Author's response to reviews

Title: Novel affordable medical devices: case studies of innovative companies from India

Authors:

Szymon Jaroslawski (szymjaroslawski@o2.pl)
Gayatri Saberwal (gayatri@ibab.ac.in)

Version: 4 Date: 1 April 2013

Author's response to reviews:

1 April 2013
To,
The Editor
BMC Health Services Research
Re: Covering Letter

Dear Ms. Pafitis,

Please find enclosed a revised manuscript ('Novel affordable devices and diagnostic kits for the Indian market.' by Szymon Jaroslawski and Gayatri Saberwal) that takes into account the comments of the two referees. Our response to each is as follows:

For referee 2
(http://www.biomedcentral.com/imedia/1163589261934216_comment.pdf):
All suggestions have been addressed in the revised manuscript.

For referee 1
(http://www.biomedcentral.com/imedia/2129347999931852_comment.pdf):
A detailed response to each comment is appended below.

Both authors have approved the version being re-submitted, and the response to the referees.

Yours sincerely,

Gayatri Saberwal

Dr. G. Saberwal, Faculty Scientist
Institute of Bioinformatics and Applied Biotechnology
Biotech Park, Electronics City Phase I
Bangalore 560 100
Response to reviewer 1 appended below.

Response to reviewer 1, where the yellow highlighted portions are the queries.

1. In the abstract, last sentence, it is stated “We have sought to understand what enablers and barriers they [the companies] encountered.” To what end is this understanding sought? How will this information be used? Notwithstanding, this is an original piece of work to the extent that such case study-type investigations have really only been done with respect to pharmaceutical producers and not for makers of medical devices. However, the paper would take on added value and importance if additional information is included.

The purpose of this study was to understand what have been the barriers and enablers for the few innovative medical device companies that exist in India today. The importance of such ventures is explained in the introduction. However, due to the novelty of commercial biomedical innovation in a developing country, there are few objective studies that shed light on the process, with most of the available material being company-sponsored publications or case studies.

Therefore, the purpose of our study was to present, in an objective manner, examples of IP-based firms that develop devices “in India and for India”. Because of obligations to their investors, these for-profit companies typically have little freedom to talk publicly about their challenges and obstacles. We have also observed that there is little information sharing between companies and each seems to work in isolation. We think that insights from our study will be useful in two ways: (i) similar companies may find herein an inspiration on how to tackle similar problems and (ii) government agencies (or other national or international bodies) that wish to promote the biomedical industry in India will hopefully make use of the findings as they develop suitable financial and other (push or pull) policies.

We believe that suitable government policies would enhance the efficiency of product development in such firms, thereby contributing to affordable healthcare in India and elsewhere.

2. Further, I struggled with finding a clear conclusion to this study. As written, and I am guilty of this as well, the conclusions look like a list of barriers and enablers, none of which seems unique to the medical device industry. There is also a 'wish list' of recommended policies (e.g., strengthen capacity and interdisciplinary work culture of the national device regulatory body, institutionalize health care payers and medical councils and associations). I would be more impressed, and I think it would add tremendous value, if authors could do at least a rudimentary stakeholder analysis (See for instance, http://www.who.int/workforcealliance/knowledge/toolkit/33.pdf) to provide an in
depth analysis of stakeholders/agendas/strengths/weaknesses.

We agree that a stakeholder analysis would be a much needed tool that could inform the development of future innovation policies in India. However, this study was not focused on the opinions of various stakeholders of the industry, which would be an entirely different study. [Even the 40 preparatory interviews were not meant to perform a stakeholder analysis, but to provide the background about an industry that the authors didn’t know much about. Along with other materials specified in the methodology, these early interviews helped us to identify the six case study companies. The results of these interviews are not included in our article, and this is now clarified in the methodology.]

The study was focused on the six selected 'case study' companies, and understanding the barriers and enablers to their novel activities were clear goals of the study. As such, the conclusion must relate to these goals.

As detailed in the introduction, we sought to understand the entrepreneurship and product development angles of IP-based medical device startups. The main conclusions, as mentioned in the Conclusion, are as follows:

1. Innovation in the medical device industry in a developing country is indeed feasible, and at a speed comparable to that in industrialized countries.

2. The availability of both funding and the human resources necessary to access the market with finished products (but not to do R&D) has been one of the major impediments to the companies. There are no local viable markets for such products, since there is high fragmentation (with no centralized 'market access point' such as NHS, and few consolidated insurers) and no national/state guidelines for the use of a new device). This makes market access a much more costly and lengthy process than R&D.

3. These companies have strong links to Western industry and academia.

4. The lack of local regulatory guidance posed a major challenge for product development (as opposed to regulators being considered a market access hurdle). Also, for these companies, the FDA, EU or WHO are not easy to work with due to high costs and distant location.

5. The low price of products is not always an advantage: the for-profit nature of the private sector demands that when pricing their products the firms need to keep in mind both (i) the affordability for the patient and (ii) the provider’s desire to generate profits.

We believe that these conclusions reflect non-obvious subtleties about the reality facing such innovative biomedical companies, and indeed are unique to the situation because (i) this kind of innovation in developing countries is a new phenomenon and (ii) the role that the regulatory agencies play, or need to play, in medical product development is often underestimated.

3. I am not really qualified to comment on details of qualitative case study
methods. However, I note that the references cited as “used by others to study medical innovation in developing countries [8, 14-16] ...” (Methodology section, first sentence) were all developed for pharmaceuticals. This raises for me the basic question of whether or not the different business models of a medical device vs. a pharmaceutical should be discussed somewhere in the paper. Indeed, these different business models may be a major driver of the results of this study. The biggest difference is the extremely rapid medical device product development cycle (certainly as compared to pharmaceuticals). Do the authors think this has an impact?

It is not very clear to us what the Reviewer is asking for.

(i) In case he is questioning the 'case study' methodology: We believe that this is appropriate wherever such companies are rare, since there aren't enough companies to do a large-scale cross-company analysis. Further, the presented companies are heterogeneous in terms of their origin, business structure and financing, as well as their products, reducing further the 'n' of each type of company. Finally, even in the case of medical devices, innovation is a complex process of trials and errors. This business risk is somewhat reflected in the fact that, as in the case of pharmaceuticals, the global medical device industry has not invested in the development of products intended for use specifically in what they perceived as uncertain or small markets. Therefore, we chose the case study methodology in order to capture the rare innovation successes and study the various paths the firms have gone through while developing new products. Nevertheless, the Methodology section has been rewritten to account for this query.

(ii) In case the Reviewer wishes us to compare the business models of device development and new molecule development in a developing country, we feel that this is premature, since no Indian company has come out with a totally new molecule, developed from scratch within the country, although a handful of companies have such molecules in trials. It is thought possible that in India all preclinical work for a new drug can be done for about $10 million, and clinical trials are expected to cost another $20 million to $50 million, depending on the indication (unpublished data with the corresponding author, based on a different set of interviews with small and innovative, drug-developing firms in India). However until a new drug actually reaches the market, and other aspects of the business model(s) are worked out, we cannot comment on this.

4. In the Methodology section, first paragraph, the authors initially did 40 interviews and then selected six companies based on several sources (BioSpectrum India Life Sciences Resource Guide 2010 etc.) but that begs the question as to what criteria were used, i.e., the largest sales by volume? Value? highest ROI? Highest profit? lowest debt ratio? This should be made clearer. Regarding the methodology section, final sentence, I wonder if the authors used any type of software such as NVivo® (http://www.qsrinternational.com/products_nvivo.aspx ) to “code” responses or develop various domains of knowledge or understanding. Essentially, I am
asking if there was any analytical process to parse out and classify the material from the interviews?

We agree that our Methodology calls for clarification on how the six companies were selected. We provide this below, and in the revised article:

Since none of the firms had achieved significant sales at the time of our research, financial measures such as profit, volumes or return on investment could not be used. Nor were details of debt or equity available for the (largely) privately held companies. We selected medical device firms located in Bangalore, arguably the most innovative biomedical hub in India, which were developing innovative, IP-based products for the Indian market, and low-resource settings in particular. This selection was based on The BioSpectrum India Life Sciences Resource Guide 2010, reference [17] and information from the preparatory 40 interviews. In the one situation where two companies with similar profiles were identified (that is inception or origin, type of product, development path) the company that was further in the product development process was chosen.

We thank the reviewer for the suggestion that we consider using software to analyze our interviews. This could be useful for our other projects where data from many more interviews is analysed.

Generally, I think they are well balanced and overall are based directly from the data. I have several questions/issues in this regard as follows:

First paragraph of Conclusion: “Although FDA, CE and WHO certifications are an alternative, the high cost of such procedures...” Please provide evidence and a reference for this assertion.

This was one of the results of our study. The sentence now reads:

“Although FDA, CE and WHO certifications are alternatives, the interviewed companies assert that the high cost of such procedures and/or distant location of these agencies are serious obstacles and result in delays.”

Last sentence of Conclusion: “Because of the complexity of such settings, accessing the market requires ground-breaking strategies also in the post-R&D phases of the product lifecycle.” I do not understand this sentence. Have I missed a discussion of these "ground breaking" strategies already in the text? What does “ground breaking” mean in this sentence?

Supplementary Table 6 contains details of the market access challenges faced by the six companies, and some of the solutions that they have developed. Overall, however, market access remains the key obstacle for such companies and will require further innovation to be overcome. Consequently, our discussion argues that as opposed to the common belief that innovative R&D is not possible in a country like India due to various shortages of skills and funds, it is the lack of viable markets for such innovative products that remain the real challenge today. The phrase now reads:
“This market complexity implies that the commercial success and survival of such companies will depend on their ability to develop ground-breaking strategies in the post-R&D phase also.”

Can the writing, organization, tables and figures be improved? I have some specific comments about this, listed below. I notice there is no “Results” section as labeled. The ‘results’ appear to start with the section called “The companies and their products”.

This is now corrected.

Third paragraph of “Background”: perhaps the authors could define “health technology assessment”

The term is now defined.

Fourth paragraph of “Background”: “In contrast, India doesn’t have a formalized national HTA process, the public health system is generally underdeveloped and not very open to new technologies...” Possibly correct, although arguable, but what is the evidence for this sweeping statement?

A suitable reference has been added to the phrase and the statement that “the regulatory body is not accustomed to licensing innovative products that have not been approved in a developed country” has been shifted to the Results/Experience with international regulatory authorities. This was the opinion of the studied companies. It is also a view that the corresponding author has heard on other occasions, from other companies and from senior academic scientists associated with the decision making process of the regulator, which is grossly understaffed.

5. Section called “Companies and their products”, second paragraph. The discussion about “… an independent assessment of the needs of health-care providers” may well be the most interesting and original part of this paper. It could be very informative and original.

How these companies ascertain "unmet medical need" with regard to devices? Much of this information is behind closed doors. Any insight into this so-called "market- and consumer- research" from a public health viewpoint is most interesting. What kind of “market” is there if most people pay out of pocket? Some more insight into what GEH did in their surveys would also be relevant.

We agree that much of the information on how product profiles are constructed is kept confidential by for-profit companies. In spite of the fact that the studied companies gave us candid interviews, they did not share with us the exact design, or results, of these surveys. However, as we explain in the Methodology and Introduction, this paper focused on companies and their evolution rather than on the detailed technical specifications of their products. We hear that there is a shortage of reference books on product design for low-resource settings, but our article does not attempt to fill this gap.
What we believe is informative and original is the description of the path that the Indian firms followed in order to design their products. This path was very different from that in the West. First, it is rare in the Western industry to start the design of a product with a low-resource user setting in mind. This has implications both for technical ruggedness and for price point. Second, because this is a virgin market and little is known about such settings, each company had to undertake original field research for its proposed products. Third, the research and subsequent design of product profiles was undertaken independent of any guidance from regulatory or coverage bodies.

Separately, we wish to clarify that in India 60-80% of healthcare expenditure is out-of-pocket (reference 11 in the manuscript). Thus, there is certainly a market, although it does mean that many people receive sub-optimal or no healthcare due to the costs.

Supplemental Table 3, in my view, is very interesting and somehow should be incorporated more in the text.

We are delighted that the reviewer is of this opinion. However, because of limitations of space, we are unable to shift it to the main text. We believe that readers with different backgrounds will find different parts of the text particularly interesting and so we have refrained from over-emphasizing any one angle. However, if the reviewer insists, and the resulting longer piece would be acceptable to the journal, we could include the table and a suitable discussion in the main article.

What about issues of intellectual property relevant to these companies? I assume there is no information here on the IP policies? Is India the only country where patents were filed? Almost NOTHING known about this subject for medical devices (as opposed to medicines).

We have now included the following statement in the manuscript, at the end of 'The companies and their products'): All the firms filed patents, in India and in other countries. There was a general tendency to first file the applications in India and then in the US and Europe. However, we formed the impression that the young companies did not have an established IP policy.

6. In my view, Table 1 already contains more information but it could be re-formatted which will force the text to be more focused. Have more columns than just the products, e.g., product/sources/IP issues/collaborators.

As clarified above, we think that different readers will find different parts of study more interesting, so we refrain from emphasizing any particular angle (such as IP or collaborators). Due to limitations of space, the main text is a general description of companies with references to details in Supplementary tables.

The last sentence of the section called “Experience with international...” talks about “high uncertainty related to the Indian public market”. I assume this is the ‘uncertainty” mentioned in the next section? If not, then this should be clarified
somehow.

Yes, this is the same uncertainty. This has now been clarified at this first mention.

7. In the “Policy implications” section, the authors should think about discussing this ‘wish list’ a bit more (see comment above about a stakeholder analysis). “...The process should be made more transparent through the incorporation of explicit evidence based decision making...” Such as? Any models in other countries? NICE in the UK? Is this likely to happen in India? “novel regulatory mechanisms...”

That begs the question, do the authors have any ideas about this? Do the authors have suggestions? Are other countries thinking about this?

We have now rewritten this section to address these questions.