Commentary

Misleading Congress about Drug Development: Reply

Joseph A. DiMasi
Tufts University

Ronald W. Hansen
University of Rochester

Henry G. Grabowski
Duke University

Abstract  The review essay by Donald Light about a Congressional Budget Office report on pharmaceutical research and development (R&D) (Light 2007) contains factual errors, leaves the reader uninformed about rebuttal responses to criticisms made in the review about studies of R&D costs, and draws erroneous conclusions about the nature of industry economics.

The review essay by Donald Light about a Congressional Budget Office report on pharmaceutical research and development (R&D) (Light 2007) contains factual errors, leaves the reader uninformed about rebuttal responses to criticisms made in the review about studies of R&D costs, and draws erroneous conclusions about the nature of industry economics. We briefly address these problems.

Nearly all of what Light writes in his section on development costs in relation to our study of pharmaceutical R&D costs (DiMasi, Hansen, and Grabowski 2003) has been published in two comments in the journal in which our study appeared (Light and Warburton 2005a, 2005b). Light, however, does not inform readers that we have rebutted all of these points in two responses in that journal (DiMasi, Hansen, and Grabowski 2005a, 2005b). Since we have already published detailed responses to the criticisms, here we simply direct readers to those publications. Light does reference one of our responses, but he makes no mention that it contains rebuttals to his criticisms. Instead, he cites it, incorrectly, as indicating that we are working on estimates of R&D costs for what he calls “me-too”
derivative products. Other factual misstatements in Light (2007) include the claim that the CEO of Merck “hosted and launched” the first public presentation of our study of pharmaceutical R&D costs (his role was only that of an invited guest speaker at the forum in which we presented our results) and the implication that F. M. Scherer’s (2001) study on the relationship between pharmaceutical industry profits and R&D expenditures was supported by the Merck Foundation and the National Pharmaceutical Council (Scherer did not receive any financial support for his study).

R&D Costs

In his section on pharmaceutical R&D costs, Light also touts the alternative estimates offered in a report by the Congress Watch division of the advocacy group Public Citizen (2001). However, the Public Citizen analysis is deeply methodologically flawed in ways that make their estimates seriously biased downward. Since we have already written about the report’s flaws in detail, we direct readers to our paper (DiMasi, Hansen, and Grabowski 2004).

One flaw in the Public Citizen report is echoed several times in Light (2007) and so is worth addressing in some detail here. Light maintains that our estimate of the cost to get a new molecular entity (NME) to market is not representative of new drug development costs because our sample excluded the (presumably lower) costs associated with all of the other new drug application (NDA) approvals made by the Food and Drug Administration (FDA) for a drug after it had obtained initial marketing approval (i.e., NME approval). These approvals, for the most part, are line extensions. Firms in this and in many other industries fill out their product lines for a basic product to better serve varied consumer needs and desires (e.g., oral solutions for children or adults who have difficulty swallowing tablets or capsules, more convenient dosing regimens, or different side-effect or efficacy profiles). In the case of drugs and the FDA statistics on NDA approvals, many of the approvals, in fact, are obtained long after the drugs have lost patent expiration by firms other than the sponsor of the original NME (often by small, specialty pharmaceutical firms or generic drug companies). Even leaving aside this substantive point about the makeup of the approval statistics, it is not appropriate to treat the incremental costs of later regulatory approvals associated with an active ingredient as though they were independent of the costs of obtaining the original approval. This would make no more sense than it would to take all of the R&D costs associated with developing a new automobile model and dividing that by
the number of trim lines of that model that the manufacturer happens to offer for sale and then use that as a measure of the R&D cost of developing a new automobile model.

Light incorrectly claims that we are currently working on cost estimates for individual line extensions and will then add them later to preoriginal approval costs. In fact, our published study of R&D costs (DiMasi, Hansen, and Grabowski 2003) already contains an estimate of the average cost for all postoriginal approval R&D, which was then appropriately added to preapproval costs to get an estimate of full life-cycle R&D cost per approved new drug ($897 million in year 2000 dollars on a capitalized basis taken at the point of original marketing approval).¹

Light (2007) also repeatedly makes the claim that $300 million is the median R&D cost per approved new drug for our data. There is no such figure in our study, nor does Light indicate how such a figure can be derived. In fact, it is impossible to construct a meaningful overall median value for these data because the R&D expenditures include costs for the bulk of new drugs that fail in testing at some point in the preclinical or clinical development process and therefore do not have costs for all development phases and because some of the early expenditures cannot be allocated to individual compounds.

Light (2007) also questions the data that we had on clinical trial sizes by comparing our average number of subjects per approved new drug to much lower figures given in Love (2003) and later updated on the Listserv belonging to the same group (Consumer Project on Technology, now called Knowledge Ecology International [KEI]). Light portrays these alternative averages as though they had been reported by the FDA itself. In fact, what KEI did was to treat whatever sample sizes they found reported in the “Clinical Studies” sections of the labels for FDA-approved drugs as if they represented the total number of subjects that had been included in industry clinical trials for the drug. What the FDA generally discusses in these sections of the label are the results for a few efficacy trials that were considered pivotal for the indication that was approved. The section does not necessarily note all phase 3 trials and typically excludes phase 1 and phase 2 trials. The result is that the KEI averages substantially underestimate the total number of subjects in industry trials. In a posting on the same Listserv that contained the KEI averages, one of us made these points and provided illustrative examples, using information in other documents.

¹. If one then wants to compare these costs to net sales, then one should look at total life-cycle sales for all product presentations containing the active ingredient.
parts of the FDA-approved label, that demonstrate unequivocally that the KEI numbers can be substantially off the mark (DiMasi 2006). Light also notes the clinical trial sizes postulated in a report on the development of a hypothetical drug for tuberculosis (Global Alliance for TB Drug Development 2001). However, this is a special case that was never meant to represent drug development as a whole, and there are numerous reasons why it should not be used to imply anything about clinical trial sizes or development costs in general. Our report critiquing the Public Citizen report also discusses the Global Alliance for TB Drug Development report (DiMasi, Hansen, and Grabowski 2004). In addition, as noted in our study (DiMasi, Hansen, and Grabowski 2003), our data on clinical trial sizes were consistent with those from another source whose estimates are not subject to the same methodological errors made by KEI (PAREXEL 2002).

**Profitability**

In his discussion of industry profitability, Light (2007) argues that the standard economic treatment of R&D costs as investment expenditures that create intangible assets is wrong simply because R&D expenditures are expensed on tax returns. One has nothing to do with the other. It is widely recognized that a more appropriate tax structure would require that R&D expenditures be capitalized and amortized over the life cycles of the products created as a result of that R&D. However, in light of the substantial uncertainties and arbitrariness that would arise in making a forward-looking assessment of the benefits that might be linked to current R&D expenditures, Generally Accepted Accounting Principles and other accounting guidelines take the most conservative route and allow for expensing of R&D expenditures. The desire of accounting guideline setters to be practical with regard to the tax treatment of R&D expenditures says nothing about how a proper economic analysis of past R&D expenditures should be conducted.

Finally, Light misconstrues industry data when he argues here and originally in Light and Lexchin (2005) that lower prices in the United Kingdom and Canada have no negative impact on R&D and that these countries cannot be called “free riders” because local R&D expenditures as a share of local sales is purportedly greater in these countries than in the United States. The markets for pharmaceuticals are typically global,

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2. Foreign free-rider arguments are more accurately referred to as “cheap-rider” arguments (Scherer 1993).
as is the R&D that creates products for those markets. This renders comparisons between local R&D expenditures and local sales meaningless. A relevant metric would be based on contributions to global quasi rents (revenues minus variable costs). Specifically, the metric would be a country’s net sales as a share of global net sales considered on a per capita basis. It is widely thought that the United States contributes most of the pharmaceutical industry’s profits in absolute terms, let alone on a per capita basis. Furthermore, Light’s arguments suggesting that drug companies could make up for the imposition of European and Canadian level prices in the United States by reducing marketing expenditures while maintaining or increasing R&D expenditures are specious. If firms can increase profits by simply reducing marketing expenditures when prices are lowered, then they could also increase profits by doing so now at current prices. In other words, Light’s implication could only be true if firms do not currently set their marketing expenditures so as to maximize profits. We doubt that Light would make that argument.

References


3. Ironically, at later points in both Light (2007) and Light and Lexchin (2005), the authors seem to acknowledge the global nature of pharmaceutical research and development (R&D) and sales, even though this conflicts with their earlier free-rider arguments.


