

CAPITAL COSTS, COST EFFECTIVENESS OF HIV APC, AND SPEED OF VACCINE DEVELOPMENT

Comment to the Commission on Intellectual Property Rights, Innovation and Public Health Open Discussion Forum, 10 December 2004

As a previous poster to the forum correctly pointed out, the idea of APCs is to encourage “large companies to invest their own resources and even encourage VCs and other funders of the small companies to help support their R&D efforts”. As a financial economist (and capitalist) I take the view that pharmaceutical firms and VC firms are not charities and would be looking for a ‘fair return’ on such investments; that is a return that compensates for ALL risks of such investment. In this case, being a high-risk investment, this would need to be a high return, and potentially form a large proportion of any APC payment, as I will demonstrate below.

I would very much appreciate it, therefore, if those who have evidence on the private capital costs of pharmaceutical firms and venture capital firms when investing their own resources into R&D for HIV vaccines, could please indicate where this evidence is to be found. It would be fine if the data were provided in the form of the per-year required rates of return on financial capital, taking into consideration ALL risks, including (amongst many other things): the risks of HIV vaccine science and the likelihood of ever getting a vaccine; the risks of not internalizing the results of privately-funded research for oneself (especially if data has to be shared or the vaccine turns out not to be a pure vaccine but instead a composite vaccine); the perceived risks of the APC mechanism itself (‘mechanism risk’); etc. Early and ‘complicated’ vaccine R&D would attract especially high rates of capital cost because all of these risk factors are much greater than for late and less ‘complicated’ vaccine R&D, as well as being compounded over much longer periods.

Since – for an HIV APC to actually work – *all* of this capital cost needs to be *fully* repaid eventually by taxpayers and philanthropic foundations through the APC, it is an important piece of empirical evidence for working out both the level at which to fix the HIV APC in advance but also for evaluating its cost-effectiveness compared to alternatives. I presume the figure or figures must be being fed into the current calculations of HIV APC figures, but I have not found them yet anywhere in the literature.

Please, can these figures be placed in the public domain? Without the figures, one can only guess, something that I will now do (all figures below are nominal,

i.e. not adjusted for inflation, and I would welcome them being challenged and recalculated in light of the actual evidence):

One would imagine that the stock market and venture capitalists would take the view that current HIV vaccine research is a particularly speculative investment – especially in the first five years or so (maybe even much longer) after an HIV APC might be fixed. It seems reasonable therefore to presume that the required rate of return on financial capital would be much higher than, say, the required rate of return calculated by TUFTS for drug development – a nominal rate of 14%-16%, with a mean of about 15% – by the very same large pharmaceutical firms now being targeted with HIV vaccine APCs. Is this a reasonable statement to make?

Let us presume for the moment that there are no layers of crowding out in the workings of an HIV APC (highly unlikely). If the required nominal rate of return to financial capital invested in early-stage HIV vaccine R&D was 25% (not outrageously high compared to speculative investments that VC firms normally make, but is it too high for this case? Or, indeed, too low?) and the average expected horizon until repayment was 10 years (given my understanding of the state of HIV vaccine science, this is being generous I would imagine, though it also depends on what is being done on the ‘push’ front), then each dollar of early pull-induced private R&D would cost about \$7.5 of eventual APC payment; that is, each \$1billion of promised APC would pay for about \$133m of early out-of-pocket research costs. So, you can see, getting a hold on the figure for capital costs (and risks) is quite important.

If there was ‘crowding out’ too of, say, half then this would lead to \$1billion of promised HIV APC paying for about \$66.5m of genuinely *additional* out-of-pocket early private R&D. ‘Crowding out’ would show up (amongst many other things) in an inability to *only* pay for privately-funded R&D and to separate out and NOT pay for non-privately funded R&D through the APC, OR an inability to generate genuine ‘addition’ to the vaccine market by preventing vaccine purchases made outside of the APC mechanism from benefiting from the APC mechanism - something that would be especially difficult to achieve for HIV vaccines. In this case, it only has to crowd out \$66.5m of out-of-pocket research expenditure. So, a notion of likely levels of crowding out would be very useful too. Again, I presume the figure must be out there entering into current calculations, and it would be useful to have it in the public domain.

As you can imagine, extending the expected horizon to 15 years or increasing the required rates of return to financial capital or increasing the levels of possible ‘crowding out’ creates increasingly dire looking figures.

It is important to get a handle on these figures, since if the ones above are even remotely correct, some of the current PPP-financed activity starts to look much more of a cost-effective way to direct fresh government (and G8) and foundation funding in the near term. Indeed, it is not clear why large pharmaceutical firms themselves would even prefer to be stimulated in the current environment by an APC.

If this is the view taken, then it becomes even less pressing to set the terms of an HIV APC any time in the near future before good information is available on how to permanently fix the terms (a permanent fix is needed to make an APC credible and to keep its risks and private capital costs down); it would be doing hardly any cost-effective pulling in the near-term (for example, if a \$10billion HIV APC were permanently fixed yet could only generate at most \$665million - \$1billion or so of genuine additional early private R&D, then the most likely reaction of private firms and venture capitalists would be to hold off R&D, and, indeed, to simply not trust that the mechanism would ever work to repay them anything they spent early on), yet it would impose higher costs by being prematurely set (other financial economists will spot that there is an expensive option-price component in fixing the terms of an APC *now* before much of the information is available on how to efficiently and correctly set it).

Even if policy-makers wished to fix APC terms now, expecting little activity in the near-term but intending that the APC be 'in place for later when it matters', it would be impossible to do so 'correctly' and cost-efficiently without resolving the relative rôle of other parts of the mechanism first. Even then, fixing now when there is no urgency to do so is not even a good idea given that policy-makers would lose the flexibility to learn from, evaluate, and scale up the much more collaborative approaches that are more likely going to be needed to generate HIV vaccines (and this itself would help to more efficiently set a later-stage HIV APC as and when a vaccine is looking much more likely).

Obsessing about an early HIV APC for the next seven months – running up to the G8 summit – to the exclusion of obsessing about the other, perhaps more difficult and collaborative, parts of the R&D framework, will put private investors off *even more* since they will come to understand (and price in to their investment decisions) that the risks of ever getting an HIV vaccine are so high, and the expected time to delivery so far off, that all the figures discussed above have to be multiplied so many fold that there is even less incentive to engage in early HIV vaccine research. I would urge those lobbying hard for an 'early' APC for HIV to the exclusion of lobbying for the collaborative parts and 'front-loaded' parts of the approach to developing a high-quality HIV vaccine, to reassess whether it is the wisest use of their influence and not, in fact, counterproductive.

The advice (for what it is worth) that I would give to those pushing heavily for an HIV APC would be to concentrate on APCs for all the late-stage areas in which they might have some strength (pneumococcus and rotavirus and many of the currently existing, but underused, vaccines such as measles, Hib-related diseases, pertussis, tetanus, etc.), where the scientific risk is relatively low, yet the market risk very high, the capital proportion of APCs (relatively) low, and the advantages of APCs in creating more certainty high. Later, use the experience gained from this to work out how APCs might ever work for complicated vaccines such as HIV. Meanwhile, if anything, totally downplay APCs for HIV, and instead push home to policy-makers that they need to bite the bullet about paying for up-front HIV vaccine work through a much more collaborative system than we now have. The hugely positive signal of success on the APCs for the diseases listed above, the credible knowledge that they will work and be used again, coupled with the bullet-bitten approach of policy-makers to doing something about driving HIV vaccine work forward and the front-loaded funding needed to do it, will make eventual HIV APCs – if ever they are used for HIV vaccines – more powerful, cheaper, and easier to set.

The way things are going at present, we will finish the G8 summit in July with policy-makers patting themselves on the back that they have \$20billion of APCs in place, but none of the really difficult and powerful parts of the mechanism for driving HIV vaccine development in place.

I would very much appreciate seeing some of the evidence discussed above.

Thank you, and good wishes,

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<http://www.economics.ox.ac.uk/members/andrew.farlow/> for papers on this issue.