement in cancer innovation ▪ Improve patient advocacy in personalized medicine to ensure access to the best care for every cancer patient ▪ Involve patient cancer organizations to empower the public discussion in each country ▪ Train patients to involve them in cancer innovation debate, assessment, and clinical trials ▪ Provide ethical information in a rigorous and understandable way	❇ ❇ ❇

Concrete Steps Forward – External Examples

Table 3 highlights a number of concrete examples of initiatives that have emerged from existing groups whose goals align with those of PACE. These data are presented as a resource for the Council in assessing what might be considered "feasible goals" as part of a PACE action plan. Included are examples of both national and international initiatives, both completed and ongoing projects, and efforts addressing both the broad field of oncology and specific cancer types. An effort was made to link the examples to barriers identified in **Table 1**.

The list is in no way comprehensive. As noted above, this discussion paper focuses on the development and uptake of pharmacological therapies, and its emphasis on innovations in cancer treatment and care naturally favors examples from developed countries. Although many activities were excluded that appeared to center on organizational or structural goals (i.e., establish a robust member community), are aspirational rather than specific, or otherwise are too general to meet the description of a "concrete step," they can be found in the fuller list of organizations and general descriptions included in **Appendix 1**.

Table 3. Examples of Concrete Steps Being Undertaken by Other Organizations

Category	Subcategory	Description	Organization
Leadership	Strategy	Under the *Recalcitrant Cancer Research Act*, drafted by the Pancreatic Cancer Action Network (PanCAN), the U.S. National Cancer Institute (NCI) will identify promising scientific advances, assess the sufficiency of qualified researchers working in relevant specialties, outline a plan to coordinate research, and include recommendations to advance research, including appropriate benchmarks for measuring progress. The legislation is a measured and balanced approach that complements ongoing research efforts at the NCI. The bill gives the NCI significant discretion to follow the best science, while encouraging the NCI to rigorously evaluate how existing efforts are, and are not, supporting progress in the prevention, detection, diagnosis, and treatment of recalcitrant cancers.	PanCAN
	Risk/Reward	The Moon Shots Program (to launch in February 2013) focuses teams that will demonstrate short-term improvement and major, long-range impact for their specific cancers across the spectrum—cancer prevention, early detection, treatment, and survival. Each Moon Shot team will receive funding and other resources needed for ambitious and innovative research ideas, prioritized for patient impact, ranging from basic research and biomarker-driven clinical trials to behavioral interventions and public policy initiatives.	MD Anderson
	Collaboration	Ten leading biopharmaceutical companies have formed a nonprofit organization to accelerate the development of new medicines. The largest ever initiative of its kind, TransCelerate, was launched to identify and solve common drug development challenges with the end goals of improving the quality of clinical studies and bringing new medicines to patients faster. Each of the founding companies will combine financial and other resources, including personnel, to solve industry-wide challenges in a collaborative environment.	TransCelerate BioPharma Inc.
Scientific	Collaboration	To facilitate sharing of information about decisions relating to Access with Evidence Generation, a web-based toolkit has been created that consists of structured questionnaires and a database for obtaining and storing information. These can be used by HTA organizations to inquire about ongoing work or to share existing work. It provides information about the level of diffusion of the technology in different health care systems, the status of any health technology assessment (HTA), monitoring	EUnetHTA

Table 3. Examples of Concrete Steps Being Undertaken by Other Organizations (Cont'd)

Category	Subcategory	Description	Organization
		actions including protocols, and results and use of new evidence for a final reimbursement/coverage decision.	
	Care	To define and pursue a coordinated national strategy for ensuring the capacity and skills of the cancer workforce, C-Change will host the 2013 "Careforce" Summit and summarize the findings and identify unique actions for C-Change and others to take. Progress Report (August 31, 2012)	C-Change
Technical	Biomarkers	Tumor characterization and individual biomarkers become standard, and companion diagnostics are eventually required to be paired with new targeted therapies for clinical and economic purposes.	Oncotyrol
	Data; Biospecimens	The American Society of Clinical Oncology (ASCO) is working with health information technology (HIT) developers and other partners to develop a rapid learning system for cancer care. This innovative system will harness cutting-edge information technology to connect cancer patients and their health care providers to a central knowledge base; collect and synthesize information from millions of physician and patient experiences in a secure environment; and provide an unparalleled, high-quality dataset for researchers to track the real-world outcomes of cancer therapy and identify new ideas for research. Data obtained from biospecimens will be electronically linked in a secure environment to patients' clinical information, allowing physicians to easily explore relationships between the molecular characteristics of a patient and their cancer, in order to choose the best treatment as well as identify the most promising clinical trial opportunities.	ASCO
	Diagnostics; Collaboration	ASCO will collaborate with partners at the NCI and the Institute of Medicine (IOM) to convene a working group with industry, academia, and other federal agencies to develop recommendations and a strategy to create a clear pathway for regulatory review and oversight of diagnostic tests that relate to use of biomarkers and therapies.	ASCO, NIH, IOM
Logistic	Clinical Trials; HTA	GPC will "produce prototype 'evidence guidance documents' which will provide therapeutic-area specific trial design recommendation, as well as general methodological advice that can be applied across therapeutic areas. The purpose of this guidance is to reduce the uncertainty currently faced by the life sciences industry regarding the evidentiary preferences of HTA and coverage bodies, to improve the relevance of clinical research, and to improve patient access to useful innovations."	GPC

Table 3. Examples of Concrete Steps Being Undertaken by Other Organizations (Cont'd)

Category	Subcategory	Description	Organization
	Clinical Trials	Since FY2007, the Japan Medical Association Center for Clinical Trials (JMACCT) has implemented a 5 Yearly Clinical Trial Activation Plan including: ▪ Promotion of cooperation among core research centers and major trial institutions ▪ Development and promotion of standardized forms to reduce the paperwork burden on industry and improve clinical trial efficiency ▪ Cooperation between core research centers/major trial institutions and clinical trials networks ▪ Support for necessary training (including changes of relevant laws and regulations) conducted by medical institutions	JMACCT
Logistic	Clinical Trials; Collaboration	ASCO will bring together government agencies, academia, and public and private trial sponsors to develop shared standards for new and flexible trial designs that allow researchers to achieve results efficiently with smaller, molecularly defined sub-populations of patients. These new trial design standards should promote the use of surrogate study endpoints that represent meaningful measures of benefit to patients and will require less time to achieve.	ASCO
	Communication	EURORDIS promotes, networks, trains, and advocates on behalf of Rare Disease Help Line Services. The website includes a full listing and cartography of existing services around Europe.	EURORDIS
	Collaboration	By pooling competencies and resources from the public and the private domain, the Innovative Medicines Initiative (IMI) will harness the know-how and expertise available across Europe's biopharmaceutical sector, making Europe more attractive for pharmaceutical R&D investments and boosting the competitiveness of European life science R&D. By directly addressing the challenges facing the pharmaceutical sector in Europe, IMI has the potential to enhance Europe's economy by strengthening the competitive position of smaller companies, enabling them to collaborate with a multitude of stakeholders.	IMI
	Education	The European Alliance for Personalised Medicine (EAPM) issued a call on March 27, 2012, for the European Commission, the European Parliament, and European Union (EU) member states. The Alliance's Call to Action sets out five key calls to policymakers, politicians, and regulators in the European Union including improving the education and training of health care professionals.	ECPC

Table 3. Examples of Concrete Steps Being Undertaken by Other Organizations (Cont'd)

Category	Subcategory	Description	Organization
		1. Ensure a regulatory environment that allows early patient access to novel and efficacious personalized medicine 2. Increase research and development for personalized medicine 3. Improve the education and training of health care professionals 4. Acknowledge new approaches to reimbursement and HTA, which are required for patient access to personalized medicine and its value to be recognized 5. Increase awareness and understanding of personalized medicine	
	HTA	The Organisation for Economic Co-operation and Development (OECD) is expanding work in the cross-national analysis of the quality of cancer care performance. The first phase, involving the development of a conceptual framework model and macro-level analysis based on readily available Health Care Quality Indicators (HCQI) and OECD Health Data, was completed in June 2009. The 2010-2011 work plan includes additional data collection for the second phase through the recently established OECD network of national cancer experts. The aim is to explain cross-country variation in outcomes by national governance and financing of cancer care.	OECD
Cultural	Clinical Trials	Under the leadership of the Patients Helping Doctors Center, *FasterCures* will cultivate a culture of participation in clinical research by: ▪ Creating a national Web-based registry of individuals willing to participate in clinical trials ▪ Orchestrating a major public relations effort to highlight the critical role patients play in the search for cures and to give them the information they need to get involved ▪ Partnering with community physicians to educate them about clinical trials, develop new incentives for their participation, and create "mini-CROs [clinical research organizations]" to ease their administrative burden ▪ Institutionalizing methods for making research protocols more patient-centered, such as revamping the informed consent process See: Clinical Trials Recruitment and Retention: Best Practices and Promising Approaches	FasterCures

Note: See **Appendix 1** for brief descriptions of key organizations referenced in this Table and links to major initiatives.

Clinical Trial Reform

During the course of this literature review and when analyzing the responses submitted by Council participants, no other issue emerged as frequently as the need to reform the current clinical trial system. This issue has been assigned a high priority by essentially all stakeholders interested in the development of innovative cancer care and treatments. The PACE Global Council must operate in the context of political, legislative, and scientific developments worldwide. There will be many opportunities for the Council participants to interact and collaborate on a large number of existing initiatives to improve the clinical trial process on a global scale and to accelerate the development of innovative cancer care and treatments. Therefore, this issue deserves a separate chapter in this review, which aims at briefly outlining the background, while focusing on current problems and controversies.

Council participants identified essentially three main problems with clinical trials today:

- cost
- ultimate relevance to medical practice
- Participation

These three problems are discussed in further detail below, along with background information regarding their current political context.

Several organizations have published concrete suggestions for necessary reforms. This review references several examples from the *ASCO Blueprint*[8] to provide guidance on concrete steps that have already been suggested. The formation of a nonprofit company by ten top pharmaceutical companies in the United States and Europe to accelerate the development of new drugs and cut costs is an exciting development in the clinical trials field.[9] Their goal is to create an infrastructure by establishing a single portal for all clinical investigators to use for all clinical studies, as well as a common language and standards aimed at increasing efficiency and cutting errors. Membership in TransCelerate is open to all pharmaceutical and biotechnology companies, with cost of membership based on how much a company spends on research and development.

The examples provided herein are meant to serve as starting points in Council discussions and in no way imply that the participants are required to endorse any or all of these suggestions; neither do they indicate any preference over solutions proposed by other organizations.

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[8]The ASCO Blueprint can be downloaded from http://www.asco.org/ASCOv2/Department%20Content/Cancer%20Policy%20and%20Clinical%20Affairs/Downloads/Blueprint.pdf.

[9] See: Wall JK. Group aims to cut costs of late-stage drugs. *Indianapolis Business Journal* (September 24, 2012), http://www.ibj.com/group-aims-to-cut-costs-of-late-stage-drugs/PARAMS/article/36866; Sherman D. Top pharma cos form nonprofit to speed drug development. Reuters (September 19, 2012), http://in.reuters.com/article/2012/09/19/biopharma-nonprofit-idINDEE88I0D420120919.

Cost

Clinical trials have become far too expensive. Numerous causes have been identified for this problem, some of the most prominent of which are

- lack of harmonization of rules leading to duplication of efforts and waste of resources
- rigid trial designs
- insurance costs

Harmonization

Ongoing and future efforts to harmonize the drug testing and approval process should seek to minimize duplication of efforts and the current waste of resources.

Skepticism toward international harmonization efforts is usually based on the notion that harmonization must lead to reduced autonomy and ignore important cultural differences. The success of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), which has established guidelines and harmonized drug approval processes in the United States, Europe, and Japan, however, suggests that harmonization is feasible.

While some stakeholders focus on eliminating the differences in regulations between different countries, others have suggested starting by setting an achievable goal first by creating resources that would allow trial sponsors to get a better overview of the specific rules and regulations that apply in each country.

After an assessment of current differences, common goals need to be identified. Furthermore, there needs to be a temporal alignment of efforts, because country- or region-specific regulations are often carried out in cycles, and knowledge about the timing and goals of these cycles will help to align international harmonization efforts.

This review cannot possibly provide a comprehensive analysis of ongoing legislative and political developments that need to be taken into account, but instead lists a few examples of important current events that may provide a starting point to align international efforts and integrate new policy ideas developed by the Council.

Europe

Since 2001, the requirements for the conduct of clinical trials in the EU are provided for in the "*Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.*"

The Clinical Trials Directive has since been modified by the "*Commission Directive 2005/28/EC laying down principles and detailed guidelines for good clinical practice as regards investigational medicinal products for human use, as well as the requirements for authorisation of the manufacturing or importation of such products.*"

Clinical trials performed in the European Union must be conducted in accordance with the Clinical Trials Directive. However, being only a Directive and not a Regulation, each member of the Union is allowed to implement it in the framework of country-specific legislation.

Clinical trials conducted outside the European Union, but submitted in an application for marketing authorization in the European Union, have to follow principles that are equivalent to the provisions of the Clinical Trials Directive (cf. Annex I, point 8 of the *"Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use*").

While the ambition of the Clinical Trial Directive was high, the results have generally been considered less than optimal. The European health commissioner John Dalli stated on July 17, 2012, that there has been a 25 percent decrease in the number of clinical trials conducted in Europe between 2007 and 2011.[10] The average delay for launching a clinical trial has increased by 90 percent to 152 days.

In 2011, the OECD Global Science Forum launched a "*Working Group to Facilitate International Co-operation in Non-Commercial Clinical Trials*." This group carried out a survey analysis to identify the hurdles encountered by the clinical research community in setting up international clinical trials. The resulting report identified three main challenges (administrative hurdles, risk management, and education) and proposed a series of policy recommendations aimed at overcoming the main difficulties.

In July 2012, the European Commission unveiled its plan to implement a regulation that is hoped to constitute a major leap forward in the harmonization of clinical trials across Europe. Drafted as a regulation rather than a directive, it will be immediately binding for all member states with much less room for country-specific interpretation. Once in place, it will repeal the Clinical Trial Directive. But before this can happen, the draft has to be approved by the member states' governments and the European Parliament.

The adoption of this "*Proposal for a Regulation of the European Parliament and of the Council on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC"* (referred to as the "Clinical Trials Regulation") was announced in a press release in July 2012 and is supported by a companion questions and answers document. In addition, a citizen summary has been made available.

Input from stakeholders is currently sought, and the regulation is expected to be finalized in 2014 and implemented in 2016. Needless to say, many stakeholders are concerned about the slow speed of this reform.

Japan

Reform of the clinical trial system also has been a priority for the Japanese government and stakeholders during recent years. The JMACCT, an organization within the Japan Medical Association, is currently conducting the "Large Scale Clinical Trial Network

[10] Cressey, D. Europe sets out to reform its clinical trial rules. *Nature Reviews Drug Discovery* 11, no. 9 (August 31, 2012): 660–661. http://www.nature.com/nrd/journal/v11/n9/full/nrd3843.html.

Project," a clinical trial promotion program subsidized by the Ministry of Health, Labour and Welfare (MHLW).

A five-year clinical trial activation plan, developed jointly by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and MHLW, has been implemented since FY2007. The goals of this plan are as follows:

- promotion of cooperation among core research centers and major trial institutions
- standardization of forms
- cooperation between core research centers/major trial institutions and clinical trials networks
- support for training conducted by core research centers and major trial institutions

Further information can be found in a recently developed brochure.

United States

In the United States, regulations to protect human research subjects (usually referred to as the "Common Rule") have been in place since 1991. In 2011, the U.S. Department of Health and Human Services (HHS) announced that the Federal government is considering several changes to the Common Rule. These changes are summarized in an Advanced Notice of Proposed Rulemaking (ANPRM). Of relevance to the current discussion of harmonization efforts is the suggestion to implement a single Institutional Review Board for all domestic sites of multi-site studies under the revised rule. Comments have been sought from all stakeholders, but no information has been released yet regarding if and when the new regulations may become law.

Another opportunity to harmonize regulations surrounding the conduct of clinical trials is during the revision cycles of the Prescription Drug User Fee Act (PDUFA), the current version of which (PDUFA V) specifically provides opportunities for continuous engagement and assessment by all stakeholders. The next reauthorization is scheduled for 2017.[11] Pharmaceutical Research and Manufacturers of America (PhRMA) and the Biotechnology Industry Organization (BIO), which represent respectively the country's leading pharmaceutical industry research and biotechnology companies, have recently expressed their strong support to implement the current regulations and to work toward implementation of a 21st century regulatory system by the next reauthorization.[12]

[11] http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm272170.htm (accessed October 21, 2012).

[12] PhRMA and BIO's joint October 1, 2012. statement can be found at: http://www.phrma.org/media/releases/pdufa-v-sets-new-course-regulatory-science-joint-biophrma-statement (accessed October 21, 2012).

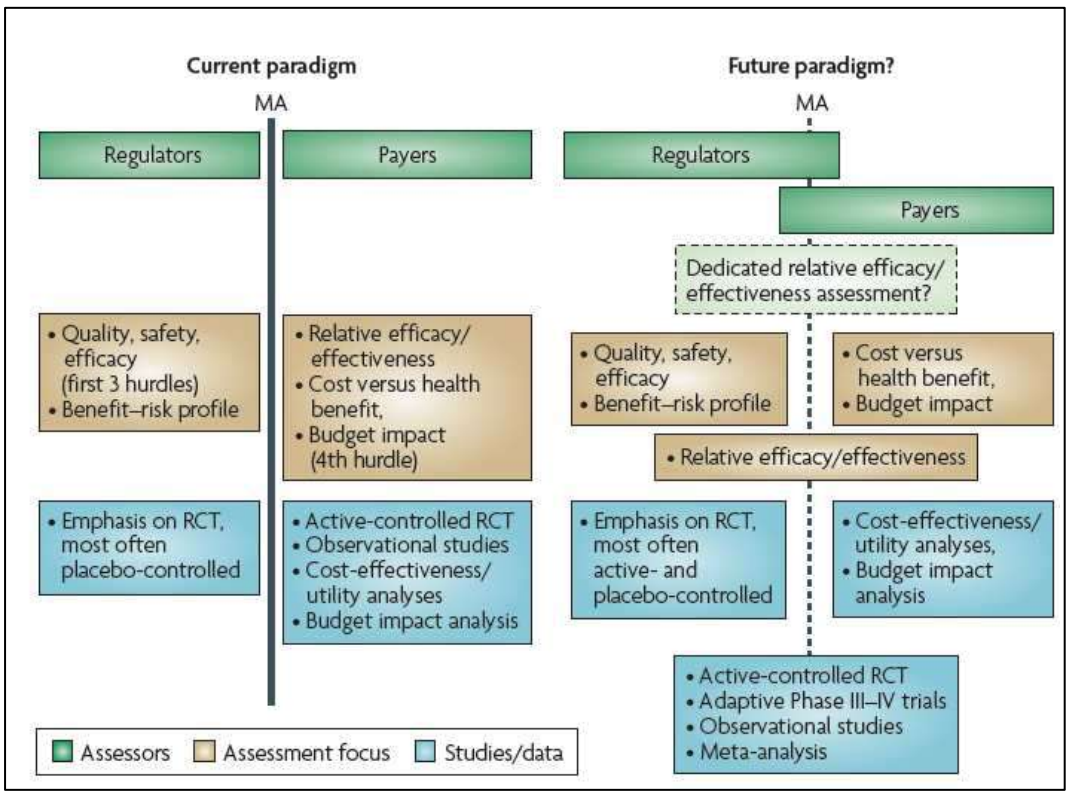
Rigid Clinical Trial Designs

Traditional clinical trial designs that recruit large cohorts of individuals and use survival as the main outcome variable are not well suited as measurement tools for new, targeted therapies in the age of personalized medicine.

Smaller trials on pre-selected patient populations, possibly employing a companion diagnostic, are becoming more common. Adaptive trial designs are another attempt at shortening the duration of clinical trials while preserving power and type II error rate.

A third, predicted evolution of the trials[13] is shown in **Figure 2.** According to this model, the current strict border between pre- and postmarket approval is likely to soften, and the future is likely to see increased interaction between regulators and payers in the assessment of relative efficacy. The model shown here contains many design elements found across different models and has been included as one example of how the clinical trial system may evolve in the future. Whether or not this development is desirable and feasible is open to discussion.

Figure 2. Clinical Trial Design Reform



Note: RCT: Randomized Controlled Trial; MA: Market Authorization.
Source: Eichler H-G, Bloechi-Daum B, Abadie E, Barnett D, Konig F, and Pearson S. Relative efficacy of drugs: An emerging issue between regulatory agencies and third-party payers. *Nature Reviews: Drug Discovery* 9, no. 4 (April 2010):277–291.

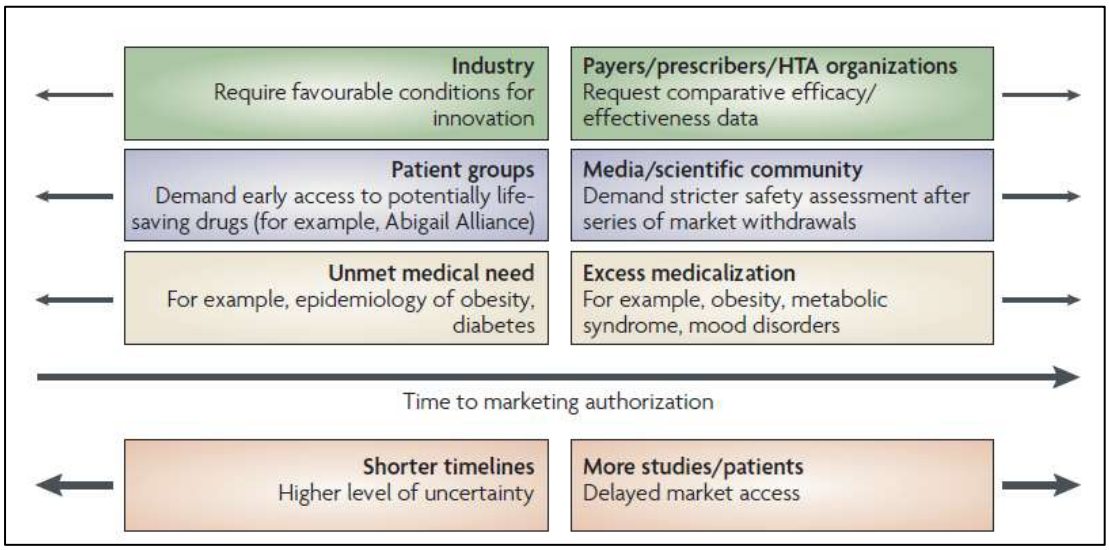
[13] Eichler H-G, Bloechi-Daum B, Abadie E, Barnett D, Konig F, and Pearson S. Relative efficacy of drugs: An emerging issue between regulatory agencies and third-party payers. *Nature Reviews: Drug Discovery* 9, no. 4 (April 2010):277–291.

Along these lines, the ASCO blueprint contains several specific goals for accelerated, modern trial designs:

- *Ensure more aggressive and timely development of biomarkers and diagnostic tests to guide treatment decisions and speed research.*
- *Develop shared standards for flexible trial designs that allow researchers to demonstrate results with smaller populations defined by specific molecular characteristics.*
- *Select trial participants primarily based on molecular characteristics, to ensure that only those who are most likely to benefit are included and that patients aren't excluded from trials because of health conditions that aren't relevant.*
- *Revitalize the National Cancer Institute's Clinical Trials Cooperative Group Program, which has been instrumental in much of the progress achieved against cancer to date. ASCO supports the continued efforts by the NCI, the Groups, and other stakeholders to fully implement recommendations issued by the Institute of Medicine in 2010 to revitalize this essential component of the nation's cancer research system.*

Traditionally, industry and payers have been viewed as opposing forces with regard to drug development timelines (see green boxes in **Figure 3**). It is, therefore, remarkable that during the preparation of this literature review, Josef Hecken, the chairman of the German Federal Joint Committee (GBA), the highest decision-making body of the joint self-government of physicians, dentists, hospitals, and health insurance funds in Germany, stated in an interview that he wants to seek an intensive dialogue with drug manufacturers to develop new strategies for drug development in personalized medicine. This indicates that the traditional roles may dissolve when the common goal of finding better, personalized treatment strategies, is at stake.

Figure 3. Traditional Opposing Forces Regarding Drug Development Timelines



Source: Eichler H-G, Pignatti F, Flamion B, Leufkens H, and Breckenridge A. Balancing early market access to new drugs with the need for benefit/risk data: A mounting dilemma. *Nature Reviews. Drug Discovery* 7, no. 10 (October 2008): 818–826.

Rising Insurance Costs

Directive 2001/20/EC introduced a mandatory insurance/indemnity. This has substantially increased the costs and administrative burden for the clinical trial sponsor. Since its implementation, insurance fees have increased by 800% for industry sponsors, while there is no evidence that the number of damages has increased during the same time period. Under the proposed new EU Regulation, member states will be obliged to set up a national indemnification mechanism on a not-for-profit basis. The question of insurance coverage also is related to more general issues of risk assessment and classification, revision of which may decrease administrative burdens, if ethically justifiable.

International companies conducting trials in European countries must, furthermore, take into account that each country will impose individual thresholds for the insurance amounts.[14]

While clinical trial insurance is not mandatory in the United States, sponsors will usually purchase insurance in order to meet requirements by participating hospitals.

In Japan, sponsors are held responsible for ensuring that adequate insurance and other necessary arrangements are in place as required by Good Clinical Practice (GCP).[15] JMACCT, in cooperation with an insurance company, has developed an insurance package for the investigator-initiated clinical trials conducted under the Large Scale Clinical Trial Network Project to provide compensation to study participants in the chance that any negative side effects are encountered. The investigators of all clinical trials funded through JMACCT's grant scheme are included in JMACCT's insurance policy. In these cases, the insurance costs are covered by JMACCT.

Ultimate Relevance to Medical Practice

What constitutes value and the importance of taking patient-reported outcomes into account has recently been discussed in a highly cited Perspective article in the *New England Journal of Medicine*: "There is more to life than death."[16]

At the same time, not all clinical trials lead to significant improvement of cancer care, and "me, too" trials and trials based on economic value rather than improved quality of life are too common. Council participants noted that current trials have a too narrow focus on survival as opposed to other outcomes valued by patients.

Concrete recommendations regarding prioritization goals for the future can be controversial given lack of consensus about what constitutes a target with the greatest promise.

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[14] http://www.mastercontrol.com/newsletter/conducting-clinical-trial-europe-from-us-perspective.html; http://www.chubb.com/journalists/chubb10064.pdf .

[15] http://www.jmacct.med.or.jp/english/whatwedo/investigator/insurance.html.

[16] Hartzband P and Groopman J. There is more to life than death. *The New England Journal of Medicine* 367(September 13, 2012):987-989.

In contrast, trials for combination therapies are scarce but would be highly valuable to practice and yet are not adequately incentivized and not necessarily encouraged by regulators.

Thus, once stakeholders have reached an agreement regarding prioritized treatments, testing of combinations of these treatments needs to be incentivized, as highlighted in the *ASCO Blueprint*: Incentivize collaboration to encourage industry and researchers to pursue high-priority targeted therapies and diagnostics in combination.

Participation

Far too few patients participate in clinical trials. This is likely due to a number of factors, such as

- extensive exclusion criteria, designed to maximize effect sizes
- lack of knowledge about available trials
- lack of access to ongoing trials
- lack of incentives to participate in trials (e.g., financial compensation)
- failure of physicians to explain clinical trials in terms that the patient can understand[17]

The lack of participation is further aggravated by inefficient use of HIT tools, such as electronic health records (EHRs). More efficient use of these tools will allow physicians and scientists to access valuable and sometimes critical information about available candidates for clinical trials. Furthermore, in silico computer-based studies can be conducted using already available information to help inform go/no-go decisions, making the clinical trial process faster and less costly overall. These studies require no additional consent or interaction with the clinical trial participant, provided sufficiently broad consent was obtained during the original consenting process for this purpose.

The ASCO Blueprint summarizes several of these ideas, as follows:

- *Use HIT tools, including EHRs and "rapid learning" systems, to allow researchers to draw upon the wealth of real-world patient information that is now locked away in file cabinets and unconnected computer systems.*
- *Standardize EHRs by defining functional requirements, harmonizing data fields and ensuring secure patient and provider access to information at any time.*

[17] Concrete steps to overcome this barrier have been provided in an editorial in Cancer World: http://www.cancerworld.org/Articles/Issues_43/Editorial/Patients_need_information%A7_Is_that_clear%3F%0D%0A.html.

APPENDIX 1: Key Organizations and Initiatives Relevant to the PACE Mission

Many key organizations have initiatives in areas directly relevant to the PACE mission. **Appendix 1** contains a selection of reports, blueprints, roadmaps, and initiatives that outline comprehensive approaches in many policy areas that seek to improve development of innovative cancer care and treatments. This list cannot be comprehensive yet demonstrates the remarkable and intense interest, as well as varying approaches, to addressing commonly identified barriers in the cancer policy environment that inhibits faster oncology innovation.

This "inventory" is provided as part of the preparation for the PACE Global Council discussion so that the meeting in New York might focus on gaps in the existing work and/or ways that PACE and its partners could augment and support these existing initiatives.

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission

Name/Organization/Company	Goals/Approach
American Society of Clinical Oncology (ASCO)	ASCO lays out a vision for transforming clinical and translational research to deliver more effective and personalized cancer therapies faster. The report also articulates recommendations for achieving that vision over the next several years and ASCO's commitment to enacting the recommendations. See: The ASCO Blueprint
Biomarkers Consortium	The Biomarkers Consortium is a major public-private biomedical research partnership managed by the Foundation for the National Institutes of Health with broad participation from stakeholders across the health field, including government, industry, academia, and patient advocacy and other nonprofit private-sector organizations. Working together, the members of the Consortium are building uniquely powerful collaborations that are increasing the development of biomarker-based technologies, medicines, and therapies for the prevention, early detection, diagnosis, and treatment of disease. Goals include the following: ▪ Facilitate the development and qualification of biomarkers using new and existing technologies; ▪ Help qualify biomarkers for specific applications in diagnosing disease, predicting therapeutic response, or improving clinical practice; ▪ Generate information useful to inform regulatory decision making; and Make consortium project results broadly available to the entire scientific community.
Biotherapy Development Association (BDA)	BDA's mission is to provide a unique platform to interface academia, industry, and regulatory authorities to improve the efficiency of drug development in oncology. It does this by organizing meetings and workshops focused on specific oncology themes to translate science into clinical practice, advising on drug development strategies and latest trends in biotherapy development in oncology, and advising on the set-up of translational research accompanying early clinical studies. See: Strategies for harmonization of next-generation oncology drug development. A report from the third Alpine meeting of the Biotherapy Development Association
Boston Healthcare	Boston Healthcare provides reimbursement, business development, and market analytics services to drug, device, and diagnostic clients worldwide. Boston Healthcare's White Paper on Recognizing Value in Oncology Innovation discusses a framework for understanding the true clinical value of a therapy over time that may prove informative to the PACE Global Council.

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
Bridging Interventional Development Gaps (BrIDGs)	As part of the National Center for Advancing Translational Sciences (NCATS) Division of Pre-Clinical Innovation, BrIDGs (previously the National Institutes of Health [NIH] Rapid Access to Intervention Development [RAID] program) makes available, on a competitive basis, certain critical resources needed for the development of new therapeutic agents. BrIDGs is intended to advance promising therapies into the clinic by providing in-kind services to overcome late-stage preclinical therapy development obstacles. Successful applicants receive not grant funds but access to NIH contractors who conduct preclinical studies at no cost to the investigator. In general, synthesis, formulation, pharmacokinetic, and toxicology services in support of investigator-held Investigational New Drug (IND) applications to the Food and Drug Administration are available.
Brookings Institution – Engelberg Center for Health Care Reform	The Engelberg Center is conducting a range of projects that support comprehensive health care reform. These projects and partnerships enhance the Center's ability to implement change at all levels and bring academic and technical expertise to bear on practical solutions to state and national health care challenges.
Cancer Care Ontario (CCO)	As the provincial agency responsible for continually improving cancer services, and the government's cancer advisor, CCO directs and oversees close to $700 million to hospitals and other cancer care providers to deliver high-quality, timely cancer services. ▪ Implements provincial cancer prevention and screening programs designed to reduce cancer risks and raise screening participation rates. ▪ Works with cancer care professionals and organizations to develop and implement quality improvements and standards. ▪ Uses electronic information and technology to support health professionals and patient self-care and to continually improve the safety, quality, efficiency, accessibility, and accountability of cancer services. ▪ Plans cancer services to meet current and future patient needs, and works with health care providers in every Local Health Integration Network to continually improve cancer care for the people they serve. ▪ Rapidly transfers new research into improvements and innovations in clinical practice and cancer service delivery.

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
Cancer World	The aim of Cancer World is to help reduce the unacceptable number of deaths from cancer that is caused by late diagnosis and inadequate cancer care. Success in preventing and treating cancer depends on many factors. Tumor biology, the extent of available knowledge, and the nature of care delivered all play a role. But equally important are the political, financial, and bureaucratic decisions that affect how far and how fast innovative therapies, techniques, and technologies are adopted into mainstream practice. Cancer World explores the complexity of cancer care from all of these very different viewpoints, and offers readers insight into the myriad decisions that shape their professional and personal world.
C-Change	C-Change assembles key cancer leaders from the private, public, and not-for-profit sectors — and from across the cancer continuum (prevention, early detection, treatment, and quality of life). Its stated mission is to eliminate cancer as a major public health problem at the earliest possible time by leveraging the expertise and resources of its unique multi-sector membership.
The Center to Reduce Cancer Health Disparities (CRCHD)	CRCHD initiates, integrates, and engages in collaborative research studies with NCI Divisions and NIH Institutes and Centers to promote research and training in cancer health disparities research and to identify new and innovative scientific opportunities to improve cancer outcomes in communities experiencing an excessive burden of cancer.
Clinical Data Interchange Standards Consortium (CDISC)	CDISC is a global, open, multidisciplinary, non-profit organization that has established standards to support the acquisition, exchange, submission and archive of clinical research data and metadata. The CDISC mission is to develop and support global, platform-independent data standards that enable information system interoperability to improve medical research and related areas of healthcare. CDISC standards are vendor-neutral, platform-independent and freely available via the CDISC website: http://www.cdisc.org/.
Clinical Trials Transformation Initiative (CTTI)	CTTI is a public-private partnership to identify practices that will increase the quality and efficiency of clinical trials. It was established by the U.S. FDA and Duke University, and now comprises more than 60 organizations from across the clinical trial enterprise. Members include representatives of government agencies, industry representatives, patient advocacy groups, professional societies, investigator groups, academic institutions, and other interested parties.
Critical Path Institute (C-Path)	C-Path is a nonprofit, public-private partnership with the Food and Drug Administration (FDA) created under the auspices of the FDA's Critical Path Initiative program in 2005. C-Path's aim is

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	to accelerate the pace and reduce the costs of medical product development through the creation of new data standards, measurement standards, and methods standards that aid in the scientific evaluation of the efficacy and safety of new therapies. Although C-Path's work can be looked at as a series of projects funded by grants and performed by collaborations and consortia, the work generally falls under the goal of creating tools to enable personalized medicine that improves health and saves lives.
Developmental Therapeutics Program (DTP)	As the drug discovery and development arm of the NCI, DTP plans, conducts, and facilitates development of therapeutic agents for cancer and acquired immune deficiency syndrome (AIDS). It acts as a resource for research materials, including Web-accessible data and tools, vialed and plated compounds, tumor cells, animals, and IND-directed studies.
European Cancer Patient Coalition (ECPC) European Alliance for Personalised Medicine (EAPM)	The EAPM brings together professional and patient advocacy groups with extensive scientific, clinical, caring, and training expertise in personalized medicine and diagnostics, as well as leading academic institutions, industry, and other expert stakeholders. The alliance is co-chaired by former member of the European Parliament John Bowis and former EU health commissioner David Byrne. See: Ensuring a regulatory environment which allows early patient access to novel and efficacious personalised medicine
European Federation of Pharmaceutical Industries and Associations (EFPIA)	The EFPIA represents the pharmaceutical industry operating in Europe. Through its direct membership of 33 national associations and 35 leading pharmaceutical companies, EFPIA is the voice on the EU scene of 1,900 companies committed to researching, developing, and bringing to patients new medicines that will improve health and the quality of life around the world. EFPIA supports a vision of modern and sustainable health care systems in Europe, where patients have equal and early access to the best and safest medicines, which supports innovation, empowers citizens to make informed decisions about their health, and ensures the highest security of the medicines supply chain.
European Network for Health Technology Assessment (EUnetHTA)	EUnetHTA's mission is to support collaboration between European HTA organizations that bring added value to health care systems at the European, national, and regional level. Through its activities, EUnetHTA ▪ supports efficient production and use of HTA in countries across Europe ▪ provides an independent and science-based platform for HTA agencies in countries across

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	Europe to exchange and develop HTA information and methodology ▪ provides an access point for communication with stakeholders to promote transparency, objectivity, independence of expertise, fairness of procedure, and appropriate stakeholder consultations ▪ develops alliances with contributing fields of research to support a stronger and broader evidence base for HTA while using the best available scientific competence.
European Patients' Academy on Therapeutic Innovation (EUPATI)	Funded by the Innovative Medicines Initiative (IMI), the consortium project, EUPATI, will provide scientifically reliable, objective, comprehensive information to patients on medicines research and development. It will increase the capacities and capabilities of well-informed patients and patient organizations to be effective advocates and advisors in medicines research, e.g., in clinical trials, with regulatory authorities and in ethics committees.
European Patients' Forum (EPF)	EPF is the umbrella organization of pan-European patient organizations active in the field of European public health and health advocacy. EPF was founded in 2003 to become the collective patients' voice at the EU level. EPF's vision is high-quality, patient-centered, equitable health care for all patients throughout the European Union. EPF facilitates exchange of good practice and challenges of bad practices on patients' rights, equitable access to treatment and care, and health-related quality of life between patient organizations at the European level and at the member state level. Its Value+ Toolkit Resource Kit for patients' organizations "provides patient organizations with information on how they can be involved as equal partners, on principles around consultation and how to use and disseminate projects outcomes in the most efficient way. It is available in English, German, French, Spanish, Lithuanian and Bulgarian." Regarding the EU Transparency Directive (Council Directive 89/105/EEC), EPF contends that further steps are needed to strengthen good governance and improve patients' access to therapies. Regarding HTA, EPF has just released three consecutive reports to help patients gaining a foothold in the HTA process.
European Society for Medical Oncology (ESMO)	ESMO is the leading European professional organization, committed to advancing the specialty of medical oncology and promoting a multidisciplinary approach to cancer treatment and care. Since 1975, ESMO's mission has been to advance cancer care and cure. ESMO achieves this through fostering and disseminating good science that leads to better medicine and determines

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	best practice. In this way ESMO fulfills its goal to support oncology professionals in providing people with cancer with the most effective treatments available and the high-quality care they deserve. ESMO 2012 Press Release: Many cancer patients unaware of the personalised medicine revolution in oncology, survey shows
EURORDIS – Rare Diseases Europe	EURORDIS is a nongovernmental, patient-driven alliance of patient organizations and individuals active in the field of rare diseases. It is dedicated to improving the quality of life of all people living with rare diseases in Europe. Currently, EURORDIS represents more than 500 rare disease organizations in 49 different countries (of which 24 are EU member states), covering more than 4,000 rare diseases. EURORDIS aims at improving the quality of life of people living with rare diseases in Europe through advocating at the European level, supporting research and drug development, networking patient groups, and raising awareness and other actions designed to fight against the impact of rare diseases on the lives of patients and family.
FasterCures – Milken Institute	FasterCures is an "action tank" that works to improve the medical research system—to accelerate the time it takes to get important new medicines from discovery to patients. Its mission is to accelerate the progress of discovery and development of new medical solutions for deadly and debilitating diseases. It aims to be nimble and independent and a "safe place" for key stakeholders of the medical research enterprise to come together to get things done.
The Green Park Collaborative (GPC)	The GPC is an international pilot initiative that is exploring the scientific feasibility of developing guidance for the life sciences industry on the design of clinical studies to meet the needs of HTA organizations and coverage bodies. The aim is to produce prototype "evidence guidance documents" that will provide therapeutic-area specific trial design recommendation, as well as general methodological advice that can be applied across therapeutic areas. The purpose of this guidance is to reduce the uncertainty currently faced by the life sciences industry regarding the evidentiary preferences of HTA and coverage bodies, to improve the relevance of clinical research, and to improve patient access to useful innovations. Prototype guidance documents produced by the GPC are not intended to represent consensus statements on the part of all participant organizations, but rather demonstrate the feasibility of and inform the subsequent development of guidance beyond the prototype phase.

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
Guidelines International Network (G-I-N)	Founded in 2002, G-I-N is a global network that has grown to comprise 86 organizations and 107 individual members representing 45 countries from all continents. The network supports evidence-based health care and improved health outcomes by reducing inappropriate variation throughout the world. G-I-N's mission is to lead, strengthen, and support collaboration and work within the guideline development, adaptation, and implementation community. It has three principal aims: ▪ Provide a network and partnerships for guideline organizations, implementers, end-users, researchers, students, and other stakeholders ▪ Assist in reducing duplication of effort and improving the efficiency and effectiveness of evidence-based guideline development, adaptation, dissemination, and implementation ▪ Promote best practice through the development of opportunities for learning and building capacity, and the establishment of high-quality standards of guideline development, adaptation, dissemination, and implementation. Its Toolkit on Patient and Public Involvement in Guidelines assembles international experiences and best practice examples of successful patient involvement and aims at supporting guideline developers who consider involving patients in guideline development or dissemination. It provides practical advice for the involvement of patients and the public for a variety of reasons, be it well-informed choice, accountability, equality, quality of care, or improved implementation.
Health Technology Assessment International (HTAi)	HTAi is the global scientific and professional society for all those who produce, use, or encounter HTA. HTAi embraces all stakeholders, including researchers, agencies, policymakers, industry, academia, health service providers, and patients/consumers, and acts as a neutral forum for collaboration and the sharing of information and expertise. With members from 59 countries and 6 continents, HTAi's mission is to support and promote the development, communication, understanding, and use of HTA around the world, as a scientifically based and multidisciplinary means of informing decision making regarding the introduction of effective innovations and the efficient use of resources in health care. See: HTAi Policy Forum 2013
Innovative Medicines Initiative (IMI)	IMI is Europe's largest public-private initiative aiming to speed up the development of better and safer medicines for patients. IMI supports collaborative research projects and builds networks of industrial and academic experts in Europe that will boost innovation in health care. Acting as a

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	neutral third party in creating innovative partnerships, IMI aims to build a more collaborative ecosystem for pharmaceutical R&D. It will provide socioeconomic benefits to European citizens, increase Europe's competitiveness globally, and establish Europe as the most attractive place for pharmaceutical R&D. IMI is a joint undertaking between the European Union and EFPIA.
Institute of Medicine (IOM)	The IOM is an independent, nonprofit organization that works outside of government to provide unbiased and authoritative advice to decision makers and the public. It asks and answers the most pressing questions about health and health care in the United States. Its aim is to help those in government and the private sector make informed decisions by providing evidence upon which they can rely. Although the expert, consensus committees are vital to the IOM's advisory role, it also convenes a series of forums, roundtables, and standing committees, as well as other activities, to facilitate discussion, discovery, and critical, cross-disciplinary thinking. See: Transforming Clinical Research in the United States
International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use	ICH's mission is to make recommendations toward achieving greater harmonization in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration, thereby reducing duplication of testing carried out during the research and development of new human medicines. ICH is a unique undertaking that brings together the drug regulatory authorities and the pharmaceutical industry of Europe, Japan, and the United States. Regulatory harmonization offers many direct benefits to both regulatory authorities and the pharmaceutical industry including: preventing duplication of clinical trials in humans and minimizing the use of animal testing without compromising safety and effectiveness; streamlining the regulatory assessment process for new drug applications; and reducing the development times and resources for drug development. Harmonization is achieved through the development of ICH Tripartite Guidelines and the commitment of the ICH regulators to implement the final Guidelines.
International Network of Agencies for Health Technology Assessment (INAHTA)	INAHTA is a network of 53 member agencies from 29 countries including North and Latin America, Europe, Africa, Asia, Australia, and New Zealand. All members are nonprofit organizations producing HTA and are linked to regional or national government. Many organizations throughout the world assess health care technology. INAHTA´s mission is to provide a forum for the identification and pursuit of interests common to HTA agencies. The

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	network aims to ▪ accelerate exchange and collaboration among agencies ▪ promote information sharing and comparison ▪ prevent unnecessary duplication of activities
International Society for Pharmacoeconomics and Outcomes Research (ISPOR)	ISPOR promotes the science of pharmacoeconomics (health economics) and outcomes research (the scientific discipline that evaluates the effect of health care interventions on patient well-being including clinical, economic, and patient-centered outcomes) and facilitates the translation of this research into useful information for health care decision makers to increase the efficiency, effectiveness, and fairness of health care to improve health. ISPOR is an international, educational, and scientific, member-driven society, with more than 6,500 members from 100 countries.
The Japan Medical Association Center for Clinical Trials (JMACCT)	The JMACCT conducts the "Large Scale Clinical Trial Network Project," a clinical trial promotion program subsidized by the Ministry of Health, Labour, and Welfare. See: JMACCT's 5 Yearly Clinical Trial Activation Plan
The Lancet Oncology Commission	This Commission gathers expert opinion from health care professionals, policymakers, and cancer survivors to address the barriers and solutions to delivering affordable cancer care. Urgent solutions range from re-engineering of the macroeconomic basis of cancer costs (e.g., value-based approaches to bend the cost curve and allow cost-saving technologies), greater education of policymakers, and an informed and transparent regulatory system. The Commission sees a radical shift in cancer policy as also required, and it considers unacceptable the political toleration of unfairness in access to affordable cancer treatment. It believes that the cancer profession and industry should take responsibility and not accept a substandard evidence base and an ethos of very small benefit at whatever cost; rather, what is needed is delivery of fair prices and real value from new technologies. See: Delivering affordable cancer care in high-income countries
Manhattan Institute Center for Medical Progress (Project FDA)	Project FDA aims to reform the FDA to meet 21st century challenges. Under the leadership of former FDA commissioner Dr. Andrew von Eschenbach, Project FDA promotes reforms that can enable the FDA to offer a more predictable, transparent, and efficient pathway for bringing safe and effective new products to patients. Project FDA believes the FDA can become a bridge for

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	innovation, rather than a barrier to it, and that this can be achieved without sacrificing patient safety. Project FDA will educate the public on the FDA's vital role in advancing medical innovation; highlight the potential for new sciences to improve health while also lowering costs; and collaborate with patients' groups, industry stakeholders, and policymakers to modernize the FDA's policies and procedures.
MD Anderson Cancer Center	Inspired by America's drive generations ago to put a man on the moon, The University of Texas MD Anderson Cancer Center has launched an ambitious and comprehensive action plan, called the Moon Shots Program, to make a giant leap for patients—to dramatically accelerate the pace of converting scientific discoveries into clinical advances that reduce cancer deaths. It is hoped that what is learned from these initial cancer "moon shots" will lead ultimately to cures for all types of the disease.
Multidisciplinary Assessment of Technology Centre for Healthcare (MATCH)	MATCH is a well-established research collaboration between four leading UK universities (Birmingham, Brunel, Nottingham, and Ulster) and a cohort of industrial partners, also supported by stakeholders from the National Health Service (NHS) and other public sector organizations. MATCH, funded since 2003 by the Engineering and Physical Sciences Research Council (EPSRC) and partner subscriptions, provides a critical research mass in the field of HTA in its widest sense, bringing together expertise in health economics, engineering and social sciences.
National Cancer Action Team (NCAT)	Improving Outcomes: A Strategy for Cancer sets out an ambitious vision for the delivery of world-class cancer services. NCAT's role is to support the NHS in translating this vision into reality. From supporting cancer networks in the development of early diagnosis initiatives through to developing better information for cancer patients, NCAT is working across the cancer patient pathway. NCAT is a key element of the National Cancer Programme, working with the Department of Health, NHS Improvement, the NHS Cancer Screening Programme, and the national initiatives that are helping to implement different aspects of the new strategy.
National Cancer Institute (NCI)	The NCI is part of the NIH, U.S. Department of Health and Human Services. The NCI coordinates the U.S. National Cancer Program and conducts and supports research, training, health information dissemination, and other activities related to the causes, prevention, diagnosis, and treatment of cancer; the supportive care of cancer patients and their families; and cancer survivorship. The NCI has a large intramural program and funds cancer researchers around the

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	United States. Over the years, legislative amendments have maintained the NCI authorities and responsibilities and added new information dissemination mandates as well as a requirement to assess the incorporation of state-of-the-art cancer treatments into clinical practice.
National Cancer Research Institute (NCRI)	The NCRI is a UK-wide partnership between the government, charity, and industry that promotes cooperation in cancer research among the 22 member organizations for the benefit of patients, the public, and the scientific community. See: NCRI Strategic Plan 2012 - 2017
National Institutes of Health Research Cancer Research Network (NCRN)	NCRN provides researchers with the practical support they need to make cancer clinical studies happen in the NHS, so that more research takes place across England, and more patients can take part. ▪ Its 32 Local Research Networks coordinate and facilitate the conduct of cancer clinical research and offer researchers a range of services to support study set-up and delivery. ▪ It currently supports 600 open studies. ▪ More than 330,000 people have taken part in NCRN-supported research studies since 2001. ▪ It has a proven track record and world-class reputation for increasing participation in cancer clinical research. Prior to its creation less than 4 in every 100 newly diagnosed cancer patients were estimated to be entering clinical studies. By 2011, more than 20 out of every 100 newly diagnosed patients took part in cancer studies (23.1%). This is thanks to NCRN's partnerships with the NHS, researchers, funders, patients, caregivers, and the public.
National Institute for Health Research (NIHR) HTA Programme	The HTA Programme produces independent research about the effectiveness of different health care treatments and tests for those who use, manage, and provide care in the NHS. It identifies the most important questions that the NHS needs the answers to by consulting widely with these groups, and it commissions the research it thinks is most important through different funding routes. It provides ongoing help and support for the investigators it funds, before publishing their findings in its internationally acclaimed journal series, Health Technology Assessment.
Office of Health Economics (OHE)	The OHE Research program stimulates discussion and debate about critical issues in health economics and health care policy at the UK, European, and international levels. Although specifics vary over time, OHE research falls into three categories: the financing and delivery of health care, HTA methods and processes, and the economics of the life sciences and pharmaceutical industries. Activities include undertaking original research on a range of topics,

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	as well as seminars and workshops, publications, and expert commissions. See: Assessment and Appraisal of Oncology Medicines: NICE's Approach and International HTA Experience
Oncotyrol	Oncotyrol is the Austrian address for translational research of personalized cancer medicine in a public-private partnership. Oncotyrol seeks to bridge the gap between research and commercial development in order to bring scientific progress to the patient—quickly, safely, and more comprehensively than today.
Ontario Health Technology Advisory Committee (OHTAC)	As part of Health Quality Ontario (HQO), OHTAC is an arms-length expert committee that makes recommendations to the Ontario health care system and the Ontario Ministry of Health and Long-Term Care (MOHLTC) about the best health technologies for Ontario. Established in October 2003, OHTAC bridges the worlds of science and health care decision making by applying the best available evidence from around the world and across the province, to the unique needs of Ontario patients, providers, facility administrators, and policy decision makers. The Evidence Development and Standards (EDS) team works with clinical experts, scientific collaborators, and field evaluation partners to provide a sound evidence base for recommendations to Ontario's MOHLTC, clinicians, and health care decision makers. EDS conducts systematic reviews of scientific evidence and consults with experts in the health care services community to produce the Ontario Health Technology Assessment Series, one of the world's premier databases.
Organisation for Economic Co-operation and Development (OECD)	The mission of the OECD is to promote policies that will improve the economic and social well-being of people around the world. The OECD provides a forum in which governments can work together to share experiences and seek solutions to common problems. It works with governments to understand what drives economic, social, and environmental change. It measures productivity and global flows of trade and investment. It analyzes and compares data to predict future trends. It sets international standards on a wide range of things, from agriculture and tax to the safety of chemicals. Drawing on facts and real-life experience, it recommends policies designed to make the lives of ordinary people better. It works with business, through the Business and Industry Advisory Committee to the OECD, and with labor, through the Trade Union Advisory Committee.

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
Pancreatic Cancer Action Network (PanCAN)	PanCAN is a nationwide network of people dedicated to working together to advance research, support patients, and create hope for those affected by pancreatic cancer. It is a national organization that seeks to create hope in a comprehensive way through research, patient support, community outreach, and advocacy for a cure. The organization raises money for direct private funding of research and advocates for more aggressive federal research funding of medical breakthroughs in prevention, diagnosis, and treatment of pancreatic cancer. Raise the Cure and the subsequent legislation requires the NCI to create a long-term plan for pancreatic and other recalcitrant cancers that includes evaluating its current efforts in the disease and making recommendations on ways to accelerate progress and improve outcomes.
Personalized Medicine Coalition (PMC)	PMC was launched in 2004 to educate the public and policymakers, and to promote new ways of thinking about health care. Today, PMC represents a broad spectrum of more than 200 academic, industry, patient, provider, and payer communities, seeking to advance the understanding and adoption of personalized medicine concepts and products for the benefit of patients. PMC educates federal and state policymakers and private-sector health care leaders about personalized medicine, helping them understand the science, the issues, and what is needed for the positive evolution of personalized medicine. The PMC works closely with existing organizations in a way that avoids duplication of efforts. See: Sustaining Progress Against Cancer in an Era of Cost Containment
Pharmaceutical Research and Manufacturers of America (PhRMA)	PhRMA represents the United State's leading pharmaceutical industry research and biotechnology companies, which are devoted to inventing medicines that allow patients to live longer, healthier, and more productive lives. PhRMA members alone invested an estimated $49.5 billion in 2011 in discovering and developing new medicines. PhRMA's mission is to conduct effective advocacy for public policies that encourage discovery of important new medicines for patients by pharmaceutical and biotechnology research companies. To accomplish this mission, PhRMA is dedicated to achieving these goals in Washington, the states, and the world: ▪ Broad patient access to safe and effective medicines through a free market, without price controls; ▪ Strong intellectual property incentives; and ▪ Transparent, efficient regulation and a free flow of information to patients.

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
Prostate Cancer Research Institute (PCRI)	PCRI was founded in 1996 by oncologists Mark C. Scholz, MD, and Stephen B. Strum, MD, with support from Daniel Freeman Hospital Foundation. Drs. Scholz's and Strum's vision was that: "an organization providing insightful clinical research in combination with high-level educational activities directed at both the patient and physician, would greatly enhance outcomes for prostate cancer patients everywhere." A patient who understands his disease and his treatment options is empowered to communicate more effectively with his physicians and will obtain a better outcome.
Quintiles	Quintiles is a biopharmaceutical services company offering clinical, commercial, consulting, and capital solutions worldwide. It helps biopharmaceutical companies develop and commercialize products to improve and lengthen patients' lives while demonstrating value to stakeholders. Its white paper on Oncology Drug Development and Value-Based Medicine argues for the need to redefine the clinical trial process that may have implications for PACE.
Rare Cancers Europe (RCE)	RCE has been established as a partnership of cooperating organizations that work together to place the issue of rare cancers firmly on the European policy agenda, to identify and promote appropriate solutions, and to exchange best practice. RCE campaigns to implement the Political Recommendations on Stakeholder Actions and Public Policies that emerged from the conference "Rare Tumours in Europe: Challenges and Solutions", held in November 2008 in Brussels. RCE has launched the Call to Action that urges policymakers and stakeholders to give priority to the issues linked to rare cancers. In the future, the campaign will also propose potential events or other initiatives if and when the opportunity arises. See: Rare Cancers Europe: joining forces to tackle a common problem.
The Rarer Cancers Foundation (RCF)	RCF works with government, political parties, and its members to ensure that patients with rarer cancers have access to high-quality services that are among the best in Europe. Its manifesto, Towards the Best in Europe (March 2010), received the support of more than 200 parliamentary candidates, and a number of its recommendations have already been adopted, including the introduction of measures to improve access to treatments and of outcome measures on cancer.
The Swedish Council on Health Technology Assessment (SBU)	For more than 15 years, SBU has stayed on the leading edge of HTA and has been instrumental in promoting scientific assessment in Sweden and abroad. Many routine methods of diagnosis and treatment are, in fact, obsolete and ineffective. Some newer methods are widely used, even

APPENDIX 1. Key Organizations and Initiatives Relevant to the PACE Mission (Cont'd)

Name/Organization/Company	Goals/Approach
	though their benefits, risks, and costs have never been critically evaluated. At the same time, there are methods that should be used on a much broader scale—methods shown by scientific assessment to be both beneficial and cost effective.
TransCelerate BioPharma Inc. (TransCelerate)	TransCelerate is a nonprofit organization formed in early August 2012 by ten top pharmaceutical companies from the United States and Europe to accelerate development of new drugs and cut costs. Each company will contribute financial and other resources to meet specific objectives and established guidelines for sharing information and expertise. The goal is to create an infrastructure by establishing a single portal for all clinical investigators to use for all clinical studies, as well as a common language and standards aimed at increasing efficiency and cutting errors. Membership in TransCelerate is open to all pharmaceutical and biotechnology companies, with cost of membership based on how much a company spends on research and development.
Union for International Cancer Control (UICC)	UICC is a membership organization that exists to help the global health community accelerate the fight against cancer. UICC works closely with key international United Nations (UN) agencies including: the World Health Organization (WHO), with whom it is in official relations, the International Agency for Research on Cancer (IARC), and the Programme of Action for Cancer Therapy (PACT), and has consultative status with the UN Economic and Social Council (ECOSOC). In addition, UICC offers corporate partners a unique opportunity to demonstrate social responsibility on a global scale. UICC is committed to reducing the global cancer burden through delivering the 11 targets of the World Cancer Declaration.

APPENDIX 2. List of Acronyms

Acronym	Definition
AIDS	acquired immune deficiency syndrome
ANPRM	Advanced Notice of Proposed Rulemaking
ASCO	American Society of Clinical Oncology
BDA	Biotherapy Development Association
BIO	Biotechnology Industry Organization
BrIDGs	Bridging Interventional Development Gaps
CCO	Cancer Care Ontario
CDISC	Clinical Data Interchange Standards Consortium
C-PATH	Critical Path Institute
CRCHD	The Center to Reduce Cancer Health Disparities
CRO	clinical research organization
CTTI	Clinical Trials Transformation Initiative
DNA	deoxyribonucleic acid
DTP	Developmental Therapeutics Program (of the Division of Cancer Treatment and Diagnosis at the National Cancer Institute)
EAPM	European Alliance for Personalised Medicine
EC	European Commission
ECOSOC	UN Economic and Social Council
ECPC	European Cancer Patient Coalition
EDS	Evidence Development and Standards
EEC	EEC, European Economic Community
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHR	electronic health record
EPF	European Patients' Forum
EPSRC	Engineering and Physical Sciences Research Council
ESMO	European Society for Medical Oncology
EU	European Union
EUnetHTA	European Network for Health Technology Assessment
EUPATI	European Patients' Academy on Therapeutic Innovation
EURORDIS	Rare Diseases Europe
FDA	U.S. Food and Drug Administration
GBA	German Federal Joint Committee ("Gemeinsamer Bundesausschuss")
GCP	Good Clinical Practice
G-I-N	Guidelines International Network

APPENDIX 2. List of Acronyms (Cont'd)

Acronym	Definition
GPC	The Green Park Collaborative
HCQI	Health Care Quality Indicators
HHS	U.S. Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HIT	health information technology
HQO	Health Quality Ontario
HTA	Health Technology Assessment
HTAi	Health Technology Assessment International
IARC	International Agency for Research on Cancer
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
IMI	Innovative Medicines Initiative
INAHTA	International Network of Agencies for Health Technology Assessment
IND	Investigational New Drug
IOM	Institute of Medicine
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
JMACCT	The Japan Medical Association Center for Clinical Trials
MATCH	Multidisciplinary Assessment of Technology Centre for Healthcare
MEXT	Ministry of Education, Culture, Sports, Science and Technology
MHLW	Ministry of Health, Labour and Welfare
MOHLTC	Ministry of Health and Long-Term Care
NCAT	National Cancer Action Team
NCATS	National Center for Advancing Translational Sciences
NCI	National Cancer Institute
NCRI	National Cancer Research Institute
NCRN	National Institutes of Health Research Cancer Research Network
NHS	National Health Service
NIH	National Institutes of Health
NIHR	National Institute for Health Research
OECD	Organisation for Economic Co-operation and Development
OHE	Office of Health Economics
OHTAC	Ontario Health Technology Advisory Committee
PACE	Patient Access to Cancer care Excellence
PACT	Programme of Action for Cancer Therapy

APPENDIX 2. List of Acronyms (Cont'd)

Acronym	Definition
PanCAN	Pancreatic Cancer Action Network
PCRI	Prostate Cancer Research Institute
PDUFA	Prescription Drug User Fee Act
PhRMA	Pharmaceutical Research and Manufacturers of America
PMC	Personalized Medicine Coalition
R&D	Research and Development
RAID	Rapid Access to Intervention Development
RCE	Rare Cancers Europe
RCF	The Rarer Cancers Foundation
RCT	randomized controlled trial
SBU	The Swedish Council on Health Technology Assessment
UICC	Union for International Cancer Control
UK	United Kingdom
UN	United Nations
US	United States
WHO	World Health Organization