Editor-in-Chief's Commentary: Integrating Economics Into Innovation

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Therapeutic Innovation & Regulatory Science 47(4) 395-396

➡ DIA 2013

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I am not a health economist, nor for that matter an economist at all. However, it is obvious that economic considerations are going to play a major role in the success (or failure) of thera- peutic innovation and of regulatory science. Thus, it strikes me that we need to engage in economic discussions at DIA and in the pages of TIRS. The challenge always is to have these dia- logues relate to real issues of medical product discovery, devel- opment, regulation, and utilization. We face enough challenges in discussions across molecular biology, systems biology and pharmacology, and biostatistics, each with its own jargon and disciplinary thinking. And yet, we must accept the challenge to move beyond our own areas of specialization; talk we must with economists, and hopefully they with us.

Stepping back to what we in the "healing arts" have been engaged in for millennia, it has always been to try and under- stand the basis of human health and disease and to develop the most effective, safest, highest quality interventions; to skill- fully use these in our patients; and now ever more so to do this "at an affordable price." The "value proposition" of the best medicine with the highest benefit:risk ratio for each patient (and thus patients in aggregate), improving outcomes that are clinically relevant and individually meaningful without bank- rupting the health care system, appears straightforward enough. Implementation in the real world, though, is far from easy. Is a very expensive intervention "worth it" compared to the disease itself and all other interventions for the disease for both the individual and for society as a whole? The prospect of targeted,

"precision" therapeutics with much higher likelihood of enhanced individual benefit:risk is appealing. Yet, as Robert Frost put it, "We dance round in a ring and suppose, while the secret sits in the middle and knows." The history of medi-cine, and our future history, will always be built on evolving knowledge and underlying uncertainty. We rightly ask for "evidence," for continuous improvement in all we do. How-ever, we need to acknowledge uncertainty up front; honest appraisal is that every patient encounter is ultimately an

"n of 1" experiment. There is a cost to uncertainty, but since that is the reality of the human condition, we need to figure out how to factor it in and move forward.

The current moment finds us excited by the elegance of new scientific insight into disease pathogenesis and interventions. Simultaneously, we worry about the some of the costs: of risk and investment; of time frames for product development and recovery of investment costs; of financial burden of extremely expensive new drugs to the individual patient and to all of us who ultimately "pay the bills" one way or another. We need to address many questions urgently (I do not pretend to have answers, only to try to encourage discussion):

- 1. How do we ensure sustainable investment in biomedical science and innovation? This includes basic science, and many concerns have been raised about how to fund basic science in our universities and other institutions. The bud- get for the National Institutes of Health is increasingly under pressure during times of fiscal constraint. Increasing shortage of grant monies can act as a major deterrent to stu- dents to pursue a career in science, and cutbacks in training funds likewise can have a profound impact in the years to come. We need to have discussions about the value of scientific inquiry—from basic through applied—and find ways to more effectively communicate the centrality of such pursuits to our future, both domestically and internationally.
- 2. How do we sustain investment in new product discovery and development? So much discussion at present revolves around risk and return on investment. Recent successes in precision medicine and drug development, and of the response of the regulatory community to new science are encouraging. Yet, honest discussions of the inherent com- plexity of human biology and of medicine often do not occur or are supplanted by exercises in advocacy or hype. This is confounded by expectations of time frames. We are seeing increasing efficiency in drug development and of the regulatory review process with better alignment of sci- ence. However, even some of the most expedited programs we have seen to date (6 years from investigational new drug application to approval for several new drugs in the past couple of years) may be considered "too long" for some in the investment community.

As we move to new paradigms of shorter, more focused clinical trial periods, we will also need new approaches to postmarket observa- tional studies of both effectiveness and safety in the real world, with complex economic issues inherent in these arenas. We need to engage in discussions not only of sci- entific innovation and regulatory scientific approaches to efficiency in the development process, but also how this will affect economic models for investment, marketing, and utilization of new products. We need to address the heterogeneity of incentives in different aspects of product development. For example, the time frames, risks, and cost structures for the development of diagnostics and therapeutics are quite different, and changing rapidly as diag- nostic technologies change. Looking forward to an era of increasingly diagnostic driven precision medicine, there is real urgency to this discussion. The level of scientific innovation needs to be matched by new levels of economic innovation.

3. What are sustainable pricing structures for new innovative products and for old generic drugs? On the one hand, we are seeing prices for many new drugs in the hundreds of thousands of dollars per year range. Many of these compounds are truly innovative, unimaginable only a few years ago, and yet third party payers are already beginning to look in distress at these trends internationally. On the other hand, we are experiencing severe drug shortages of commonly used generic medicines, particularly sterile injectable products—from components of intravenous solutions and parenteral nutrition to anesthetics, crucial resuscitation medicines, and chemotherapy drugs for cancer (see Woodcock and Wosinska¹).

Prices are being forced down to the point where manufacturing of high-quality sterile products becomes financially untenable, with some manufacturers abandoning products and others running into significant quality issues. A critical question is, How can we clearly value and incentivize quality manufacturing and recognize high-quality products as a crucial aspect of therapeutics? As new, innovative products reach the end of their patent lives, are we simi-larly going to face shortages of these drugs when they become generic and the price point is forced too low to sus- tain high-quality product availability? We need to engage in innovative dialogues about these issues now, and meet them head on. One of my greatest fears after 40 years in medicine is to see innovation go for naught, products dis- appear for the wrong financial reasons, and patients (and that means all of us at some time in our lives) needlessly suffering because we have not engaged in difficult discussions.

We stand in the midst of medicines too costly to be sustain-able members of our therapeutic armamentarium and others too cheap to ensure high-quality manufacturing and availability. Even for non-health economists, the irony is striking; for those of us who treat patients, and for all of us who are patients, the prospect is frightening. Solutions—innovative, novel and focused on ultimate needs of all who are sick—will require complex, honest interactions among all concerned. All of us—those who discover, develop, manufacture, regulate, mar-ket, pay for, prescribe, and take medicines—"own" the responsibility to ensure access to the very best medicine and science have to offer. I hope that through our Editorial Board and authors we can use the pages of TIRS to help engage in this discussion, and to be one practical vehicle leading to a new path forward.

Reference

1. Woodcock J, Wosinska M. Economic and technological drivers of generic sterile injectable drug shortages. Clin Pharmacol Ther. 2013; 93(2):170-176.