International Programme for Microbicides (IPM)

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Financing Mechanisms for Microbicide R&D and Future Introduction

Final Report

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TABLE OF CONTENTS

ABBREVIATIONS

AMC	Advance Market Commitment
ARV	Anti Retroviral
BMGF	Bill and Melinda Gates Foundation
DFID	Department for International Development (UK)
EC	European Commission
GAVI	GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunisation)
GDP	Gross Domestic Product
GFATM	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human Immunodeficiency Virus
IDA	International Development Association
IDPF/UNITAID	International Drug Purchase Facility
IFF	International Financing Facility
IPM	International Partnership for Microbicides
MDG	Millennium Development Goal
ODA	Official Development Assistance
OTC	Over The Counter
PEPFAR	President's Emergency Plan for AIDS Relief
PMPA	Tenofovir
PSI	Population Services International
STI	Sexually Transmitted Infection
TB	Tuberculosis
TMC120	Dapivarine
UNAIDS	Joint United Nations Programme on HIV/AIDS
USAID	United States Agency for International Development
VAT	Value Added Tax

EXECUTIVE SUMMARY AND KEY MESSAGES

This report uses a scenario planning approach to explore possible cost ranges for the introduction of future microbicides. Although no microbicide has yet been registered for use, several products are currently in clinical development. Three 'first generation' microbicides are presently in, or completing, phase 3 clinical trials. These are all gel based and must be used each time sexual intercourse takes place ('coitally dependent'). The data from the first of these trials will be available by the end of 2007, with results from the other two trials anticipated by 2010. A 'second generation' of products are currently in safety trials. These products are based on topical antiretroviral drugs and are being developed in a number of non-coitally dependent formulations.

In advance of the availability of a registered product, no attempt is made in this paper to model the uptake of a future microbicide based on the complex relationships among, and assumptions about, effectiveness, cost, financing, delivery approaches and consumer demand. Rather, the scenarios used in this paper are based on assumptions about countries which are likely to be among the first to adopt a future product and the actual experiences of the introduction of other relevant health commodities aimed at a similar target population (sexually active women).

It is important to note that this paper does not look at the benefits of microbicides or the relative benefits of different microbicide products. Only total costs are examined, with no analysis of relative cost-effectiveness between potential microbicides or with other HIV prevention approaches

As a starting point, it is assumed that the developing countries participating in the current phase 3 microbicide clinical trials will be among the first to introduce future products. Three uptake scenarios – slow, medium and fast - for introduction and uptake volumes of a future microbicide over a 10-year period have then been derived from experiences of introducing female condoms and injectable contraceptives in developing countries. Assumptions about unit product costs have been based on current costs associated with microbicides in clinical trials. Programming and delivery costs have been based on those associated with the delivery of male and female condoms and injectable contraceptives.

Using data from these commodities to develop more or less aggressive possible uptake trajectories for future microbicides, the baseline scenario suggests that **microbicide programme costs may be of the order of $118m per annum by year 10** in the eight countries considered in this analysis but could up to $284m if uptake is rapid in all countries in which initial introduction takes place. It could be as high as $275m under the medium uptake scenario if the product is introduced throughout India rather than being concentrated in four southern states as assumed under the base case. Costs would increase if more countries introduce microbicides or if broader national roll out is undertaken in very large countries, such as India.

Projected Annual Costs of Early Generation
Microbicide Introduction
according to the different demand uptake scenarios
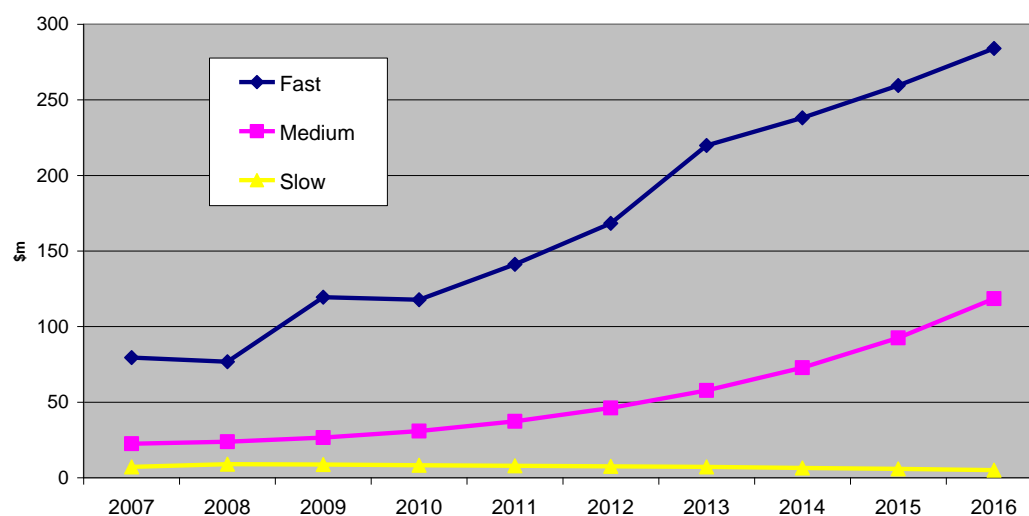
As can be seen from the graph above, the results are highly sensitive to the uptake assumptions being made. These cover a range of issues and will be influenced by a range of policy decisions which will need to be thoroughly scrutinised. They range from assumptions about the choice of countries of first introduction and patterns of subsequent country adoption (p10), to the impact of possible reductions in product or programme costs (annex 2) and to patterns of sexual behaviour in the general population (annex 1/table 2). The results presented here are dependent on rates for microbicide uptake being similar to the experiences of the commodities chosen to guide this analysis. To some degree this assumes that financial, structural and system factors are as least as important in determining product introduction, uptake and use in developing countries as product characteristics; there are many health technologies that could improve health in developing countries but which are constrained by limited financing or poor health infrastructure.

Key Findings

Firstly, it is likely that **it will take time to reach relatively modest coverage levels** of women of sexually active age in the developing countries considered. This will partly reflect historical financial and system constraints to the introduction of new health technologies but also more consumer driven factors – it take time to build demand for new products. The impact of current international efforts to rapidly scale-up HIV responses and improve health in developing countries may present opportunities to achieve more aggressive introduction objectives, but this is difficult to predict and will require ongoing analysis as these efforts unfold.

Secondly, based on available unit cost data for microbicides currently in clinical trials and programme costs for other commodities, **product costs will represent a relatively large proportion of overall programme costs**. This is true for both early generation and next generation products, with the latter representing – at current estimates for unit costs – higher overall costs. This finding suggests that achieving economies of scale in microbicide manufacturing will play an important role in reducing costs over time. The size of the potential market plays an important role in

influencing decisions about investment in manufacturing capacity. The size of the market for microbicides in the 8 countries included in this study would be around $330m over the first 10 years under the medium uptake scenario. Introduction in additional countries or wider national use in very large countries, such as India, would increase this market size.

Thirdly, as product costs are likely to represent a relatively high proportion of overall costs, **there will be scope for continued subsidisation of product costs** – including in more commercial distribution networks - **to ensure they remain affordable for potential users**. Charging users may be one way of reducing net introduction costs to the public sector but runs the risk of reducing demand, especially among poorer and more vulnerable groups, which is likely to run counter to many programme goals.

Fourthly, past experience with other sexual and reproductive health commodities suggests that **there will be a need to rely heavily on donor funding, at least in the initial stages of introduction**. The scale and predictability of donor funding for future microbicides are thus likely to be key factors determining the goals and success of introduction programmes..

Fifthly, reliance on domestic Government funding is likely to be more sustainable and predictable but it is not clear how realistic this might be given increasing strains on country budgets. Shifts in donor funding to general budget support approaches might facilitate a shift to higher levels of domestic budget financing. However, such funding is, by definition, not earmarked, and may not send sufficiently strong demand signals to potential manufacturers to secure commitments to high volume microbicide production. This trend is likely to be more relevant for some donors (e.g. DFID, Nordics) than others (e.g. GFATM and the US where funding is likely to remain heavily earmarked).

Finally, while this paper does not set out a comprehensive argument making the investment case for future microbicide introduction, it does demonstrate that the costs of introduction will merit early consideration of both the evidence base that will required and the financing mechanisms that will be needed to support introduction decision making and implementation.

INTRODUCTION

This paper is intended to aid thinking around the introduction of microbicides. It does not attempt to predict the future. That would be premature – an effective microbicide has yet to be developed and the timing and characteristics of any such product are, as yet, uncertain. Rather the paper attempts to map out a series of possible scenarios to explore one factor that will be important in planning and implementing microbicide introduction - cost.

No microbicide products have yet been approved for use. Consequently, there is no historical demand or cost data available for microbicide programmes on which to draw. Instead, this paper builds on the experiences of the introduction of a number of other health commodities in low income countries that share some characteristics with microbicides. The cost ranges presented here are therefore premised on the assumption that microbicides introduction, uptake and use will follow similar patterns to these commodities. The paper examines total and constituent costs of possible microbicide introduction scenarios over time and makes a number of observations on how these relate to possible financing instruments and other policy decisions.

As with any scenario planning exercise, the results of this study are determined by the underlying assumptions. These are clearly open to challenge and, indeed, we welcome this. The model developed is not intended to be a definitive analysis of microbicide introduction costs, but a useful planning tool that can contribute to an iterative discussion that can be strengthened as more information on actual products becomes available and as understanding of the contexts into which they will be introduced evolves. In order to facilitate this we have been explicit about the assumptions used. An outline of the methodology is presented in the main report and details are given in the various annexes.

This report focuses solely on product and programme costs. While these are clearly important for planning, they are not in themselves sufficient. It is beyond the scope of this paper to model the potential benefits of future microbicides in improving the effectiveness of HIV prevention programmes, nor to look at the cost-effectiveness of different microbicides or in comparison to other HIV related services.

1. OVERVIEW OF MICROBICIDE DEVELOPMENT AND RATIONALE OF REPORT

Microbicides are products currently being developed with the aim of reducing transmission of Human Immunodeficiency Virus (HIV) during vaginal intercourse. Microbicide products could potentially take the form of gels, creams, films, tablets, sponges or be contained in a vaginal ring. One 'early generation' microbicide has recently completed in phase 3 efficacy trials, with data due to be reported late in 2007. Two further 'early generation' microbicide are in phase 3 efficacy trials, with results expected before 2010. These products utilize a similar mode of action to prevent HIV transmission. They must all be used each time sexual intercourse takes place ('coitally dependent') and they are formulated as gels delivered intra-vaginally using some form of applicator.

A 'next generation' of microbicides, that utilize a different mode of action, are also in development, with one proof of concept efficacy trial now underway and others in safety trials. These products are based on the topical application of antiretroviral drugs that are highly active against HIV. They can be formulated in a number of different ways including as daily or longer acting products.

The aim of this report is twofold. Firstly, based on comparisons with the experiences of existing health commodities used in developing countries, plausible cost ranges for different microbicide introduction and use strategies are developed. Secondly, the implications of these costings for the possible financing of microbicide introduction are discussed.

2. COSTS OF INTRODUCING MICROBICIDES

The overall aim of the costing analysis is to initiate discussion related to the eventual resource needs for the distribution of microbicides, once an effective product has been identified. While longer-term estimates for the cost of scaling up comprehensive HIV responses have been developed in recent years, these do not generally include the costs associated with new technology introduction.

There have been previous estimates related to costs or potential market size of potential microbicide products. This section first reviews the methodological approaches previously used and then presents the methods and results for this current study.

2.1 Scenarios for the Initial Introduction and Scale-up

Previous studies have aimed to make the broad economic and public health case for investment in microbicide research and development. In general, while these studies covered both costs and benefits, they used simplified assumptions regarding the scale and speed with which future microbicides would be introduced and adopted at country and global levels. This study differs in that it only addresses costs and focuses particularly on plausible scenarios for the scale and speed of introduction of a future product. By developing scenarios based on the introduction and use of existing health commodities the study does not focus on how the specific characteristics of a microbicide, such as efficacy or price, will affect demand. For each of the scenarios developed, it is assumed that there will be a ready supply of an microbicide, that it is effective enough to be introduced and that financing is available. The study does not address the relative merits of different products or the relationship to other HIV prevention approaches.

The key assumptions underlying two base cases and the additional sensitivity analyses are highlighted in the table below and explained in the following sections (or in some cases in the annexes).

Table 1: Summary of Key Assumptions

	Base Case – Early Generation Product	Base Case – Next Generation product	Sensitivity Analyses
Product Characteristics	Coitally dependant	Long-lasting delivery method (30 days). Non-coitally dependent	Daily method; Non-coitally dependent
Time Horizon	10 years	10 years	
Country Coverage	Countries with phase 3 trial (Aug 2007) and potentially key countries for HIV prevention All countries begin in year 1	Same	Phasing of initial countries in years 1, 3 and 5 Broadened to allow wider country roll out
Population Group	All women aged 15-49 in urban areas	Same	Assumes uptake in rural areas
Uptake	Fast, Medium, Slow 90% of women 15-49 are sexually active, 75% of whom are in regular partnerships, 5% in commercial sex work, and 10% in casual relationships, Assumed annual number of sexual sex acts (66, 200, 25 respectively) Consistency of microbicide use is assumed to be 80%.	Same Same Assumes complete consistency of use	
Distribution Channel	Assume to be reflective of public sector and quasi market (using social marketing data)	Same	
Costs	Product Cost: constant $0.6/unit Initial Market Development Costs Delivery Costs	Product Cost: constant $15 Same Same	Impact of economies of scale in product costs – assumes unit costs decline from 60 cents to 20 cents per unit as production increases from 50m to 250m units per annum Impact of different products e.g. ring method 30 and 90day Impact of increased upfront costs Impact of charging users on net costs

Time horizon
For the purposes of the costing analysis we adopted a **10-year time horizon**. Based on previous product experience, this is a relatively short period of time when talking about market development. However, the increasing scale of uncertainties related to product, epidemiological, financing and country developments over time reduce the utility of longer-term scenario planning[1]. Consequently, this study examines the initial costs of introducing and market development for microbicides, rather than the evolution to a mature programme. For illustrative purposes the analysis assumes introduction begins in 2007.

Country selection for initial introduction
We assumed that initial introduction would first be **focussed on countries where phase 3 trials are currently (Aug 2007) or countries which would be priorities for HIV prevention efforts, given the potential acceleration of the epidemic.** These countries will have some familiarity with microbicides and will have justifiable claims to prioritisation based on the contributions that communities living in them have made to the development process.[2] Hence, the following countries have been included: Uganda, Tanzania, Zambia, Malawi, Zimbabwe, South Africa. In addition, Nigeria and India have also been included in this study. These two large countries could have major impacts on the scale of initial microbicide introduction and have both been identified as important targets for HIV prevention. In addition, both were, until February 2007, participating in phase 3 microbicide trials, which have now been discontinued.[3] With the exception of India, all urban settings are considered in the baseline coverage scenarios. However, it is more realistic that introduction in India would follow a state-level roll-out rather than nation wide launch.[4] Thus the baseline scenario considers roll-out to the higher HIV prevalence (>1%) states of Southern India - Kerala, Karnataka, Andhra Pradesh and Tamil Nadu.

Actual product introduction over the first 10 years of microbicide availability is likely to include more countries than those selected for this study. **Consequently, this study is likely to underestimate considerably the total potential global market for microbicides.** However, as predicting which and when countries may introduce microbicides is very difficult, this paper chose to focus only on those that have participated in Phase 3 trials. The figures presented here **are not global estimates**.

This country selection does not represent a recommendation for the selection of the first countries to introduce a microbicide. The choice to introduce a microbicide will be made by countries themselves, with technical support from agencies such as WHO. Donors will also play an important role in providing financing to support country decisions.

Population Covered
The study assumes a **general population approach** to microbicide introduction and does not consider targeted strategies based on specific groups that could be differentiated by epidemiological or behavioural criteria. The potential users of microbicides for the purposes of this report are **sexually active women 15-49**

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[1] Full market maturation may take up to 30 years..
[2] A number of product developers have made clear that they would work with countries and others to ensure that communities participating in trials will have access to microbicides shown to be efficacious.
[3] The Cellulose Sulphate Trial, with sites in Burkina-Faso, Benin, Nigeria, South Africa, Uganda, Kenya and India, was stopped at the end of January 2007. A preliminary review of results by the Independent Data Monitoring Committee suggested that cellulose sulphate could lead to an increase risk of HIV infection.
[4] The sensitivity analysis considers national introduction in India.

residing in urban areas[5]. The scenarios developed look at uptake and coverage rates based on this population. The focus on an urban population is a simplification based on the assumption that early introduction is likely to target this more accessible group of women.

Distribution Channels
There are a number of potential distribution channels for a microbicide product including through public sector facilities (such as general health and reproductive health clinics), social marketing and through the private sector. We assumed for the initial 10-year period of the analysis that **distribution is undertaken through the public sector and through social marketing programmes**.[6] Historically, contraceptive market development – which aims at a similar population group - has largely started in this manner, with the emergence of the private sector as the market matures over a 10-15 year period. Public and quasi-public channels have played an important role in countries in developing a minimum level of uptake of contraceptive products, before commercial suppliers enter the market (Hanson et al, 2000).

One key issue that will drive distribution strategies will be whether future microbicide products will be registered and available as Over-the-Counter (OTC) products or as prescription only products. The human resource and infrastructure requirements needed for prescription only products are likely to place constraints on the scale and speed of introduction for microbicides registered as such. It is not clear at the moment into which category the first registered and subsequent microbicides will fall, or how easy it will be for an initially prescription only product to move to an OTC designation. While this paper does not explicitly factor in this issue, a prescription only product (an injectable contraceptive) was included among those examined to provide data for possible introduction and uptake scenarios.[7]

Product Mix
Data from a phase 3 clinical trial of an early generation product (Carraguard®) will be available in late 2007, with results from a further 2 trials expected by 2010. A next generation microbicide entered a proof of concept efficacy trial in the summer of 2007 (PMPA gel). Additional next generation products are in safety studies and a further efficacy trial is anticipated to start in 2009. As is usual for the R&D process, the results of clinical trials could show no, limited or higher levels of product efficacy in reducing HIV transmission. There is still considerable uncertainty regarding when and where a first microbicide product will be registered and with what mode of action and formulation.

Two product profiles are developed for use in the baseline scenarios for this study. **Product 1** is coitally dependent and delivered in a gel formulation with an applicator. **Product 2** is a long-acting (30 day) product that is not coitally dependent. For the purposes of this scenario, unit costs for product 2 have been based on initial estimates of the costs of a vaginal ring.

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[5] see table 2 annex 1 for further detail

[6] Note that this does not mean that private sector providers may not be involved in microbicide delivery, but that financing and market development will be driven by public health objectives rather than purely commercial market concerns.

[7] Note, that while a prescription only designation for a microbicide would limit distribution options (at least officially), the introduction of an injectable contraceptive Uganda provides the basis for the most optimistic uptake curve from the data that was available. Uganda has successfully instituted community based distribution programmes to increase coverage of injectable contraceptives. See http://www.fhi.org/en/RH/Pubs/servdelivery/cbd_dmpa/brief1.htm . PSI's programme included detailed training of providers (doctors, pharmacists and paramedics). Similar training activities would be required for microbicide delivery by prescription.

In sensitivity analysis, **product 3** is defined as a daily, non-coitally dependent product. There are a number of formulations currently under development that could provide such product, including gels, tablets and films. For the purposes of this scenario, unit costs for product 3 are based on initial estimates for a gel/applicator delivery model.

As uptake scenarios for this study are not based on product focused modelling, no assumptions are made regarding the importance of product efficacy or formulation in determining introduction and use decisions. Rather, it is simply assumed that a product that is introduced is 'effective' and 'acceptable' enough to generate demand and to secure necessary financing. Nor are potential differential uptake rates based on the degree of coital dependence related to different products, which may influence rates of consistent use, examined.

Scenario Development
To keep the analysis in this paper focussed, we developed three scenarios that could be used to represent alternative microbicide introduction and market development (Table 2) trajectories. In reality, the scale and speed of microbicide uptake will be related to the interaction of a wide range of factors including; product characteristics, intensity and effectiveness of marketing, supply of product, availability of financing, the availability of alternative HIV prevention methods, the preferences of women and their partners, cost, OTC or prescription only registration and the capacity and coverage of potential distribution channels. However, rather than attempt to undertake detailed modelling of the interaction of these factors to estimate demand and uptake, the three scenarios used are assumed to represent different combinations of these factors resulting in more or less rapid and broad microbicide uptake.

Table 2: Scenarios for Microbicide Introduction and Scale Up

Fast	Higher and earlier levels of mature demand, reflecting a rapid scale-up and fast adoption of microbicide products. The fast scenario assumes only limited barriers to uptake e.g. that sustained financing is available, that there is good coverage of target populations by accessible services and socio-cultural factors do not hinder acceptability and use
Medium	Initial slow levels of uptake, then maturation of market. Microbicide products are less quick to be adopted but markets will eventually reach mature levels of use.
Slow	Low levels of demand, with little maturation of the market and slow scale-up. Microbicides are adopted only as a niche product. This scenario could be consistent with larger cultural and social barriers to uptake of microbicides, relatively low efficacy or constrained financing.

2.2 Development of Uptake Trajectories for Scenarios

In order to develop realistic trajectories of market development, historical information for products similarly targeted to sexually active women were examined. The assumptions draw heavily from the experiences of Population Services International (PSI) as this dataset was readily obtainable and collated.[8] Clearly, there are a number of limitations with relying one dataset and one type of delivery mechanism. The uptake information may not be typical of public sector strategies in general. The uptake data will also be affected by the market share that PSI might have in a particular country (in contrast to broader public sector distribution). However, in the

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[8] PSI is one of the world's social marketing organisations and their detailed data was made available for this study. Clearly, there are limitations in focussing on the experience of one provider to shed light on microbicide uptake, but must be traded-off with the richness of the data that is available. Similarly data from other providers is not freely available and would require extensive negotiation and consultation, as well as primary data collection beyond the range of this study

absence of detailed country-specific public sector data, the PSI data allows an initial examination of likely trajectory paths, which could be further refined as comparable and standardised data from different delivery channels become available.

In order to develop the uptake trajectories, actual annual sales of products were used for female condoms and injectable contraceptives. Coverage was estimated by comparing sales relative to the size of the urban female population aged 15-49. In order to generalise the uptake trajectories, for each country and product a regression analysis was undertaken to estimate the predicted sales trends through time. These predicted sales were then compared with the urban female population aged 15-49 to estimate predicted coverage rates for product uptake by country and product.

Product Uptake
Fast, medium and slow uptake scenarios were developed. The first is based largely on experiences with injectable contraceptives in Uganda, the second on female condoms in Zimbabwe and the last for female condoms in Tanzania. This is detailed in **annex 1.** The choice of these technologies was based on their similarity to aspects of potential microbicide introduction. First the target groups (sexually active women) are broadly similar. The female condom is a coitally dependent product that is available OTC. It's costs are in a similar range to gel/applicator microbicide delivery systems (based on initial costings for these). The female condom also offers dual protection against STIs and HIV. The injectable contraceptive is a prescription only product that is non-coitally dependent and provided on 90-day cycles. Injectable contraceptives are currently in the $5 - $10 price range.

The estimated population coverage (defined as proportion of sex acts covered)[9] for urban women of microbicide sales for these three scenarios are summarised in Figure 1 below. Both the fast and medium scenarios show increasing sales, while the slow scenario shows a small and relatively stagnant market. Coverage is just below **6% by year 10 under the fast scenario**, is **less than 3% for the medium scenario** and **negligible for the slow scenario**.[10]

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[9] to arrive at coverage figures assumptions need to be made about the number of sex acts covered and the consistency of use – these are outlined in table 1

[10] The fast trajectory reflects the prescription-based injectable product, which seems somewhat counter-intuitive as one would expect OTC sales to increase faster. However, these uptake curves also suggest that a prescription-basis product need not be a barrier to rapid uptake.

Figure 1: Projected Population Coverage
different uptake scenarios
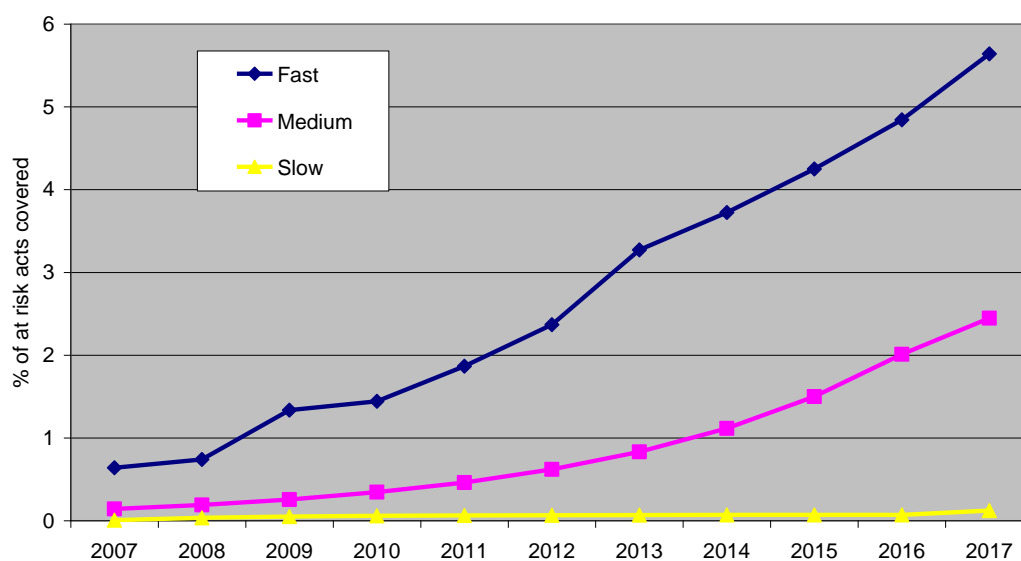
Introduction Costs

Product 1 is used as the base case for estimating costs and assumes unit commodity costs of $0.60 (see annex 4 for rationale). Upfront market development costs (made up of advertising and promotion and mass media) were based on PSI experience and the levels assumed depend upon the scale and maturity of the programme (with larger programmes having higher costs but with costs declining over time in all cases). The cost analysis takes the perspective of an incremental costing, adding to existing infrastructure. It does not assume the development of parallel delivery systems. The costs include incremental costs of training. Estimates of delivery costs were based on PSI data and assumed to be amenable to significant economies of scale. The background to the costing analysis is at **annex 2**.

3. ESTIMATED COSTS OF INTRODUCING MICROBICIDES

3.1 Baseline Analysis

How Much Could It Cost?
For the eight countries included in this study, the total projected cost for the **Product 1** baseline scenario, over the 10-year period from 2007 to 2016 is $1.70bn, $529m and $73m under the fast, medium and slow scenarios respectively (note that this includes selected-state introduction in India – in Tamil Nadu, Kerala, Karnataka and Andhra Pradesh - and country-wide introduction in Nigeria). Figure 2 presents the annual costs by scenario. Both the fast and medium scenarios show increasing costs through time, with the slow scenario showing decreasing costs. Under the fast scenario the annual cost is just under $285m by year 10 and around $119m under the medium scenario.

Figure 2: Projected Annual Costs of Early Generation Microbicide Introduction
according to the different demand uptake scenarios
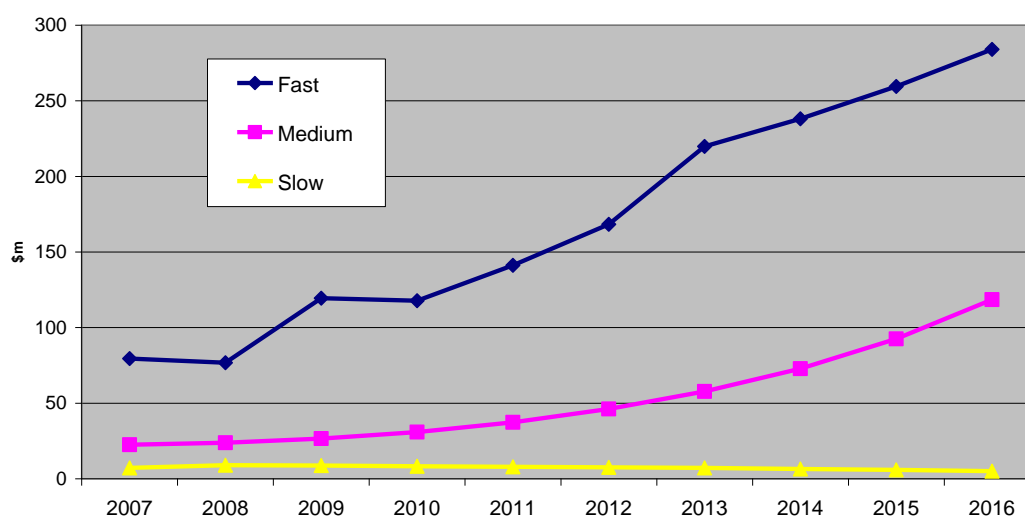
Figure 3 (below) presents the cost of the baseline scenarios for **Product 2**. In this case a constant unit product cost of $15 is assumed for a monthly microbicide. Marketing and per unit delivery costs are assumed to be the same as for Product 1 (see annex 4 for costing assumptions). Under these assumptions, the cost of product 2 for the medium scenario would be $1.14bn, compared to $529m for product 1.

Figure 3: Projected Costs of Introducing Next Generation Product

medium uptake scenario - 30 day coverage: $15 per application
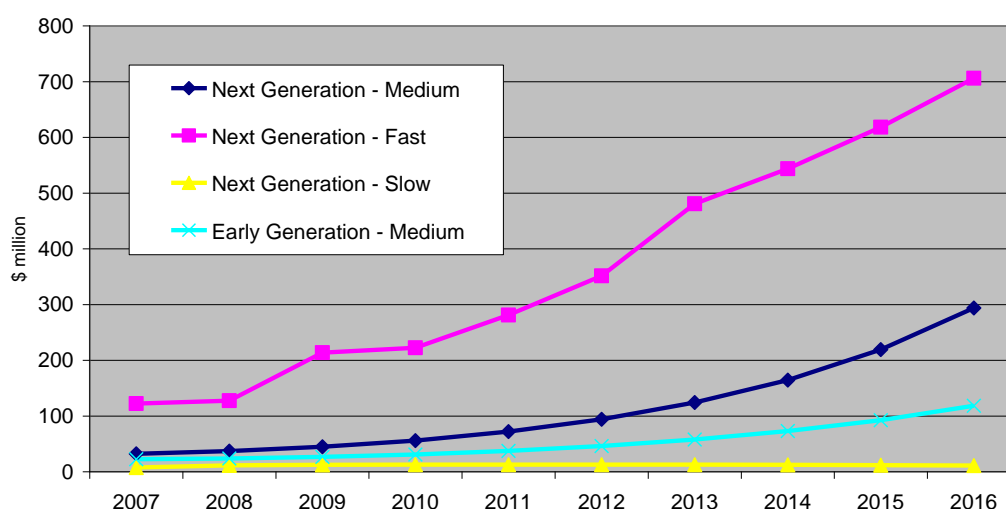
These findings are heavily dependent on assumptions regarding the unit costs of Product 1 and Product 2. It is important to note that unit product costs are driven strongly by the formulation chosen for a microbicide. Costs may vary from a few cents to several dollars. Next generation products can be delivered in a range of formulations with different unit costs. However, cost needs to be considered alongside the acceptability of any particular product formulation for women using microbicides and the degree to which different formulations are likely to support high levels of consistent use (adherence). Coitally dependent and daily formulations may be less costly to produce but may not support the same levels of adherence that women using longer acting formulations (such as vaginal rings) may be able to achieve. There is currently limited data on comparative adherence rates by women using different formulations. Further information on these, unit costs and the importance of consistent use in achieving health impact in different populations will be needed before informed decisions regarding product selection can be made.

Where?

 In the base line scenarios for product 1 and product 2, the country wise requirements are driven by relative population size. India alone accounts for around 37% of the total cost and Nigeria a further 32% as shown in Figure 4 for product 1. In practice, it is more likely that microbicides would be introduced on a state by state basis in large countries, including Nigeria. **Total costs are clearly very sensitive to the large population countries** (although note the relationship between economies of scale and product price under sensitivity analysis 4 below)**.**

**Figure 4: Country Wise Breakdown of Costs - Early
Generation Base Case Scenario**
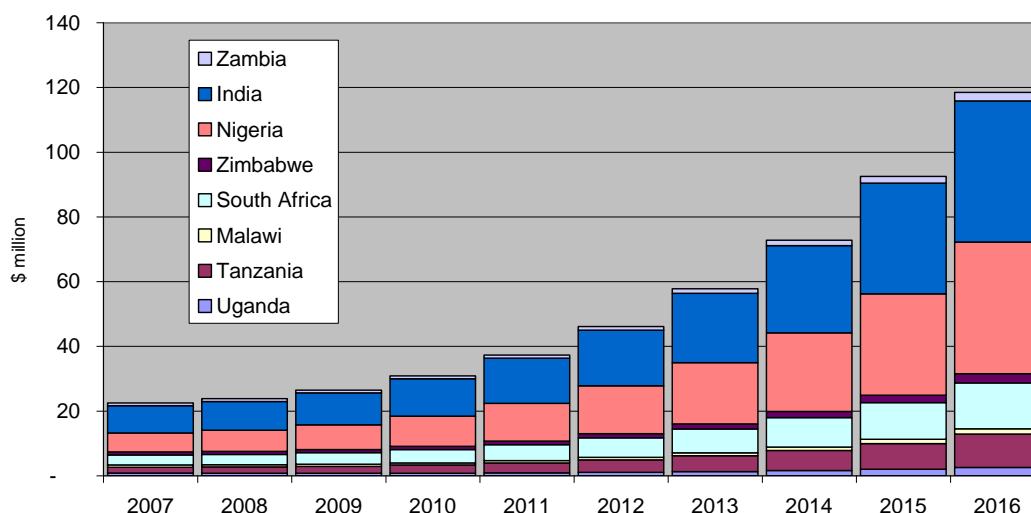
On what?

The cost structure for microbicide introduction varies considerably in the different **scenarios**. For example, **initial development expenditures** account for a large share of the costs where uptake is slow. For the fast uptake scenarios, product unit costs are more important as high sales cover the **initial** fixed costs and also allow significant **economies of scale** to be gained in terms of delivery costs**. Product expenditure represents a fairly minor share of total costs in the first 5 years but subsequently assumes an increasing share.**

**Figure 5: Cost Breakdown - Early Generation Product
Medium Uptake Scenario**
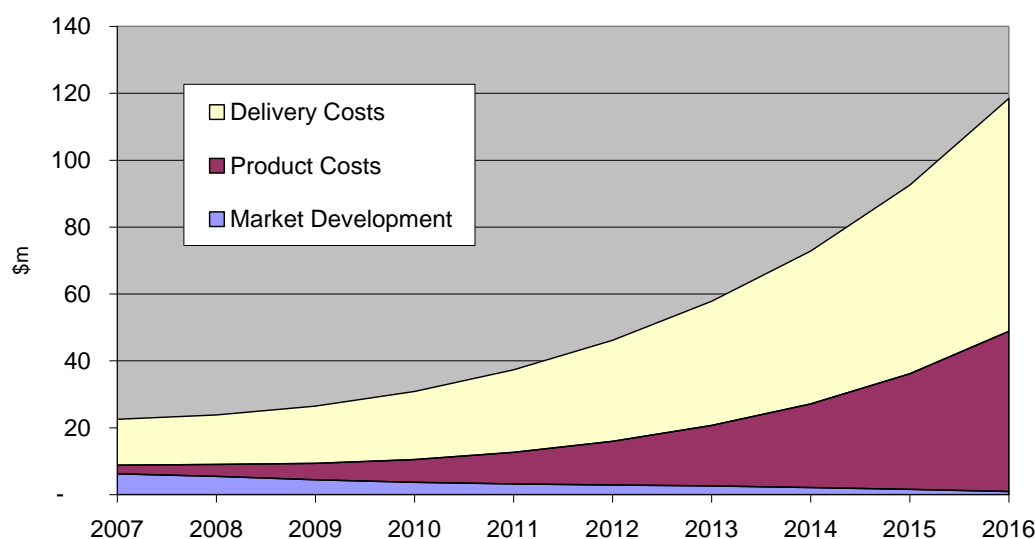
Figure 6 shows possible funding requirements for products over the next ten years according to the different scenarios. This is also useful in that it is also an indicator of possible market size and a possible signal for manufacturers to invest in production capacity (although this would need to be backed up by early indications from donors as to the availability of such funding and its predictable delivery). It shows a total

market size of around $166m under the medium uptake scenario to 2016 increasing to just over $535m under the fast uptake scenario
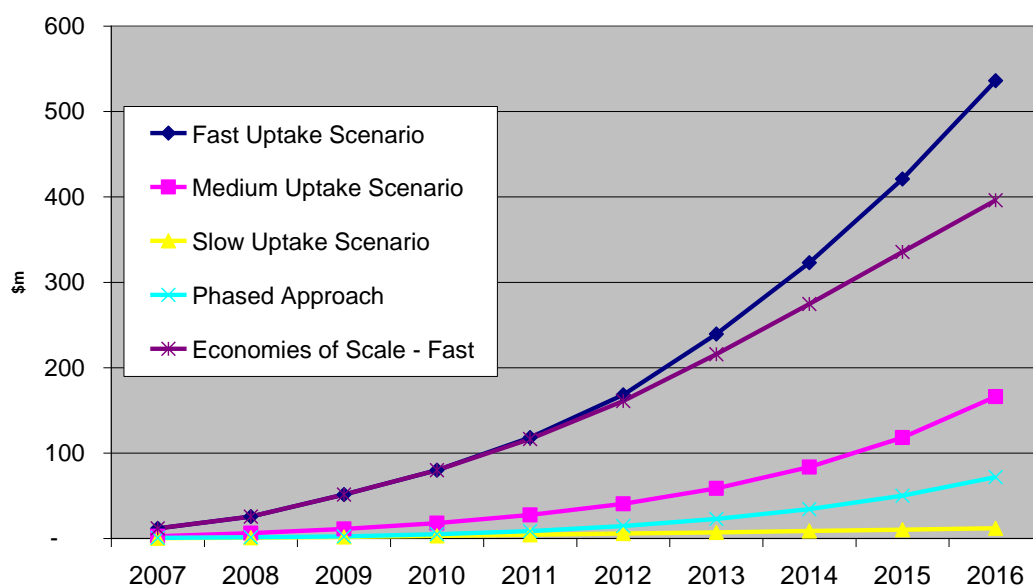
Figure 6: Estimated Cumulative Product Costs

Figure 7 shows possible costs of delivery over the period. Figures range from $330m under the medium uptake scenario to $1.13bn under the fast uptake scenario. Taken together total programme costs (combining product and delivery costs) vary from just under $500m under the medium uptake scenario to $1.67bn under the fast uptake scenario.

Figure 7: Estimated Cumulative Delivery Costs
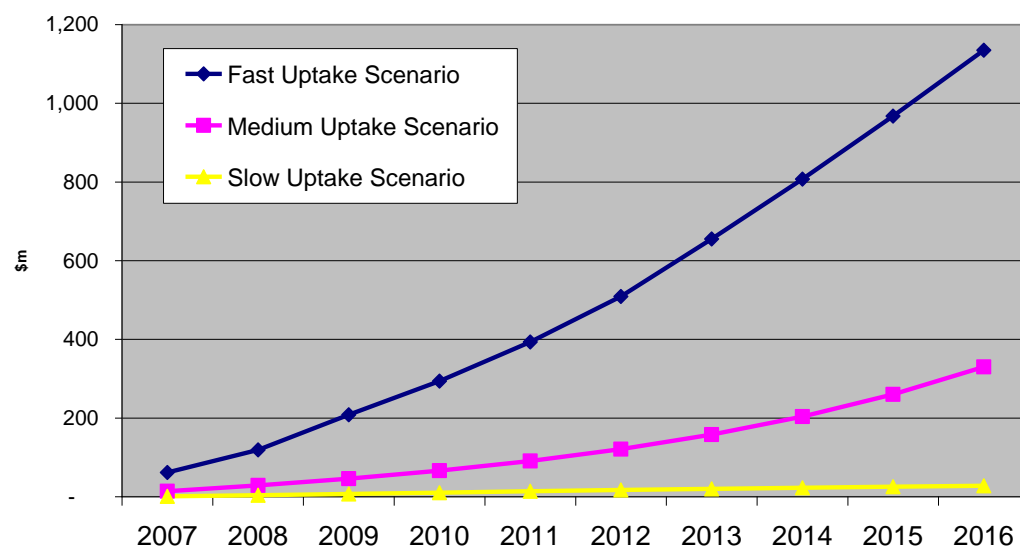
Finally Figure 8 shows both annual and cumulative development costs and are shown separately as some donors may be willing to meet initial up front costs but not subsequent running costs

Figure 8: Development Costs - All Scenarios
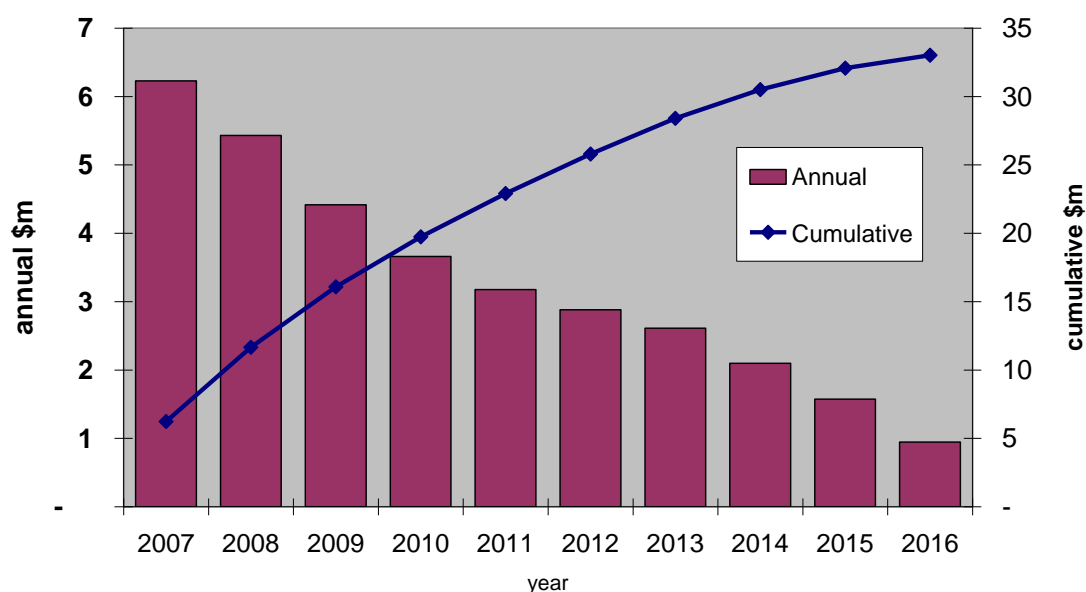
In all cases expenditures for product 1 ultimately account for around half of costs, assuming an incremental costing for programme/delivery costs (Figure 9). This is higher than for many other products and has implications for future subsidisation of any programmes.[11] The speed of uptake alters the structure of costs – with product costs accounting for a lower share of total costs under the slow scenario

Figure 9: Product Costs as a Share of Total Costs
Early Generation Product
Different Uptake Scenarios
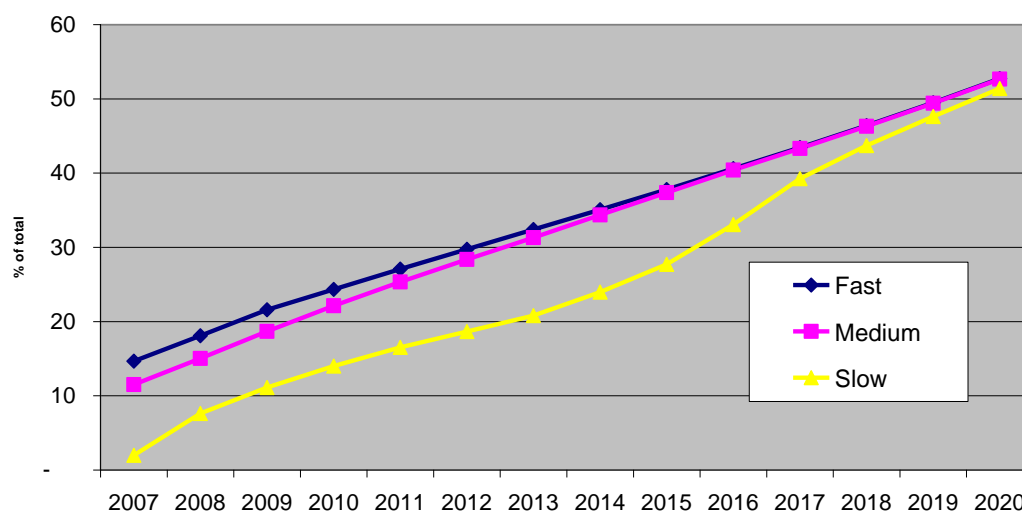
A more detailed analysis of the baseline scenarios is presented in **annex 3**

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[11] Analysis of PSI data suggests that the share of product costs depends heavily on the "maturity" of the programme – in some cases the share exceeds 60% somewhat higher than that projected for microbicides.

3.2 Sensitivity Analyses

As discussed earlier the nature of this scenario planning is hypothetical, given the large uncertainties around the nature and timing of any future product and its introduction. The sensitivity analyses below examine the role of some of the key assumptions made in this scenario planning exercise and how they affect results. For simplicity, the sensitivity analyses are based around the medium uptake scenario (unless stated otherwise).

Sensitivity 1: Reducing Product Price
Rather than assuming constant product costs, we considered a scenario where significant economies of scale can be achieved as manufacturing volumes increase. Initial costs for **Product 1** of $0.6 are based on the relatively small volumes of gel and applicators produced for use in clinical trials. While it is difficult to make definite estimates of potential reductions, the analysis assumes unit costs decline from 60 cents to 20 cents per unit as production increases to 250m units per annum[12]. More detail on these assumptions and their implications for unit product costs under the various scenarios are shown in **annex 4.**

Based on these assumptions significant reductions in unit product prices, which are reliant on volume, are only possible under the fast scenario with very limited reductions possible under the medium case (due to lower levels of production) and none under the slow case.

Figure 10: Impact of Production Economies of Scale on Product Costs: Early Generation Product
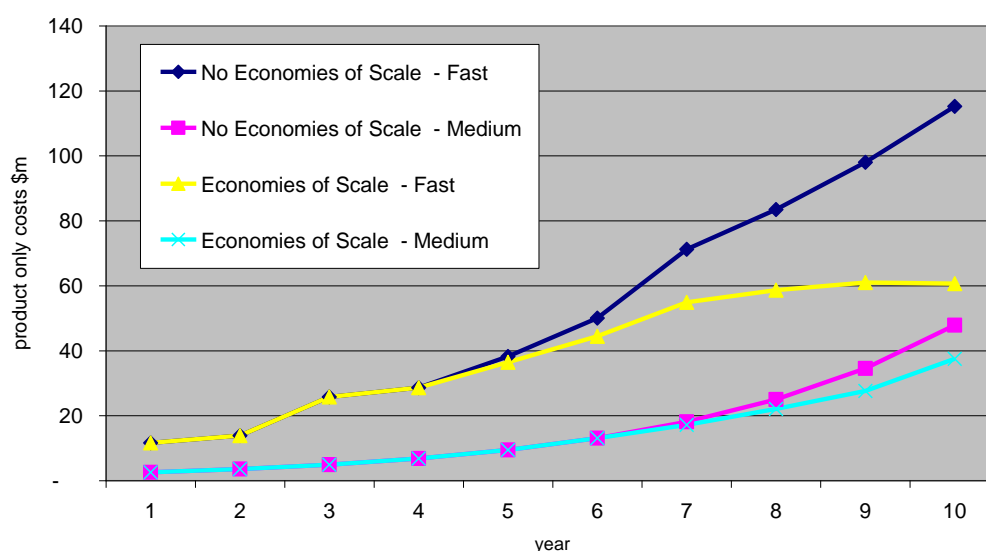
As shown in Figure 10 economies of scale under the fast scenario would reduce product costs by around 26% over the 10 year period and by year 10 annual product costs would be around three quarters of what they would have been in the absence of such cost reductions. Under the medium scenario economies of scale would reduce total product costs over the period by 12.7%.

While caution is needed in focusing on the figures generated from this analysis, it is clear that a positive relationship between product cost and volume has as particularly significant impact on overall programme costs. This is due to the relatively high

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[12] the analysis assumes a linear decrease. In practice stepwise decreases may be more likely

proportion of total costs made up by product cost. This positive relationship has important implications for planning introduction. More aggressive strategies are likely to deliver greater cost effectiveness and may, depending on actual cost/volume relationships, even reduce overall programme costs.

Sensitivity 2: Different Formulations and Costs for Next-Generation Products
Next generation products can be formulated in a number of different ways resulting in different use and cost characteristics. Figure 11 shows costs for **Product 2** assuming two different unit costs ($15 and $6) and two different durations (a 30 day and a 90 day product).

Costs for **Product 3** (a daily, non-coitally dependent product costing a constant $0.6) are also included.

While these figures are dependent on very preliminary assumptions (and the exact figures generated should be treated with caution), they demonstrate the importance of unit product costs in determining overall programme costs (assuming that distribution costs are incremental to existing programmes rather than new systems being put in place from scratch).

Figure 11: Projected Costs of Next Generation Products
under different costing and coverage assumptions
medium uptake scenario
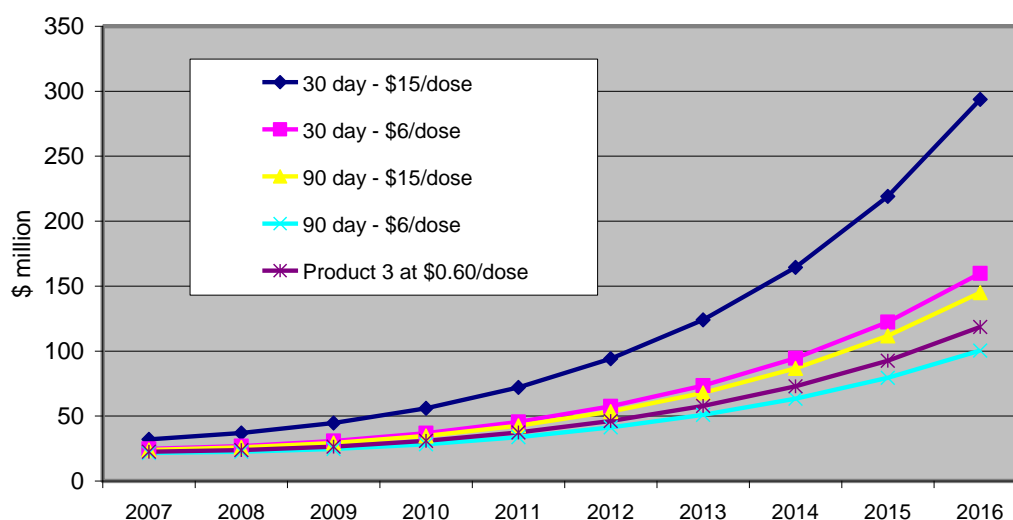
*Sensitivity 3: Changing the Phasing of Microbicide Introduction*
The initial scenarios assume *all* countries start immediate introduction. However, even amongst this small group, it is likely that countries will be phased in over time. As an alternative we considered the financial implications of phasing according to the sequence in Table 3. The sequence is somewhat arbitrary, suggesting that high-burden HIV countries with Phase III trials would start first.

Table 3: Assumed Phasing of Introduction

Year 1	Year 3	Year 5
South Africa	Nigeria	India
Zimbabwe	Malawi	
Uganda	Tanzania	
Zambia		

Phasing in of countries would substantially reduce costs (product 1, medium uptake) - by around 48% in total over the 10 year period.

Figure 12: Effects of Phasing In Country Wide Introduction
based on medium uptake scenario - Early Generation Product
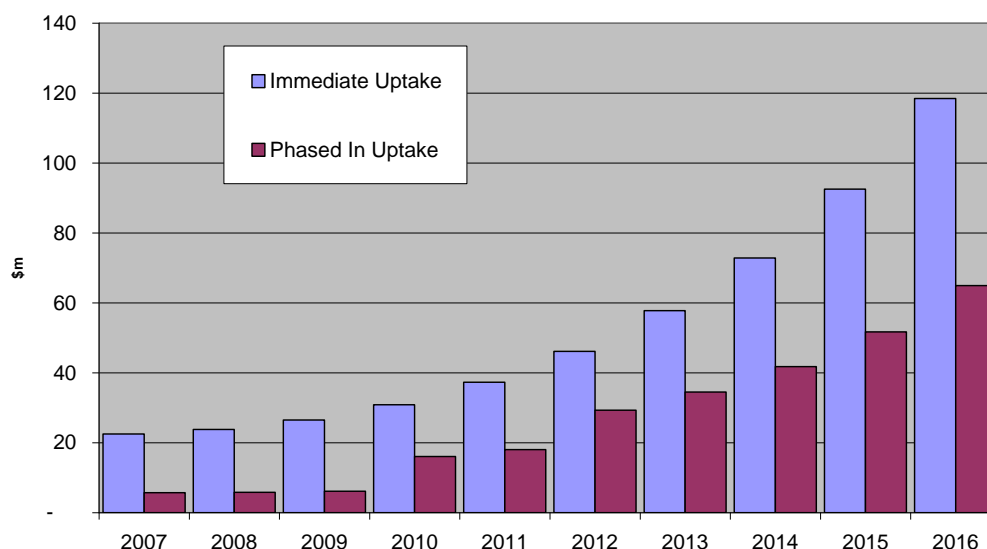
Sensitivity 4: How Much Will Users Pay for Microbicides?
 Policy makers face a number of options regarding if and how much to charge consumers for purchase of a new product. A low or zero price strategy may be chosen to stimulate initial demand for a new product. However, as demand increases and programme costs grow it may then be politically challenge to introduce a product charge. However, charging a higher price at launch may choke demand, particularly where cheaper alternatives options may exist.

Charging users reduces the costs to Governments of making microbicides available by transferring a proportion of costs to users (very few consumers in the countries discussed would be able to bare the full cost of programme and product). It might also further reduce programme costs by limiting demand. This is particularly likely to be the case for poorer and vulnerable groups who would probably be a key target group for such programmes.

In this sensitivity we assume users pay 10 cents per application[13] and we assume that this price increase would be associated with a 20% fall in demand.

Figure 13 shows that the impact is quite large – reducing costs by 23.2% over the initial 10 year period.

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[13] This is about the cost of the price per use for male condom, but significantly lower than the price per user for the female condom, which range from 10-20 times higher. This scenario does not allow for economies of scale. If it had cost recovery would have increased from just over 15% of the initial price for product 1 to around 50% of the cost once scale economies have been achieved

**Figure 13: Possible Financial Implications
if User Pay 10 Cents per Application**

based on Product 1 - medium uptake scenario
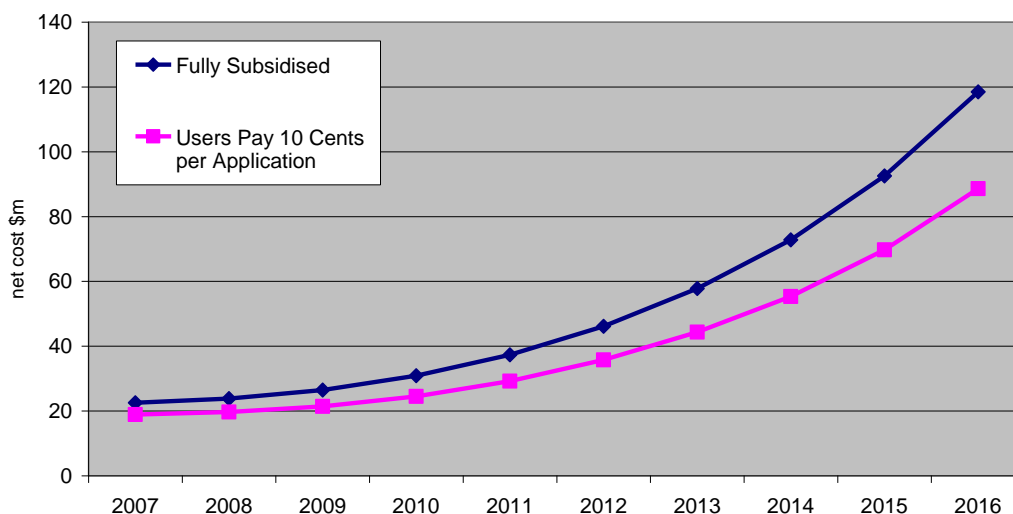
Experience suggests that once market become established and the costs of subsidy mount donors begin to think seriously about sustainability and push the charging route quite heavily. Were product costs to be fully covered – as noted above – costs could, in theory, be reduced by 50% and much more probably given expected effects on demand.

Sensitivity 5: Impact of Country-Wide Introduction in India
A final sensitivity analysis considers the impact of country-wide introduction in India.

Figure 14: Effects of Phased Approach in India

Product 1 - medium uptake scenario
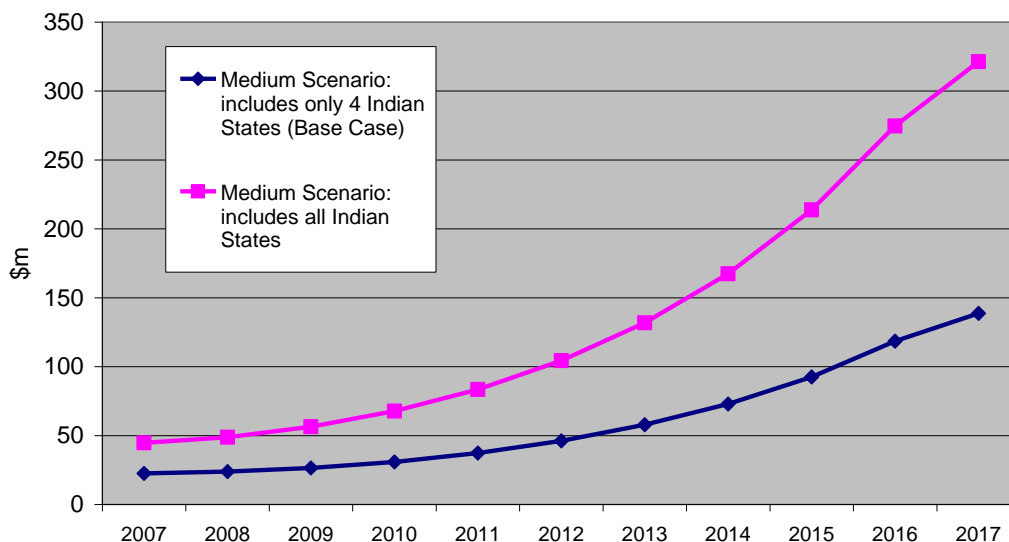
Inclusion of the all states in India results in an almost 5 fold increase in the India programme costs and a 125% increase in overall programme costs over the 10 year period.
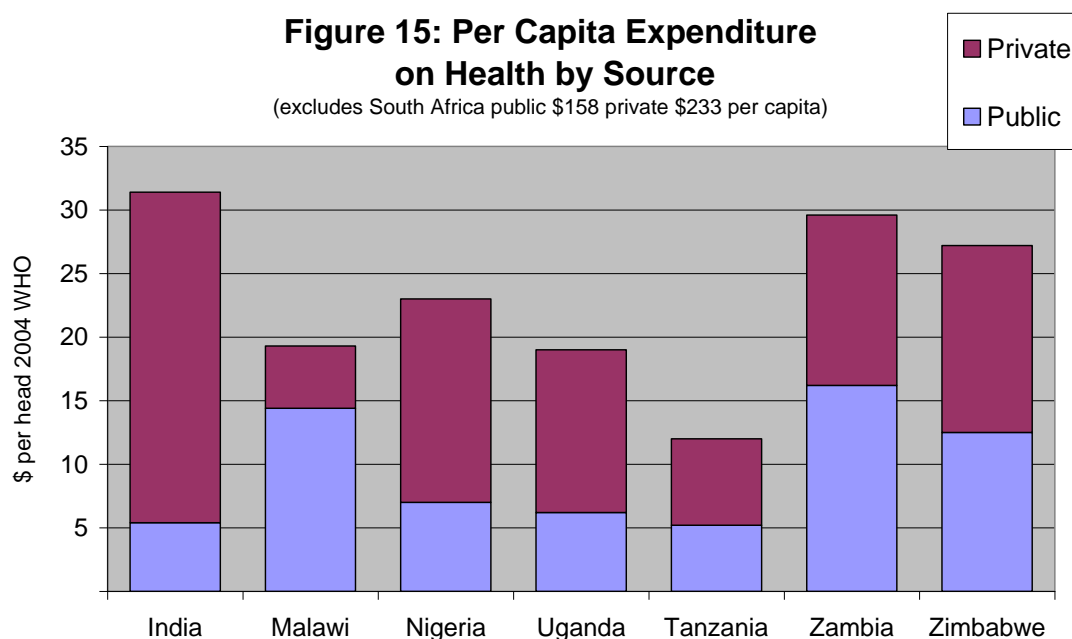
4. AVAILABILITY OF FUNDING

This section considers first whether the magnitudes of costs identified in section 3 seem affordable in the light of likely funding for health programmes over the coming years. It also considers the advantages and disadvantages of possible funding sources (whether donor/foundations, Government or users) and financing mechanisms (whether Government systems traditional bilateral or multilateral support, global health initiatives or alternative innovative financing mechanisms)

4.1 Assessing the Affordability of Introducing Microbicides

4.1.1 The Challenge

Public spending on health in low income countries remains extremely low - well below levels considered necessary to provide a basic package of essential services (see Figure 15 below). Current assessments suggest that it can cost anything between $30 and $50 per head to achieve the MDGs in low income countries. There is a large degree of uncertainty over such figures as they tend to be based on bottom up costing approaches. They do not necessarily account for additional costs of increasing the range and coverage of individual health services, such as those required for health systems strengthening (or do so in a rather arbitrary fashion). The direct effects of economic growth on the health MDG targets are also often excluded.

Figure 15: Per Capita Expenditure on Health by Source
(excludes South Africa public $158 private $233 per capita)

Disease specific costings, such as those produced by UNAIDS estimating the costs of scaling up HIV and AIDS services to provide universal access, do not include projections for the introduction and use of new technologies.[14]

Domestic resource generation efforts are hampered by a low revenue base in most developing countries and the scope for future increases is limited. Current allocations in Africa also average little over half the 15% target set out in the 2001 Abuja Declaration.

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[14] UNAIDS. 'Financial Resources required to Achieve Universal Access to HIV, Prevention, Treatment, Care and Support' September 2007

Donor support for health has increased rapidly – particularly so in recent years - although much of this has been earmarked for particular services. Aid dependency is generally high in sub-Saharan Africa, and likely to remain so, especially in East and West Africa. South Africa and India have low donor dependency, although donors may continue to play and important role in supporting piloting of new programmes and at the state/provincial level.

Reliance on donor financing can cause problems for countries, as they tend to be much less predictable than domestic revenue sources. The IMF reports that overseas development assistance funds are up to 7 times more volatile than domestic budget funding. Uncertainty about the long term availability of funds to support programmes can lead to developing country reluctance to commit to investing in human resources and infrastructure capacity building. Volatility in donor financing also make predictable demand forecasting for health commodities in developing countries very difficult.[15]

Creating the Fiscal Space for Microbicide Introduction

In order to finance the introduction of microbicides on a reasonable scale, countries will need to generate the **fiscal space** (space in the budget) to ensure that the necessary funds are available.

Fiscal space can be created in a number of ways. Domestic revenue is one way - ideally through increased domestic revenue mobilisation but also possibly from more borrowing or through the reallocation of existing resources. Increased donor support provides another potential source, and has been key in driving much of the additional investment in the health sector in recent years (see table 4 below).

Table 4: Recent Trends in Aid Flows

$m		2001	2002	2003	2004	2005
All Development Assistance	Commitments	71,705	81,113	98,222	98,311	119,108
	Disbursements	34,954	55,765	66,680	69,002	101,663
Health ODA	Commitments	5,262	6,579	8,408	8,434	9,316
	Disbursements	2,421	4,223	5,493	5,971	6,893
Health as % of Total	Commitments	7.3	8.1	8.6	8.6	7.8
	Disbursements	6.9	7.6	8.2	8.7	6.8

Source: DAC

4.1.2 Future Resource Prospects

Future prospects for health financing are relatively good. Economic prospects are much better than they have been for some time and long term projections suggest modest increases in per capita income over the coming decades in sub Saharan Africa (although rather less than in Asian regions). Likewise prospects for increased aid flows are good – with potential for a doubling of aid to sub Saharan Africa by 2010 – if commitments made at the Monterrey 'Financing for Development' meeting in 2002, by EU Member States in 2005 to reach 0.7% of GNP by 2015 and at the Gleneagles G8 Summit are honoured.

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[15] The Paris Declaration does include commitments from DAC members to move towards longer-term and more predictable financing as a means to improve aid effectiveness and to reduce the macro-economic impacts of ODA uncertainty in highly dependent countries.

There are also hopes that aid effectiveness will continue to improve. However, as the harmonisation and alignment agenda continues to influence funding decisions, it is likely also that aid funding for health will increasingly be provided *indirectly* through general budget support rather than *directly* as earmarked support. However, it should be noted that a large proportion of donor funding for HIV and AIDS (as well as support for malaria and TB) has, so far, continued to be provided through specific financing instruments, such as the Global Fund for AIDS, TB and Malaria, the World Bank's Multi-Country AIDS Programme (MAP) and the President's Emergency Plan for AIDS Relief (PEPFAR).

As part of this work an attempt was made to estimate the levels of resources (the *fiscal space*) likely to be available to support health spending in the medium to long term. Details of this analysis are in **annex 5.**

4.1.3 Key Results for Microbicide Trials Countries

So what are the prospects for funding microbicides? The following charts show how the costs of microbicide introduction compare to projected future Government spending on health. Note all the figures refer to the base case scenario where no economies of scale in production are assumed. To this end costs may be overstated

Under the medium case scenario the costs of microbicide introduction would account for less than 1.5% of the Government health budget in all countries except Tanzania over the next 10 years. Costs are typically in the range of 0.5-1% of the health budget.

Figure 16: Microbicide Introduction Costs
as % of total public spending - Early Generation Product medium uptake scenario
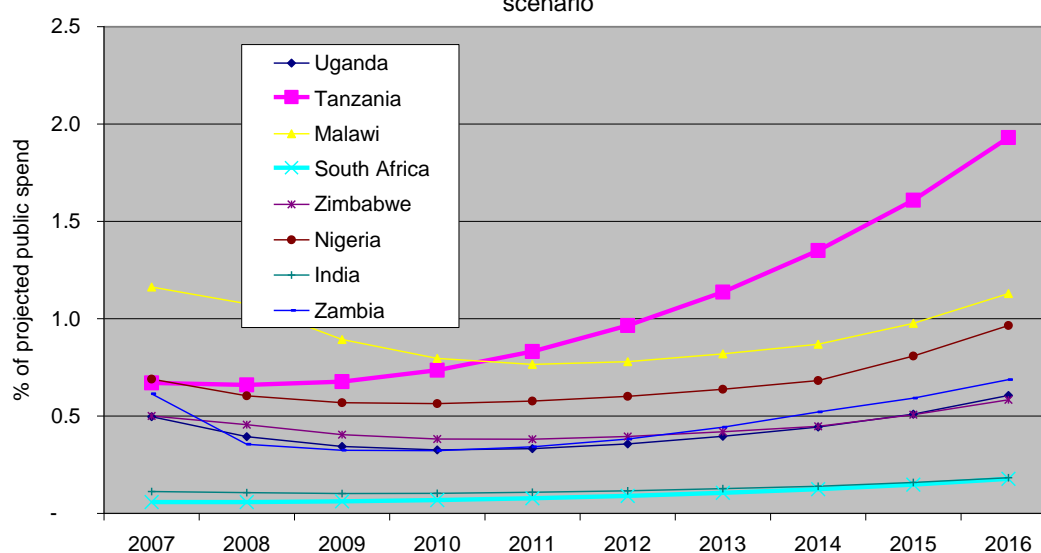
Under the fast uptake scenario affordability is likely to be more of an issue. In Uganda, if microbicides were funded publicly introduction would take up more than twice the share of the budget in the fast uptake scenario in comparison with the medium scenario (Figure 17).

Figure 17: Projected Effects of Different Scenarios on Affordability: Uganda

Early Generation Product
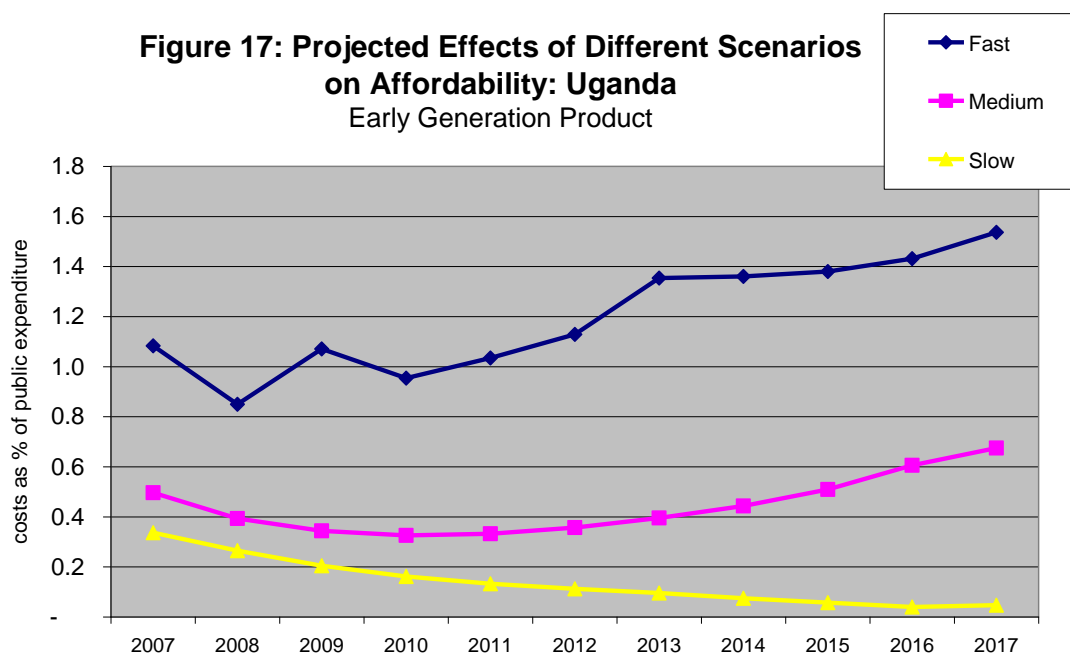
It is also important to distinguish between Government and donor financed public spending. In practice, very few countries have funded the costs of new product introductions through domestic budget resources – they have typically been funded by parallel donor funds. If this approach continues it may mean that microbicides will be particularly dependent on donor funding within a country rather than the total amount of available resources. In countries where donors play an important role in supporting pilot programmes but where overall donor dependency is low (such as South Africa and India), successful microbicide introduction would require strong government commitment. In the more aid dependant countries microbicides would, in general, account for 1% of less of aid flows for health.

Figure 18: Projected Microbicide Introduction Costs as % of Projected Donor Support:

Early Generation Product Medium Scenario
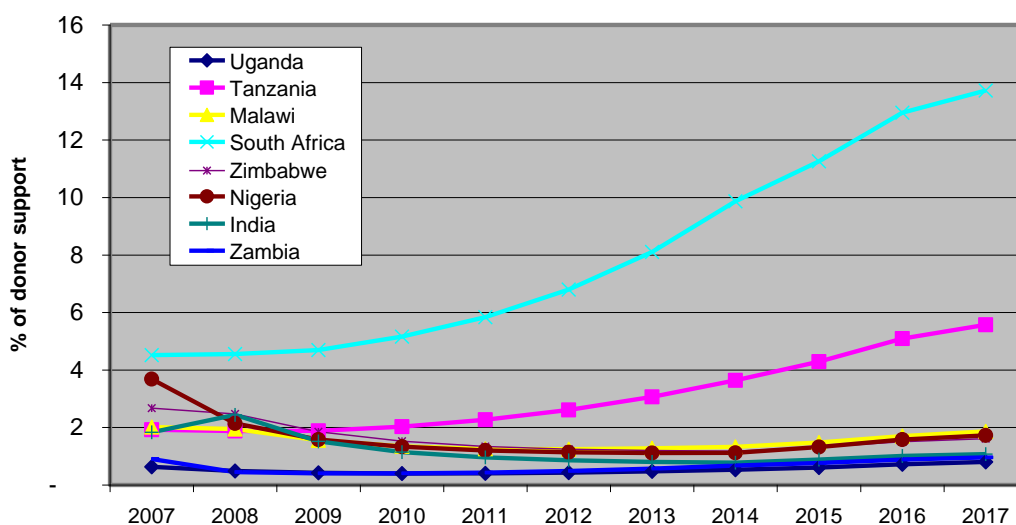
### 4.1.4 Affordability in the Context of HIV/AIDS Funding

Are microbicides competing with other development programmes as a whole or will they be competing with other HIV interventions? If heavy reliance is placed on donors it may be useful to consider the requirements in the context of existing and likely future funding for HIV/AIDS programmes rather against overall aid flows as above. It is important here to consider the overall context in which, to take a pessimistic view, the golden years for HIV/AIDS funding may have passed as:

Some donors are actively considering shifting resources away from the social sectors (including the World Bank a major funder of HIV/AIDS programmes)
There is greater recognition that huge amounts of HIV/AIDS spending has distorted allocation patterns with the examples of Rwanda and Ethiopia recent cited at High level Forum and other Aid Effectiveness fora as examples of this[16])

Figure 19 below shows donor *commitments* for HIV/AIDS control activities since 2000. The key messages are the tailing off in commitments since 2003 as well as the heavy reliance on a small number of donors (between 2003 and 2005 three donors the US, the UK and the Global Fund accounted for 67.6% of all commitments)

Figure 19: Commitments for HIV/AIDS Control Activities
2000-2005 by Donor: Source DAC - Creditor Reporting System
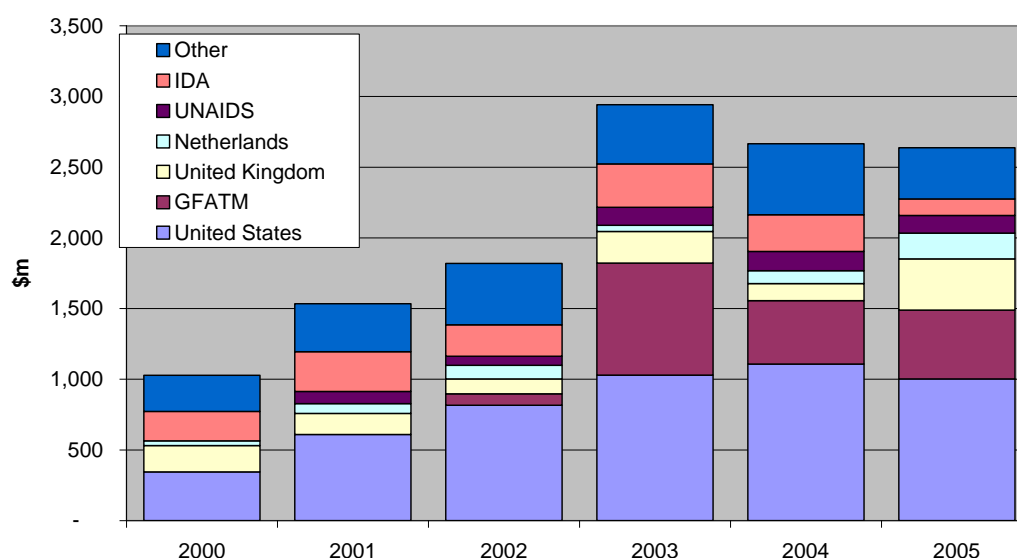
4.2   Review of Funding Mechanisms

4.2.1 Modelling the Financing Mix

The analysis above assumes an *all or nothing* approach with donors either funding all of the costs or Government doing so. The reality is that the funding burden is likely to be shared and that the pattern may vary between countries and evolve over time.

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[16] 55% of Ethiopia's health ODA is for HIV/AIDS; "gross misallocation of resources ….. with $18mn earmarked for malaria (the biggest cause of mortality and morbidity) and just $1mn for the integrated management of childhood illnesses, compared to $47mn for HIV/AIDS, grossly disproportionate in a country with a 3% infection rate" Scaling Up to Achieve the Health MDGs in Rwanda: A Background Study for the Tunis High-Level Forum Meeting June 2006

A number of funding scenarios were considered. In broad terms the scenarios assume heavy reliance on donor funding from the outset with the real differences arising from the speed with which Governments and/or users take on the financing burden.

Donor or foundation led – it is assumed that initial funding will be external - coming from the donor community or foundations. Governments and users progressively bear a larger share of the cost as programmes become more established. Such a scenario is consistent with most recent experience of new product introductions (e.g. donor support for female condoms and donor/Foundation support for vaccines through the Global Alliance for Vaccines and Immunisation)

Government led – under this scenario committed Governments may make provision for funding through their own budgets, with the donor community acting only as a contributor or funder of last resort.

User Financed – under this scenario it is assumed that prices are set at higher levels to maximise revenue and minimise the costs faced by funders

The specific assumptions underlying these approaches are set out in table 5 below.

Table 5: Key Assumptions: Financing Sources

FUNDING SOURCE	ASSUMPTIONS
Donor or Foundation led	Assumes introduction is fully donor funded in the first 5 years. Government funding share 5% in year 6 increasing by 5% per annum thereafter. No charges to users
Government led	Assumes Governments contribute 10% of costs from year 2 increasing by 10% per year thereafter except South Africa and India where Governments fund 25% of costs in year 1 increasing by 25% each year thereafter. No charges to users
User Financed	Fully donor funded for 5 years. In year 6 Government takes on 2.5% of costs and users a further 2.5%. Government and user contributions increase by 2.5% per annum thereafter

The results are shown in figure 20. Again all refer the medium uptake scenario of the base case. Not surprisingly Governments account for most of the costs (81.8%) under the Government led approach, donors most under the donor led approach and private led approach (83.7%). More speculatively, were these trends to continue to 2030 the patterns change markedly as the changes in funding patterns begin to have a major effect. For example, the private led approach which is still heavily reliant on donors to 2017 would by 2030 have come to rely roughly equally on donors, Government and users.

Figure 20: Financing Sources - The Overall Picture

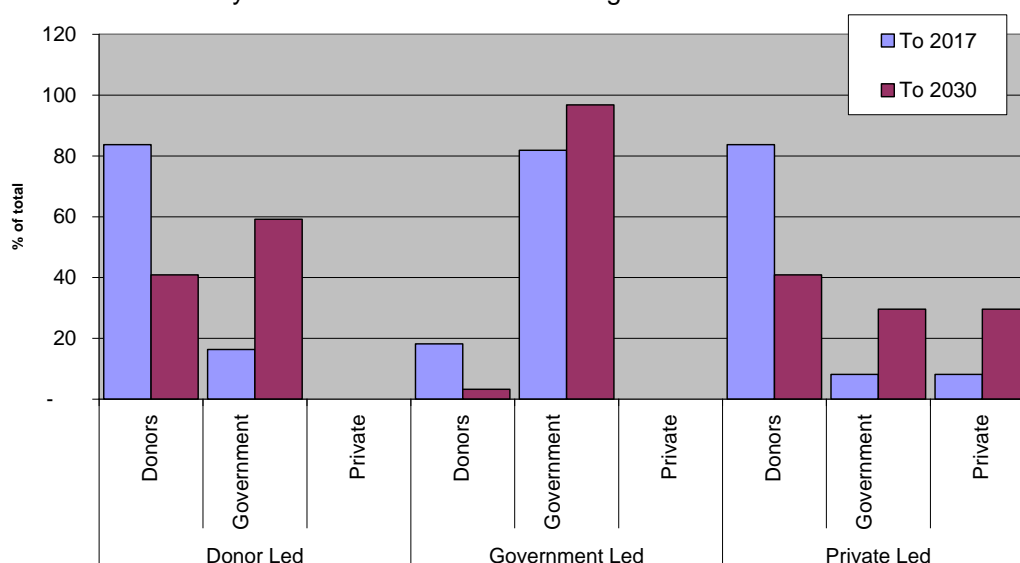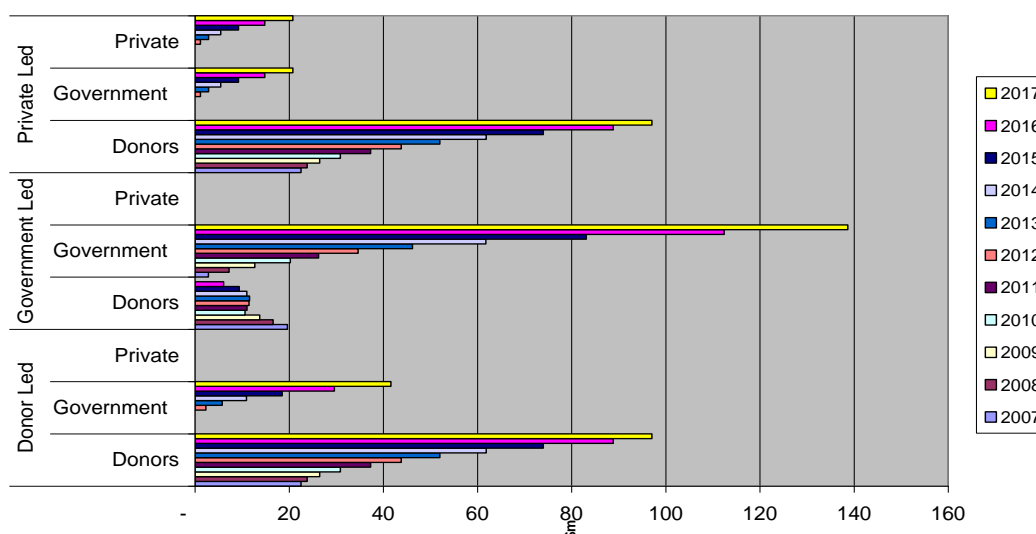Early Generation Product: according to different scenarios

Figure 21 shows how this picture builds up over time

Figure 21: Financing Sources - Changes Over Time

First Generation Product - according to different scenarios

As already noted, based on past experience, the donor led approach is most likely for initial introduction. However, such reliance places programmes at risk of unpredictable resources and the potential for changing donor priorities (which are not always synchronised with country priorities) over time. Charging users may reduce costs but as noted elsewhere it also raises the concern that it might have serious consequences for product uptake, especially by poorer groups. In reality, countries are likely to mix these potential funding streams over time and according to local contexts.

4.2.2 Fiscal Space Implications

What would such patterns mean for likely affordability? Under the donor led approach the share of donor funding required to support microbicide introduction is generally

less than 2% and declining. South Africa and India are the exceptions (reflecting low aid flows), but also the countries most capable of self-financing, particularly in the longer term.

Figure 22: Share of Donor Funding Required for Microbicide Introduction

Early Generation Product: donor led approach - medium scenario
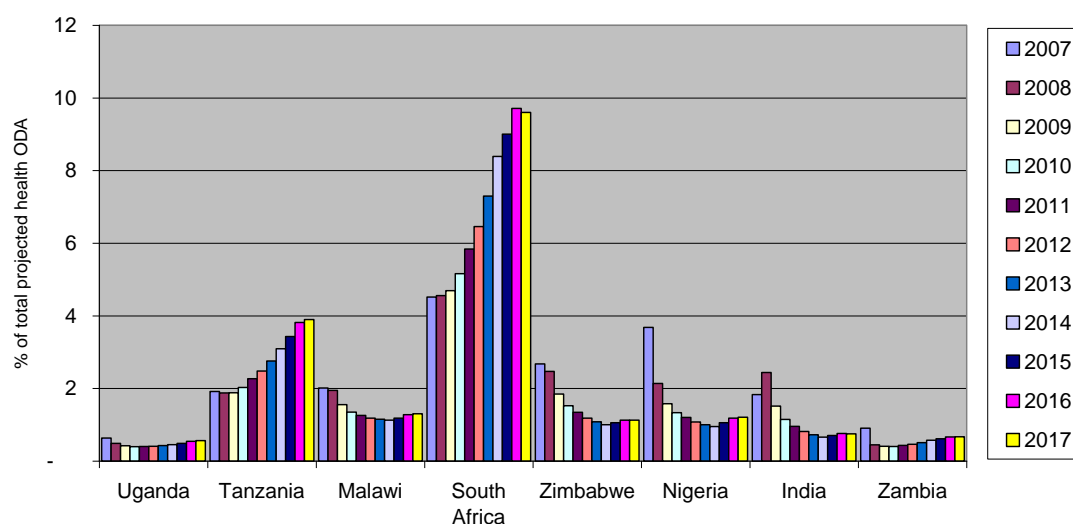
In the less likely scenario of Government led financing, the share of domestically funded health expenditure needed for microbicides would increase to up to 5% of Government funding.

It should be noted that should donor funding be increasingly channelled to general budget support – which is then regarded as a domestic funding stream - then a different picture would emerge.

The share of private expenditure which would needed to fund introduction under the private led scenario remains below 1% of total private spending on health in all cases (though it would increase beyond 2017 given greater reliance on private spending and continued increases in uptake)

In summary:

- Introduction of microbicides at the rates suggested in the scenarios does not appear to create an insurmountable hurdle as the amounts involved are relatively modest when set against likely funding flows. However, it will pose challenges in some countries.

- The ideal long term approach is to rely on Government financing – this is both more sustainable and more predictable. This is unlikely to happen in the short to medium term and heavy reliance on donors (whether bilateral, multilateral or foundations) will be required in the interim.

- There is a range of financing mechanisms many of which have a good fit with microbicide financing needs – with heavy input at the start with tapered funding later on. It is far from clear that such approaches would be supported at present for fear of further of further fragmenting the aid architecture.

- Of the alternative mechanisms none achieves all of the key requirements identified. It is quite possible a combination of approaches might meet outstanding financing needs through this would require a degree of coordination between donors – a task which would be much simpler if a key donor were to come forward to act as a supporter of last resort.

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ANNEX 1: Background to the Development of Different Trajectories

The female condom and injectable contraceptives were considered as the most relevant comparators as they are both targeted to sexually active women and were introduced relatively recently (e.g. 7-8 years ago). The female condom also has many properties - such as vaginal insertion - that are also likely to apply to a microbicide product. The specific scenarios were developed by following the trajectories of how these products were introduced by PSI in different countries.

An analysis was undertaken for both female condoms and injectable contraceptives for PSI country programmes which were 4 years and older. Three trajectory paths were then selected to reflect three scenarios, slow, medium and fast. The overall analysis of the PSI data suggested that the period until market maturation began was on average 7-8 years, so the time horizon of 10 years is realistic for examining initial scale-up. Section 2.2 has discussed some of the limitations of relying solely on PSI social marketing data. However, in the absence of available time-series data on uptake by different distribution channels, it provides an initial foundation to examine likely uptake patterns.

Fast Scenario

The trajectory follows the experience of the PSI programme in Uganda where there was rapid adoption of injectable contraceptives (Figure 1). In this scenario, there was fast adoption of the product and sales have jumped exponentially over a 7-year period, starting at over 200,000 in sales and reaching 1.4 million sales in its 7th year. This rate of increase is then extrapolated until year 10 for the cost estimation study. It is interesting that the injectable performed well despite being only a prescription-only product. This could be analogous to some of the longer-lasting formulations being considered as second generation products.

Figure 1. Annual Sales of Injectable Contraceptives in Uganda by PSI
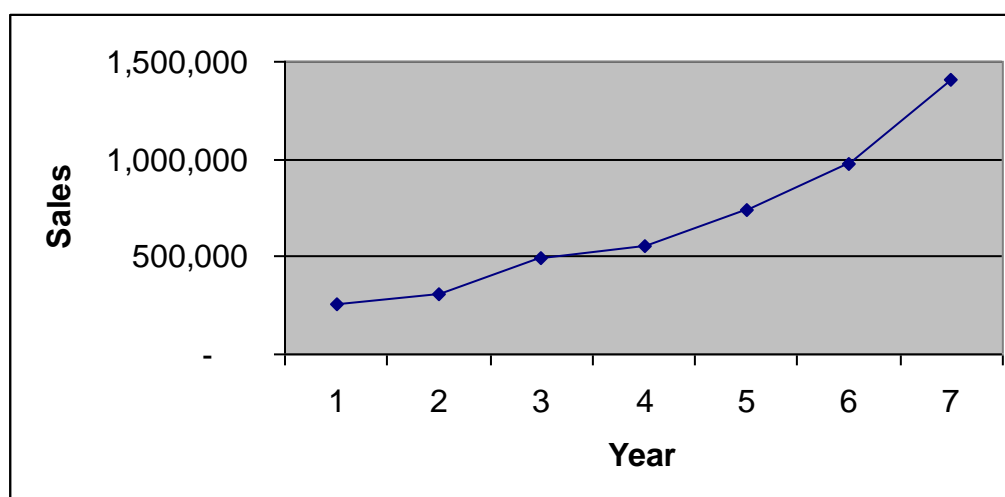
Medium Scenario

This trajectory follows the experience of the PSI programme in Zimbabwe where there was initially slow uptake but then more rapid maturation of the market for female condoms (Figure 2). In this scenario, there was a 4 year period after the introduction of the product before there was a take-off, with sales peaking at almost one million by year 7. For the purposes of the cost analysis, it is assumed that the upward trend that is observed in year 7 continues (rather than the dip seen in the Zimbabwe actual sales).   This dip was partially attributable to fluctuations in donor funding, and again highlights the limitations of relying on one source of data for examining trajectories.

Figure 2. Annual Sales of Female Condoms in Zimbabwe by PSI
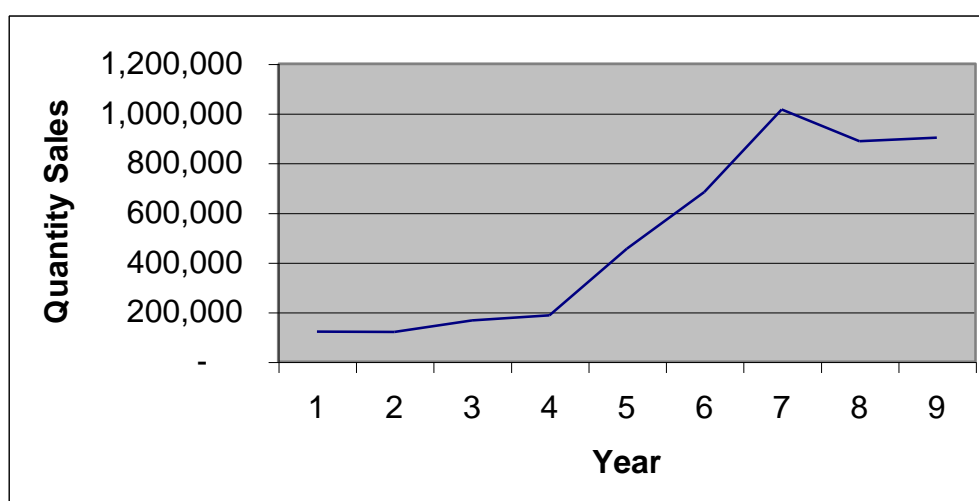
Slow Scenario

This trajectory follows the experience of the PSI programme in Tanzania where there has been persistently slower sales (apart from year 6) - Figure 3. For the purposes of the cost analysis, the trend is taken (without year 6 which could have been attributable to fluctuations in donor funding) and extrapolated until year 10.

Figure 3. Annual Sales of Female Condoms in Tanzania by PSI
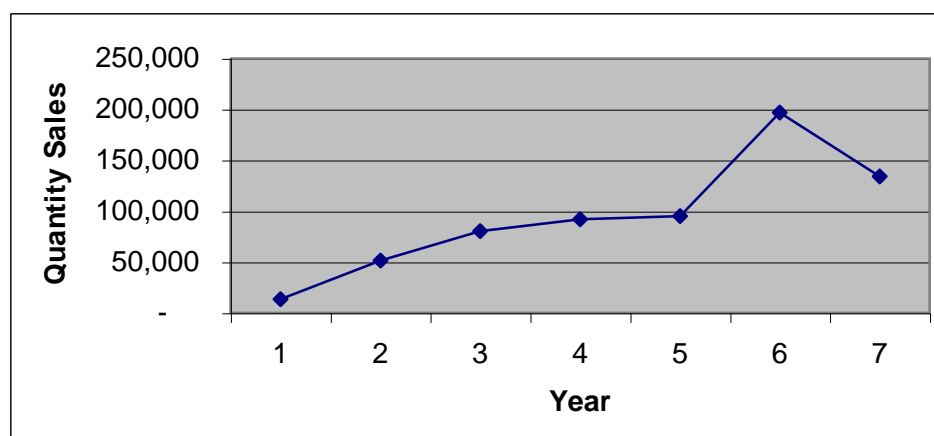
Estimation of Costs of Scale-up

In order to finalise the scenarios for the estimation of costs, the trajectories were estimated; cost data was compiled and then the costs for scaling up the introduction of microbicides over 10 years was calculated.

Estimation of Trajectory Paths

Based on the data from Uganda, Zimbabwe and Tanzania, trajectory paths were estimated. The sales data were taken from the whole of each country, however as we were interested in a target population of urban women aged 15-49, the trajectory path for sales was adjusted for this.[17] In order to estimate the trajectory paths, actual sales were taken and univariate trend regression analysis was used to estimate the trajectory path for each country. These predicted sales were then divided by the urban population of women (aged 15-49),[18] for the respective year of the sales to obtain predicted sales per women. These predicted sales per women were then applied to the size of the female urban populations in the selected countries.

In order to consider what these predicted sales per women would translate in terms of coverage, UNAIDS guidelines to defining coverage can be applied. If it is assumed that 90% of women 15-49 are sexually active, 75% of whom are in regular partnerships. 5% of women are assumed to be in commercial sex work, and 10% in casual relationships. By using the estimated annual number of sexual acts (66, 200, 25 respectively) coverage figures can be estimated. A crucial assumption is the consistency of microbicide use for sex. For the coverage calculations we adopt a 95% level of consistency in all sex acts. (Note – these assumptions are taken from the UNAIDS Global Report on the HIV/AIDS Epidemic)

Table 2: Assumptions Made to Estimate Coverage Rates

Category	Share of Population	Number per million population	Average Sexual Contacts per annum	Sales Required for 100% Coverage (million)
In Regular Partnerships	75%	750,000	66	49.5
Commercial Sex Workers	5%	50,000	200	10.0
Non Regular Partnerships	10%	100,000	25	2.5
Total				62.0

Based on these assumptions 49.6 million sales are required to ensure 100% coverage of sex acts with 80% consistency of use for the illustrative example above, using a population of 1,000,000.

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[17] Coverage figures were not explicitly used as the urban populations were relatively small compared to the optimistic and realistic scenarios, suggesting extremely high coverage figures. In reality, this masked the fact that there was high uptake in rural settings in Zimbabwe and Uganda.

[18] Population figures were all taken from UN Population Division Statistics

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ANNEX 2: Background to Costing Analysis

There are 3 components to the cost inputs used for the estimates of scaling-up. The first cost input is the cost of the microbicide.

Microbicide Costs - The costs set out below are highly provisional on two counts. Firstly, the cost of a microbicide is highly dependent on its formulation. A variety of potential formulations are currently being tested or considered and there is no certainty which will progress into clinical trials or forwards for registration. Costs could vary from a few cents through to several dollars. Secondly, estimated costs for product currently in trials (gel/applicator systems and vaginal rings) are based on low production volumes and particular technologies. Innovation in product design and scale efficiencies at great production volumes may reduce unit costs significantly. However, predicting these innovations and efficiencies is currently difficult.

Table 3: Price estimates for Microbicide Products (US dollars)

Product	Low Estimate	High Estimate
Product 1 (coitally dependent)	$0.57	$0.59
Product 2 (long-lasting product 30/90 days)	$15.02	$17.50
Product 3 (daily product)	$0.57	$0.70

Source: IPM

Estimates for products 1 and 3 are base on estimated costs for gel/applicator based systems currently in clinical trials. Consequently, they are based on low production volumes (those needed to conduct trials). For early generation and current next generation products, the cost of active pharmaceutical ingredients accounts for a small proportion of the total gel/applicator costs. For the purposes of the sensitivity analysis above, a lower cost of $0.20 per unit is estimated for higher volumes of production. However, this lower figure is largely speculative.

Estimates for product 2 are based on small scale production for a current vaginal ring technology. Caution is required with this estimate as alternative, less expensive and production scaleable ring technologies are under active consideration. For the purposes of sensitivity analysis, a low cost of $5 - $6 is considered. However, this lower figure is not based on systematic production process analysis.

Initial Market Development Costs – it is assumed that the introduction and scaling-up of microbicides will be accompanied by advertising and promotion efforts involving the mass media. In a recent review of advertising and promotion by PSI for male and female condoms (Terris-Prestholt et al 2005), average annual promotion expenditures range from $ 6,800-$2,160,240 with a mean of $316,159 for male condoms and $0-$251,072 with a mean of $40,958 per country. Promotion costs varied by scale and maturity of country programme. For this analysis, PSI data related to promotion, population size and product age were examined. The data was too short for panel estimation. First, a quadratic regression model was estimated relating promotion expenditures to population. Then based on countries for which data was available for 6-8 years, a decay function was approximated to show how promotion expenditures might decrease over time.

Delivery Costs – it is assumed that implementation is done through quasi-public channels. Given the requirement for considering the economies of scale, the study uses the experience of costs of products from the PSI data suggest that there are

significant economies of scale that can be achieved. For the purposes of the analysis we estimate a univariate price function for the price reductions seen in Zimbabwe (net of the cost of the product). The reductions in price due to economies of scale are shown in Figure 4. The delivery costs included associated training related to provision of the microbicide. In reality, these training costs will be relatively negligible overall, but we would expect an up-front loading of these in a short initial time-frame. The delivery costs are incremental to existing systems. Again, it may well be that the PSI data is not a good approximation to public sector costs, but has been used as the initial starting point in the absence of systematic data.

Figure 4: Price Reductions in Delivery Due to Economies of Scale
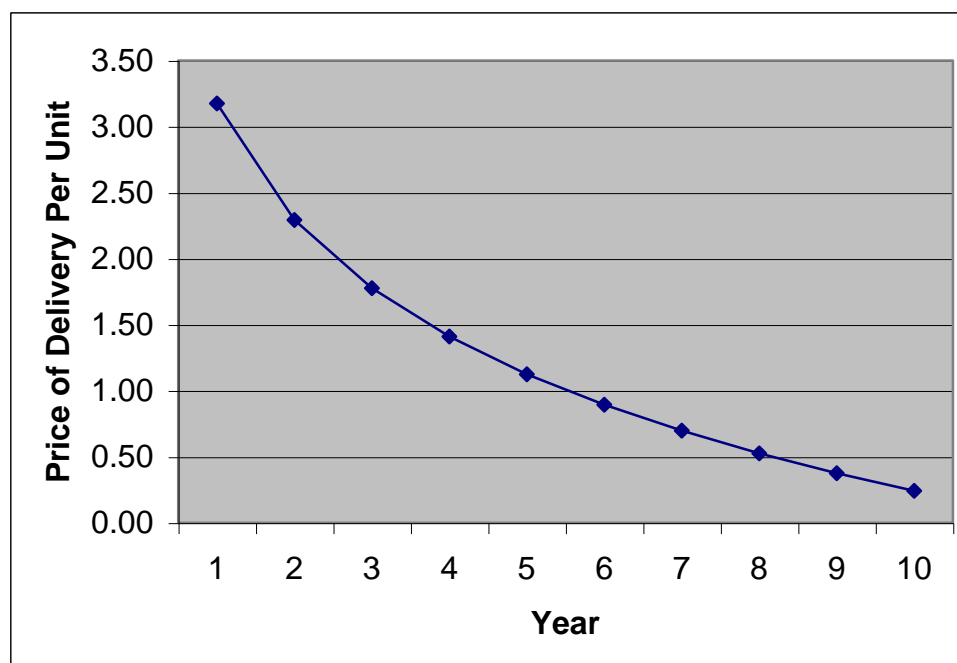
Cost Calculations

In order to estimate the costs of microbicide introduction, the three cost components (promotion, microbicide and delivery) were calculated and summed together. First, the number of sales per woman was calculated annually, according to the scenario-specific trajectory path for each country. This figure was then multiplied by the price of the microbicide to obtain the microbicide cost. These sales figures were also multiplied by the price of delivery to obtain the delivery cost. Promotion costs were estimated for each country annually according to the regression and decay functions described above and were independent of the level of sales. Promotion costs were calculated on the basis of population size and time since introduction. A summary of the cost calculation is presented below.

Annual total cost of microbicide introduction

= Predicted sales x price of microbicide

+ Predicted Sales x price of delivery (scale)

+ Promotion (population, time)

Where Y(x) indicates that the variable Y is a function of or allowed to vary by X.

ANNEX 3: Detailed Analyses of Baseline Scenarios

The baseline cost analysis for each scenario represents the following construct:

- all countries start in first year
- constant microbicide price (no adjustment for economies of scale or other factors affecting the price)
- economies of scale in delivery prices
- population size-related promotion effects (with some economies of scale due to the quadratic nature of the regression analysis).

Cost Breakdown

Figure 5 shows that in the fast and medium scenarios, the microbicide and delivery cost components increase through time, reflecting increasing up-take. In contrast, the costs of delivery decline in the slow scenario. This corresponds to the fact that the scale effect dominates the low-uptake (e.g. that the scale effect comes in relatively quickly for sales volume). Promotion costs are a decreasing component for all scenarios reflecting the assumptions of reduced annual promotion activities.

Figure 5a: Cost Breakdown - Fast Uptake Scenario
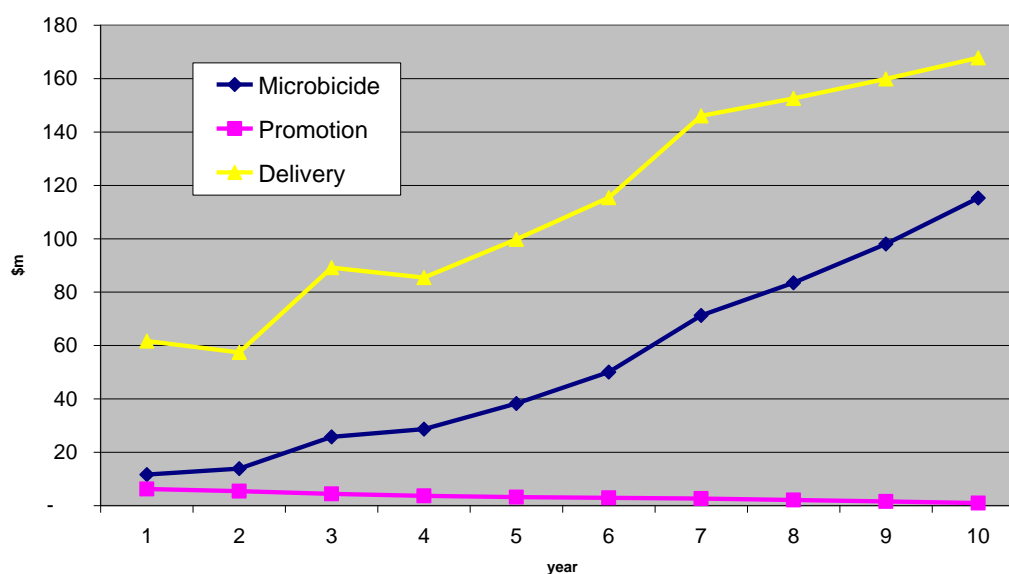
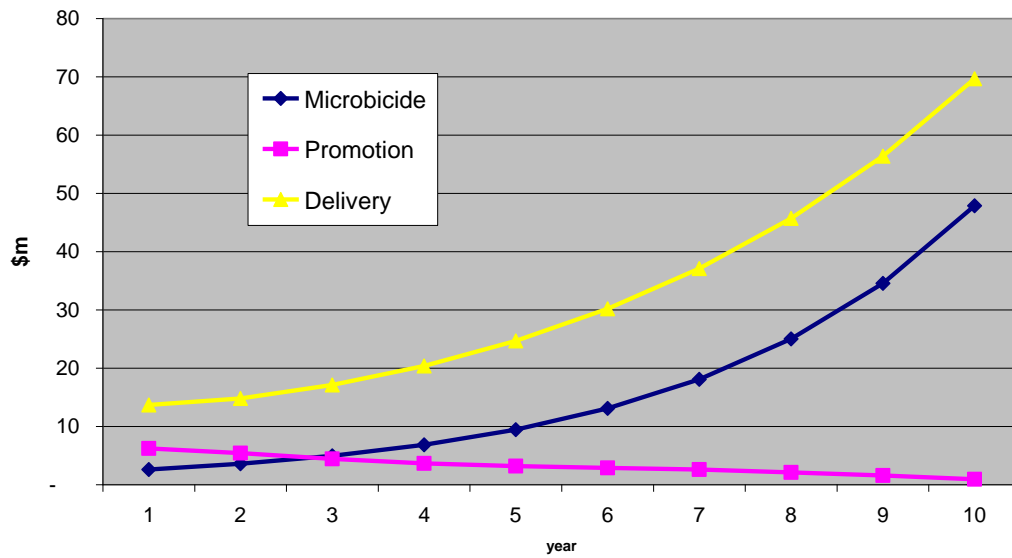**Figure 5b: Cost Breakdown - Medium Uptake Scenario**

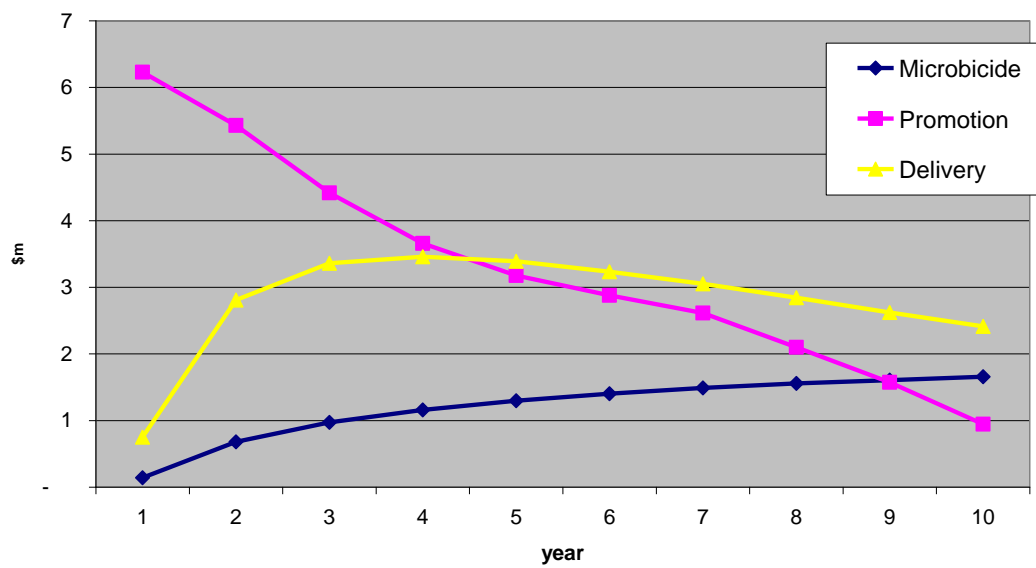**Figure 5c: Cost Breakdown - Slow Uptake Scenario**

Figure 6 shows the variation in cost structure between years 1 and 10 for each scenario. For both the fast and medium scenarios, by year 10 the microbicide and delivery components are approximately half of the cost. Scale economies achieved by delivery mean that although the delivery cost component is increasing, it is doing so at a decreasing rate. In contrast, in the slow scenario, the relative cost share of delivery costs remains the same as although there are scale effects, the volume of sales has not increased substantially. Reducing promotion costs mean that the relative share of the microbicide cost component has increased.

Figure 7 shows the country-specific total cost of microbicide introduction costs. The fast and medium scenarios show again the increasing costs of introduction reflecting higher uptake. In contrast, the slow scenario shows that costs will actually decrease by country reflecting the fact that there is slow uptake accompanied by decreasing promotion costs and some scale economies in delivery. In relative terms, the large population countries (India, Nigeria, South Africa) reflect the majority of the country costs.

Composition of Costs: Years 1 to 10 by Scenario

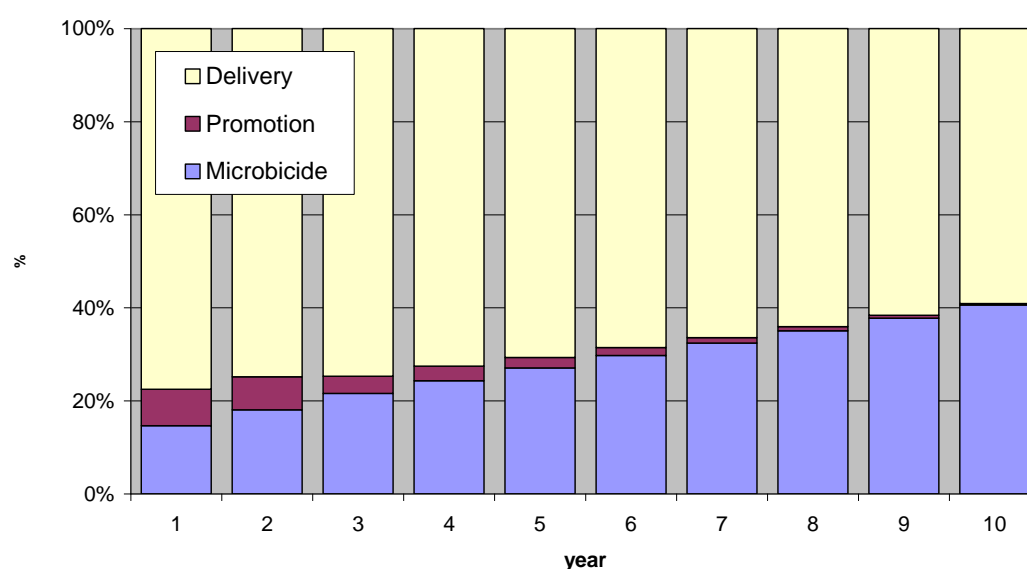**Figure 6a: Composition of Costs - Fast Uptake Scenario**

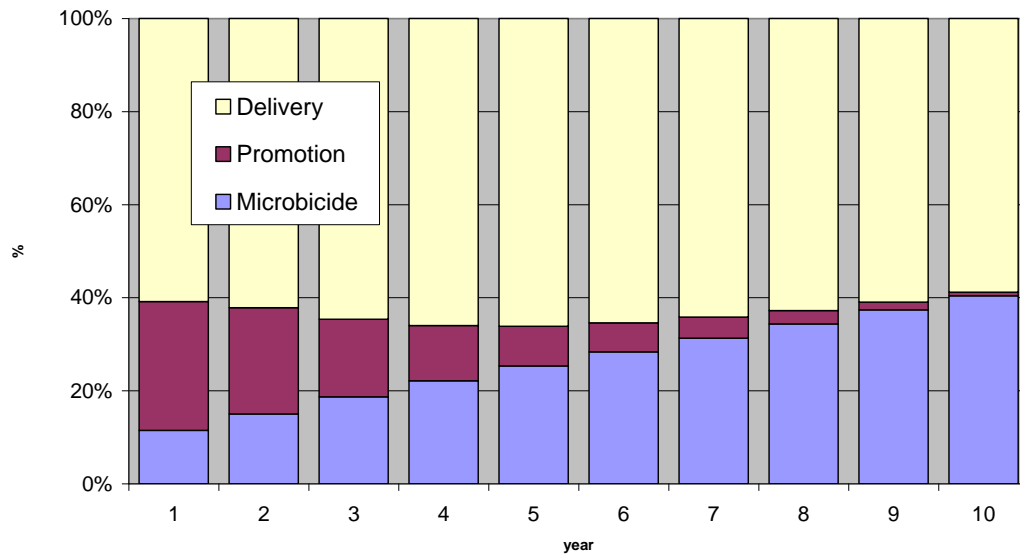**Figure 6b: Composition of Costs - Medium Uptake Scenario**
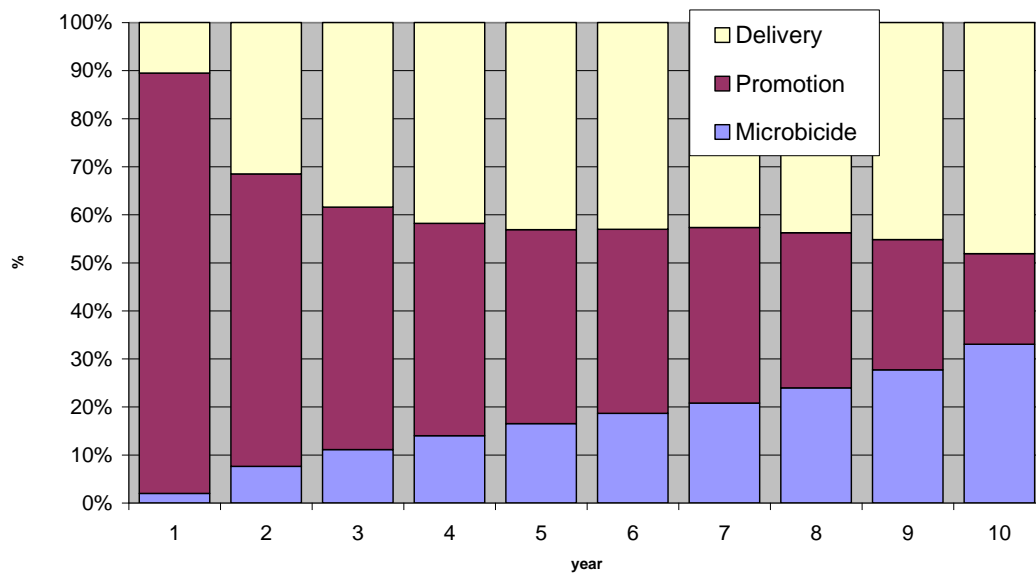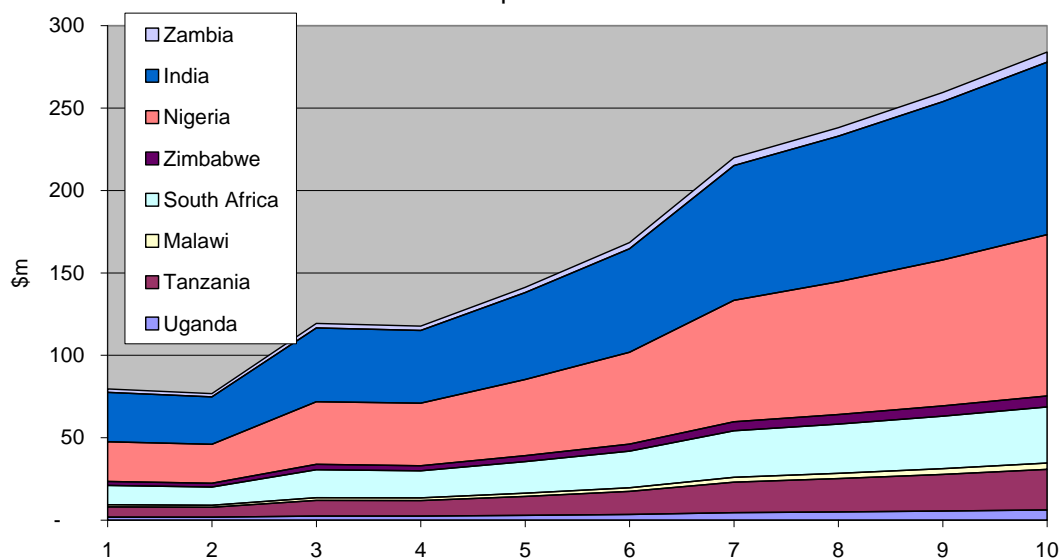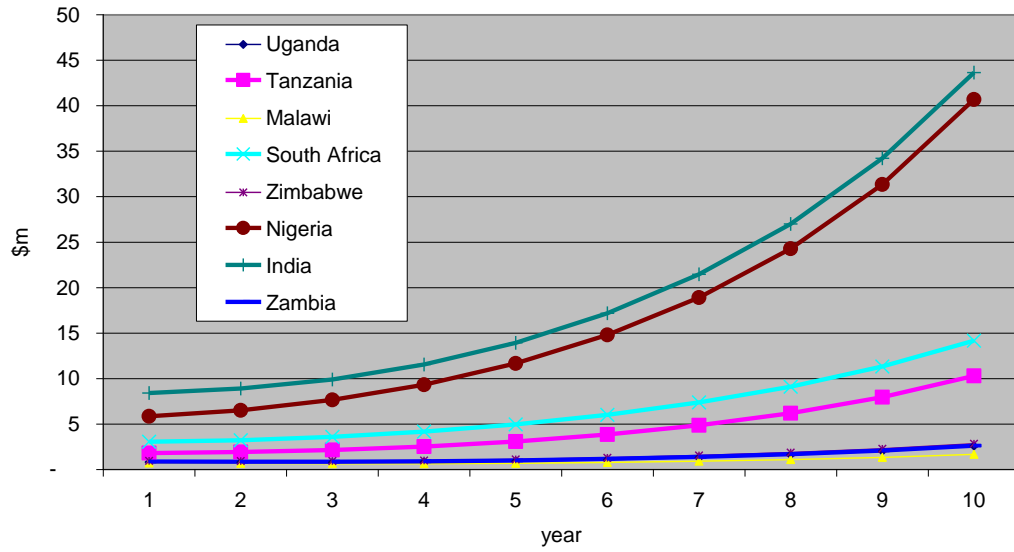

Figure 6c: Cost Composition - Slow Uptake Scenario

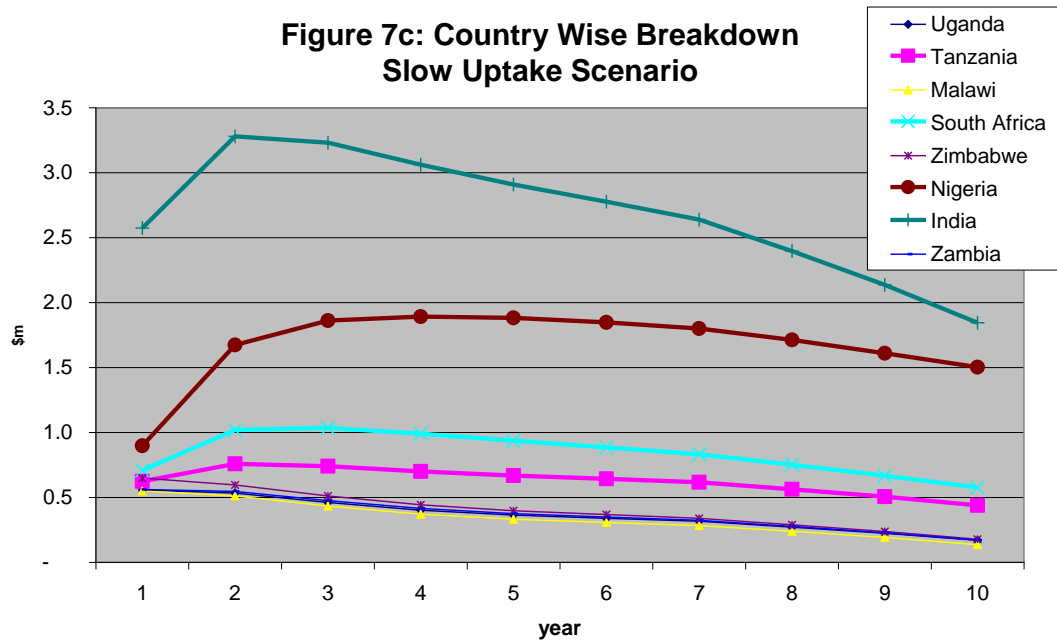**Microbicide Introduction Costs by Country**

Figure 7a: Countrywise Breakdown of Costs
Fast Uptake Scenario

Figure 7b: Country Wise Breakdown
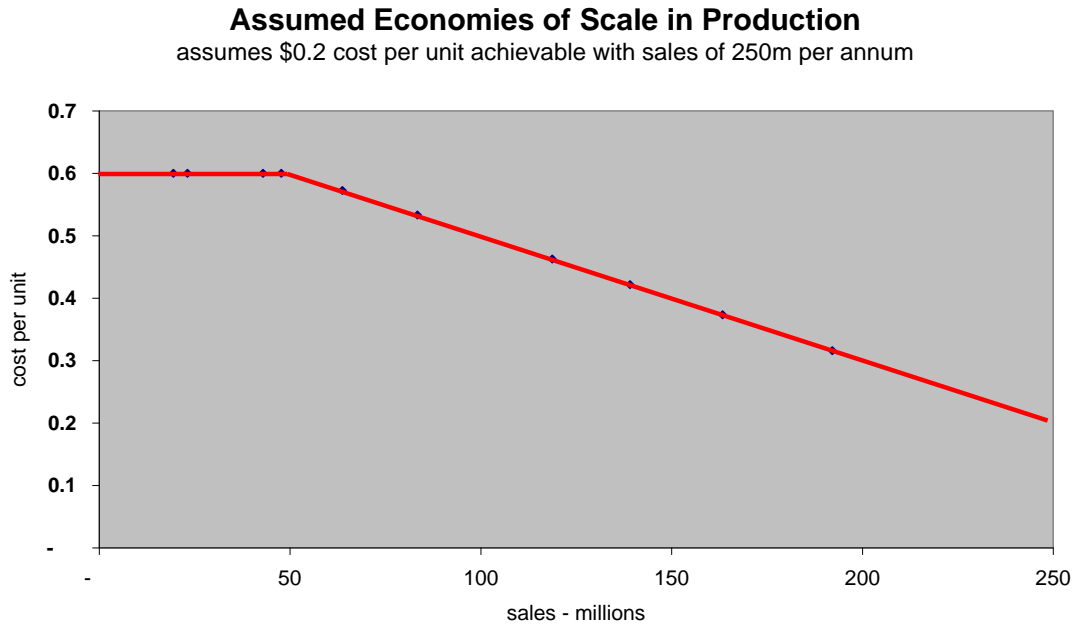## Medium Uptake Scenario

Figure 7c: Country Wise Breakdown
## Slow Uptake Scenario

ANNEX 4: Economies of Scale

The assumptions for the unit costs of production as set out in the chart below. It is assumed that costs decline to 20 cents when production reaches 250m units per annum.

Assumed Economies of Scale in Production

assumes $0.2 cost per unit achievable with sales of 250m per annum

The implications of this for unit product costs are set out in the table below. According to the assumptions used unit cost would decline to just over 20 cents with the 10 year period under the fast uptake scenario, fall to just over 50 cents under the medium scenario and remain at current levels under the slow scenario

Projected Unit Product Costs

Assuming Economies of Scale in Production: according to different scenarios
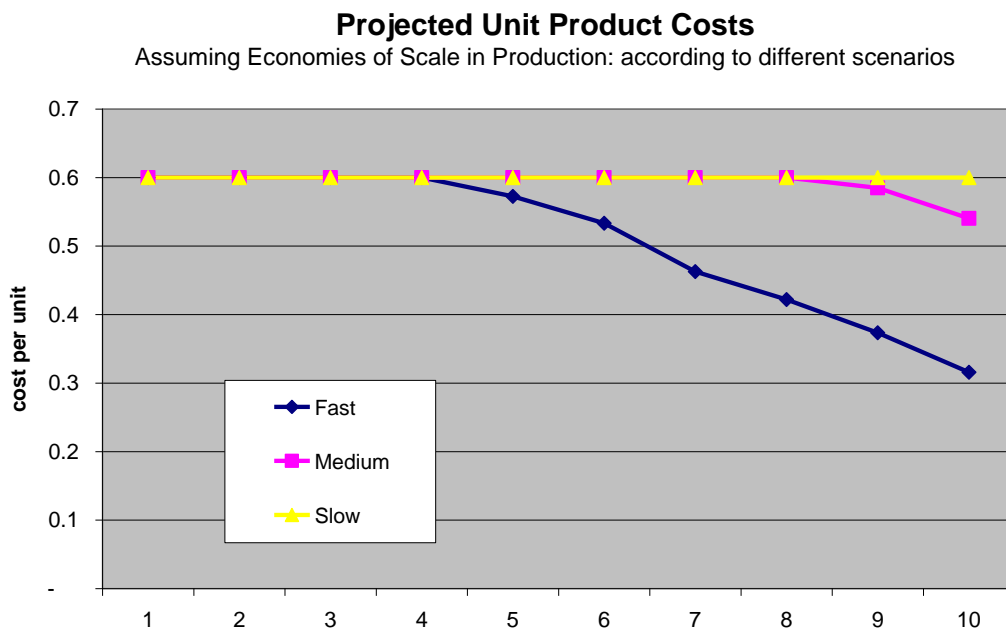
ANNEX 5: Fiscal Space Estimates

It order to estimate the level of funds likely to be available for health in coming years assumptions were made about key determinants of health spending – including economic growth, the share of public expenditure to GDP, the share of public spending to health, the extent to which private expenditure increase with income and overall aid flows and their regional and country wise allocations (the assumptions are set out in the table below). Although the availability of data is a problem the approach seems to be useful in identifying the relative importance of the key factors and assessing the likelihood of achieving financing targets. A number of sensitivity analyses were run to test the impact of alternative assumptions and thus the robustness of the findings.

Fiscal Space: Overview of Assumptions and Scenarios Tested

	Base Case	Optimistic (High)	Pessimistic (Low)
Growth in Per Capita Income	World Bank Long Term Development Indicators	Base Case +50%	Base Case – 50%
Population	UN Population Division medium estimates	UN Population Division medium estimates	UN Population Division medium estimates
Share of GDP to Public Expenditure	Increase of 0.25% of GDP per annum to a maximum of 50%	Increase of 0.5% of GDP per annum to a maximum of 50%	Constant
Share of Public Expenditure to Health	Increase of 0.25% per annum to maximum of 20%	At least 15% of public expenditure by 2010 (Abuja)	Constant
Overall Aid Flows	Consistent with G8 Commitments		
Allocation of Aid Flows	4 approaches: business as usual; additional funds population based; additional funds equity based (the base case scenario); radical equity allocation		
Share of Development Assistance to Health	Assumed to increase by 10% from 2003 levels by 2010	Assumed to increase by 10% from 2003 levels by 2010	Assumed to increase by 10% from 2003 levels by 2010
Private Expenditure	Income elasticity of 1.1	Income elasticity of 1.5	Income elasticity of 0.9

Key Data sources: Funding – World Health Report 2006; Population (Projections) – UN Population Division