



## FEATURED ARTICLE

# BEYOND REIMBURSEMENT: HEALTH ECONOMICS AS A CLINICAL AND REGULATORY STRATEGY

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In every country around the world, in every potential market for new drugs or devices, governments are considering the impact of health economics.

In the U.K., the National Institute for Health and Clinical Excellence (NICE) requires that drugs be cost effective - in addition to being effective - to gain inclusion on the government healthcare plan. In Germany, drug price reforms included an increased discount for government health insurers and a price-freeze, and new legislation may lead to price negotiations. Greece, Spain, Italy and France have all cut drug prices.

Even the United States is not immune. Under healthcare reform passed last year, a newly-formed Patient-Centered Outcomes Research Institute will commission comparative-effectiveness research to help patients and doctors make more cost-effective decisions. Already, the National Institutes of Health is conducting a trial to compare Lucentis (ranibizumab) with less-expensive Avastin (bevacizumab) in the treatment of wet age-related macular degeneration, and initial data released this year indicated the two have similar efficacy.

Additionally, while the U.S. does not have government healthcare, both government and private insurers require that sponsors demonstrate the value of their new drugs to gain favorable reimbursement status.

But health economics is expanding beyond the world of reimbursement. It is becoming an integral part of both government decisions on the approvability of drugs and sponsor decisions regarding their clinical trial strategies.

## Where Health Economics and Government Collide

The recent economic downturn has prompted finance ministers in many countries to more closely analyze the cost of healthcare. They are beginning to recognize the many hidden costs of treating disease, and the fact that new drugs - despite their potentially high prices - can decrease these costs overall by preventing hospital visits and labor hours lost. To ensure these new drugs are available in their countries, finance ministers have become increasingly eager to support clinical trials. In fact, many countries are examining the cost of not participating in trials for conditions that cost the government significant amounts of money over the long term.

In the midst of such considerations, some governments have also acknowledged that the current system for reviewing drugs is antiquated - it has not kept pace with improvements in drug research, monitoring and manufacturing or with the shift to the development of more targeted therapies.

This situation creates an opportunity for drug makers to engage governments in a discussion about health economics. If a country must wait through years of traditional clinical trials before a drug is approved, what is the resultant cost to the healthcare system? These years of clinical research cost the developer millions of dollars that they will wish to recover. Is this cost justified? For example, if a sponsor works closely with the government to design the right preclinical and Phase I trials, could a single Phase II/III trial be sufficient for approval in some indications?

The science behind new drugs - solid safety and efficacy - is the first priority and always will be. But there is room in some countries for discussions of how safety and efficacy are established. Are so many repetitive studies really necessary? Is the requirement or guidance relevant to the current technology? If a sponsor can prove to the government that a certain disease is currently costing 50 cents per person per day to treat, and a new drug would change treatment paradigms and reduce that cost to a penny, that is a compelling argument. Not compelling enough to compromise safety or efficacy, but compelling enough to perhaps move things along a little faster by partnering to agree upon the most appropriate pathway to approval.

There are no formal guidances or rules covering this, but such discussions are happening right now, all around the world. And governments are beginning to take action: even those not yet comfortable with the idea of allowing more flexibility and customization in the clinical trial process are open to the idea of reducing bureaucracy and red tape for products with the potential to significantly impact health economics. This includes providing support and in some cases funding to help develop the newest technologies and testing methods. The shared approach has great advantages; the return on investment for the governments can translate into improved, cost-effective products for the country.

For example, INC Research has used health economics analyses to successfully accelerate clinical programs in Europe. Regulators allowed sponsors that had proven their treatments made fiscal sense to have certain portions of their review conducted in parallel, provide justifications for more streamlined approaches, and collaborate to identify the areas that were no longer applicable to the new methods of development. This applied not only to clinical trials but to market approval information. By looking at the potential cost impact to the country early, buy-in was improved and, upon approval, the discussions regarding reimbursement were less cumbersome and timelines greatly improved. All of this was possible only because thought went into health economics early in the process.

Another step governments are taking to support products that are economically responsible is to give their reviews a higher priority. Again, while there are no official guidances on this and it is not standard practice, it has happened in certain countries. Even within governments there is a finite capacity for work and there is always an internal process of triage, so anything that will make a product stand out is of great benefit.

There is movement along these fronts in the U.S. as well. Healthcare in the states is not nationalized, and the FDA is forbidden from considering cost when determining the approvability of a drug. But even so, as the agency creates new approval pathways for emerging fields like biosimilars and nanotechnology, it can take health economics into consideration as it designs the requirements for development and determines the information needed to get the product approved.

Overall, the last frontier of product development is adding economic analyses to science. The two have never been good bedfellows, and it is up to sponsors to work with governments and educate them as to how they can help reduce development costs, obtain access to new drugs faster, and reduce the cost of healthcare in their countries.

### Applying Health Economics in the Clinic

While many drug makers have become adept at using economic analyses to gain favorable reimbursement status in the U.S., they are often less successful in other countries, and many are inexperienced at incorporating these discussions into the approval process.

It is the responsibility of sponsors to help governments understand how a new drug can impact health economics in their country. Presenting analyses of mechanism of action, dosing, safety and efficacy are no longer sufficient. For example, telling payers that a new diabetes drug can help get blood glucose levels under seven percent does not help them understand how that affects hospitalization rates. Sponsors must be able to explain not only the profile of their product, but the value proposition. They should be able to answer the questions: What can the patient do after treatment that they couldn't do before, and how does it save the healthcare system money?

For example, can your oral formulation replace infusions and reduce hospital visits? Can your medical device electronically track compliance with home treatments so a doctor can catch noncompliance and intervene before the patient ends up in the emergency room?

Gathering health economics data to prove a product's value must be integrated into the clinical trials process. Many sponsors don't consider health economics until they are having discussions with payers, but at that point it is too late to collect data. Health economics should become a part of the clinical trial plan - ideally before Phase III, but the earlier, the better.

Even at the preclinical stage, sponsors can hold advisory boards with payers to get a better understanding of what they are looking for and what kind of data they would need to make a decision. If scenarios arose in which certain data were generated in a trial, what would be the relevance to the payer?

During Phase II, sponsors can start working with key opinion leaders that advise payers and payers themselves to determine how a product would be positioned in the patient care pathway. How might the product's use be restricted? Would it be used only in a hospital, or only in certain patients? At this point it is also critical to understand not only the current treatments available but also those that may reach the market while the sponsor's product is undergoing clinical development.

Based on this research, a sponsor may need to modify the planned design of their Phase III program. It may be appropriate to use questionnaires to track quality of life and how the treatment affects the patients' ability to work. Additional endpoints or a comparator arm may be needed to track reduced hospitalization and other health economics outcomes.

Some countries are considering making health economics analyses mandatory for inclusion in all clinical trial plans. Fortunately, many governments also provide grants to help defray the costs of such programs, and even those who do not have official subsidies in place are often willing to entertain discussions about such a proposal.

After all, as many finance ministers are beginning to realize, the price of a new drug often pales in comparison to the net outcome that drug can have on healthcare costs. And anything that impedes that drug getting to market - be it financial constraints, onerous clinical requirements or bureaucratic red tape - is costing the government money in the long run.

### About the Author

Geoff Fatzinger brings a comprehensive scientific and legal background to the Global Regulatory Services group, plus extensive experience in global regulatory affairs including product and clinical development in both pharmaceutical and CRO environments, with extensive knowledge in Europe and Asia Pacific. He has expert knowledge in product development, including combination products and medical devices and regulatory study start-up; having successfully managed several global regulatory start-up groups with 98 percent first round approval rates and accelerated first patient in (FPI). His therapeutic experience in cardiovascular, CNS, oncology and women's health trials is well aligned with INC Research's therapeutic focus. Mr. Fatzinger is also a registered member and speaker for regulatory associations including The Organization for Professionals in Regulatory Affairs (TOPRA) and Regulatory Affairs Professionals Society (RAPS) and is a frequent lecturer on international regulatory requirements and legislation issues. In addition, Mr. Fatzinger has extensive strategic and operational experience in regards to CTD, PIP and market authorizations for Europe and Asia Pacific.