Modelling the antibiotic development process

In order to quantify the effects that different types of incentive would have on the development pipeline for antibiotics, we developed an economic model of the drug discovery process. This builds on similar efforts by the Eastern Research Group (ERG) in the US[1], and the Office of Health Economics in the UK.

Our model is not intended to perfectly represent the highly complex drug discovery process, as obviously each drug and company will be different. However, it was designed to help determine the relative effectiveness – and cost effectiveness – of different policy interventions to stimulate antibiotic development.

Cost and revenue assumptions

In gathering information for this process we sought data on the typical costs of the antibiotic development process (including marketing, manufacturing and regulatory costs) from a number of sources:

- IMS Health UK;
- a literature review; and
- large and small pharmaceutical companies.

Data on typical estimated antibiotic sales volumes and revenues were provided by companies. Both costs and revenues will differ significantly by drug, but we worked with the companies involved to establish ranges reflecting typical development costs and patterns of sales[2].

Non-cost development assumptions

The model's underpinning assumptions for factors other than development costs and revenues were defined on the following basis:

- Based on the ERG report and academic literature, we assumed that the annual discount rate used by a company would be 11%.
- The typical duration of each phase of the R&D process came from information we were given from pharmaceutical companies and ERG.
- The probability of success of each stage of development was based on research commissioned from IMS Health (on observed rates of success), and those assumptions used by the ERG modelling. In our base case we used an average of these two approaches. We felt that the IMS data may overstate the probability of success in the development of *novel*

[1] Sertkaya et al 2014

[2] Several companies generously shared data on development costs and sales projections which they regard as commercially confidential. This has been invaluable as part of the modelling process, but we are limited to publishing this data on an aggregated and non-identifiable basis.

classes of antibiotics because most of the drugs in their sample were follow-on products (reflecting patterns of antibiotic research in recent years.)[3]

What the model does[4]

Firstly, this model allows the user to choose a high, medium or low setting for all the assumptions on R&D cost, probability of success and discounting rate. Depending on these settings, the implied cost of buying out the patent of a drug changes, as does the cost of rewarding the drug developer at the end of the process.

Secondly, the model allows the user to assess the impact of different interventions on the total cost of drug development.

Thirdly, the model can forecast the cost of a complete market buyout. where drugs are then sold at cost, and a hybrid model where there is a lump sum in addition to sales.

Summary of inputs

Outlined below are the inputs used in our model. These assumptions are based on the sources outlined above, and represent what we believe is currently spent on typical development projects in these areas.

Length of trials

Phase	Length of trials	Time between phases
Preclinical	5 years 6 months	none
Phase one	11 months	3 months
Phase two	1 year 1 and a half months	6 months
Phase three	1 year 10 months	6 months
Approval	9 months	none
Post-approval paediatric and follow on trials	3 years	none

Probability of success

	Base case assumption Average of other two assumptions	ERG modelling assumptions	IMS observed data
Preclinical	17.3%	35.2%	9.3%
Phase one	33.0%	33.0%	33%
Phase two	59.3%	50.0%	75%
Phase three	75.8%	67.0%	85.7%
Approval	79.7%	85.0%	75%

[3] IMS data may also exclude some preclinical stage failures, leading to a tendency to overestimate the probably of early stage success. However we felt that this bias may be offset by the exceptionally high rates of failure of antibiotic discovery based on genomic screening, which may account for a disproportionate number of projects in their sample.

[4] We have made the model available in Microsoft Excel format.

Research costs

	Base case assumption	Lower bound estimate	Upper bound estimate
Preclinical	$10,688,946	$10,033,419	$12,814,435
Phase one	$10,072,046	$6,982,404	$15,082,141
Phase two	$26,312,760	$17,273,318	$47,221,654
Phase three	$96,295,600	$64,919,901	$117,874,527
Post-approval paediatric and follow on trials	$146,295,599	$114,919,901	$167,874,527
Notes	Based on the average input we're given from eight different sources	This was the 25th percentile from the inputs	This was the 75th percentile from the inputs

Other costs

Approval fees	**$3,676,466**
Marketing costs (for life of drug)	$401,000,000
Basis	Based on a literature review and discussions with industry experts