Phillips McDougall

The Cost of New Agrochemical Product Discovery, Development and Registration in 1995, 2000 and 2005-8.

R&D expenditure in 2007 and expectations for 2012

Final Report

A Consultancy Study for Crop Life America and the European Crop Protection Association

January 2010

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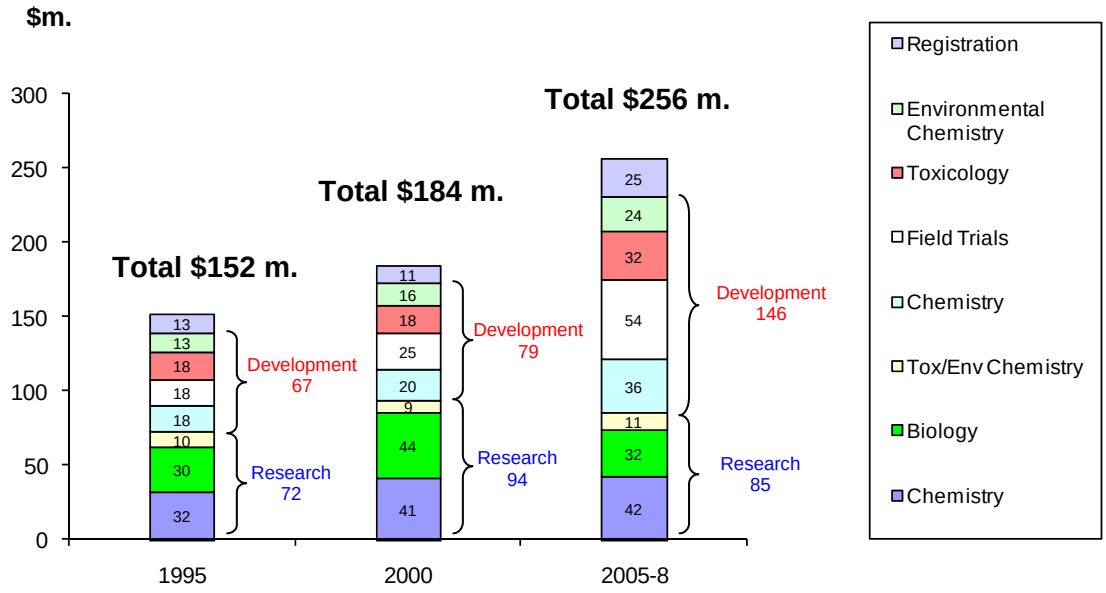
Executive Summary

This study presents the results of a survey of the leading crop protection companies designed to determine:

- The expenditure necessary for the discovery and development of a new crop protection product in 1995, 2000 and in the 2005 to 2008 period.
- The number of new molecules that have to be synthesised and tested to lead to the discovery of a new product
- The average time between initial product synthesis and product launch

Ten companies were surveyed and the results were as follows:

Discovery and Development Costs of a New Crop Protection Product



The overall costs of discovery and development of a new crop protection product increased by 21.1% from $152 m. (€115m.) in 1995, to reach $184 m. (€140m.) in 2000. From 2000 to the 2005-8 period, costs increased by 39.1% to $256 m., equivalent to Euro 189 million at constant exchange rates.

The survey results demonstrated that the cost of taking a product through development stages increased from $67 m. in 1995 by 17.9% to $79 m. in 2000 and by 84.8% to $146 million between 2005-8. Within this the greatest rise was seen in the costs of field trials which were shown to have risen by 116% from 2000 to $54 m. in 2005-8. It is likely that this increase can be attributed to a rise in efficacy data required by both regulatory bodies and companies as they target development products at an increasing number of crops and pests.

Overall costs of new product research rose by 30.6% from $72 m. per product in 1995 to $94 m. in 2000, but declined slightly to $85 m. in 2005-8. Cost savings may have been made due to greater efficiency from high throughput screening, combinatorial chemistry and genomics. All of these technology changes are aimed at increasing the overall scope and capability of the discovery process. It is also possible that with a high number of research candidates the focus is now on the development stage once a product has been accepted.

On the basis of individual costs, the most significant increase over the 2000 to 2005-8 period was found in field trials as discussed above, followed by development chemistry up 80% to $36 m. possibly due to the use of more advanced formulation. In this time period toxicology costs, also in the development phase, increased by 77.7% and environmental chemistry by 50%.

This results of the survey on product synthetic leads showed that the average number of new molecules that are synthesised and subjected to biological research in order to lead to the registration of one new crop protection product has increased between 1995 to 2000 and was sustained in the 2005-8 period.

Number of Products Processed leading to a Successful Product launch

		1995	2000	2005-8
Research	Synthesis	52500	139429	140000
Development		4	2	1.3
Registration		1	1	1

While both costs and the number of developmental leads increased over the 1995 to 2000 period, the survey results also demonstrated that the average lead time between the first synthesis of a new crop protection molecule and its subsequent commercial introduction had increased.

Crop Protection Product Discovery and Development Lead Time

	1995	2000	2005-8
Number of years between the first synthesis and the first sale of the product	8.3	9.1	9.8

This increase could reflect an increased complexity in the data requirements of regulatory bodies however it could also indicate that re-registration procedures in both the EU and the USA could have impacted on companies' internal development workload.

Introduction

During 2009, on behalf of Crop Life America and the European Crop Protection Association (ECPA), Phillips McDougall undertook a survey of the leading global agrochemical companies designed to provide information on the comparative costs involved in the discovery, development and registration of a new conventional chemical crop protection product.

This study was carried out to update previously published information which showed that the overall level of expenditure required to develop and register a new crop protection product had grown from DM 50m. ($23.1m.) in the 1975-1980 period to DM 250m.($157m.) for the 1990-1995 timeframe. (See Appendix 1)

Study Definitions

The process leading to the discovery, development and commercialisation of a new agrochemical molecule is complex, costly and time consuming. The overall process can be split into three main stages, firstly the research programme leading to the discovery of a new molecule, secondly its development and lastly its registration with the appropriate regulatory authority.

Research

For a new chemical crop protection product the discovery or research process involves the synthesis of candidate molecules. These candidate molecules are subsequently subjected to a series of biological research tests or screens which are designed to demonstrate the biological activity of the new molecule. The screening process is likely to involve a number of increasingly complex stages to ensure that the new chemical has a suitable biological activity to merit further development. Although the synthetic and biological screening programme will lead to the discovery of molecules whose biological activity has been quantified, the decision as to whether the new chemical is suitable for full development will also involve other criteria, namely it must be able to be patented, possess good toxicological and environmental properties and display good commercial prospects.

In order to satisfy these latter criteria, the research process generally includes preliminary toxicological and environmental testing as well as undertaking an evaluation of the new chemical's commercial prospects. Individual companies will set their own measure for success for these tests.

In recent years the chemical synthesis stage has been enhanced through the development of combinatorial chemical methods which have resulted in companies having the ability to synthesise large numbers of molecules. In addition the development of high throughput screening methods have enabled a greater number of molecules to be subjected to the biological research process. Biological research has also been enhanced through the use of genomics as a means for the discovery of new active molecules and potential sites of activity within target organisms.

Overall the ultimate goal of the discovery process is to provide product leads or candidates that have biological, chemical, toxicological, environmental and commercial characteristics suitable for further development.

Development

Agrochemical product development encompasses a broad range of processes which by definition are all aimed at developing the product for subsequent commercialisation.

Chemical development processes include the establishment of a pilot plant to produce suitable quantities of material for further biological and safety testing. Studies on optimising the manufacturing process for commercial production are subsequently undertaken with the aim of arriving at a suitably cost effective manufacturing process.

Another important area of chemistry development is formulation evaluation. This generally involves the testing and optimisation of a variety of formulations of the new crop protection product to ensure that the product can be delivered in a safe and effective manner for subsequent field use.

In the research stage, biological screens, normally conducted in the laboratory, will have established that a product has potentially important crop protection activity. Further biological development of the new crop protection product is designed to investigate the activity of the product against a variety of target pests, weeds or diseases in a number of crops under a variety of environmental situations. These studies are conducted in actual field situations and comprise both small and large-scale field trials. As well as testing the relative efficacy of the new product, these field trials also encompass formulation evaluation and are used as a basis for the determination of the fate of the molecule and its metabolites or residues in the environment, soil and plants.

Although some preliminary safety testing will have been undertaken at the research stage, the development programme for a new crop protection product includes significantly expanded toxicology and environmental chemistry testing to meet the statutory requirements of the regulatory bodies in the USA, the EU and elsewhere.

Registration

The results of the developmental studies are subsequently submitted to the regulatory body for review. On acceptance the product is registered by the regulatory body and commercialisation of the new crop product can then take place.

The following page contains a glossary of the main terms used the describing the research, development and registration process for a new crop protection product.

Glossary of Terms

Research	The discovery of new active ingredients, either from natural sources or by chemical synthesis, and subsequent screening to assess biological activity. Research stages generally also include preliminary toxicological and environmental testing prior to making the decision as to whether to progress the product to full development.
- Chemistry	The production of new chemical entities for assessment as potential active ingredients, either by conventional chemical synthesis that has now been enhanced by combinatorial chemistry techniques, or by extraction from natural sources.
- Biology	Assessment of the biological efficacy of a potential new active ingredient. Conventional screening has now been enhanced by rapid throughput techniques. Biological Research has also expanded to cover Genomics.
Chemical Synthesis	Production of new potential active ingredients from basic chemical entities, this process is now enhanced by combinatorial chemistry.
Combinatorial Chemistry	A rapid mechanised system for the production of a large number of potentially active ingredients from basic chemical reagents.
High Throughput Screening	Rapid, mechanised system for assessing the biological activity of very low volumes of chemical.
Genomics	The application of biotechnology to further understand genetic structure and function.
Development	The progression of selected potential products from discovery to commercialisation. Includes regulatory studies required to support product registration as well as investigating the biological efficacy of the product in the field against a variety of pests in multiple crops, the manufacturing processes and formulation chemistry.
- Chemistry	The scale up of chemical synthesis to produce volumes required for product development and then for commercial introduction. Also the development of formulations suited to the target crop applications.
- Field Trials	The assessment of activity against target weeds / pests / diseases in the field, including comparison with standard treatments already on the market.
- Toxicology	Safety assessment of the product candidate in biological systems.
- Environmental Chemistry	Investigation of the physical and metabolic breakdown of a potential product in plant, animal, soil and water systems. Identification and assessment of the residues of the compound and its breakdown products in these systems.
Registration	Preparation and submission of data dossiers to, and subsequent negotiations with, registration authorities with the aim of obtaining approval to market a new product.

Study Scope

As described above, the primary aim of this study was to determine the cost of several key parameters in the discovery and development process for a new crop protection product in the USA and the EU. The parameters to be investigated were:

- Cost of discovery, development and registration
- The number of products processed by companies in order to commercialise one new crop protection active ingredient
- The lead time between the first synthesis and the commercial introduction of the new active ingredient

Methodology

The study was conducted according to the protocol which is included as Appendix 2.

The primary data for this investigation was obtained from a questionnaire (see Appendix 3) which was sent to a group of agrochemical companies which were considered to have active discovery programmes for conventional chemical crop protection products.

The companies included in this survey were :

- BASF
- Bayer
- Dow
- DuPont
- Sumitomo Chemical
- Syngenta

On receipt, the results of each company response were added to a matrix in which each company was listed by code number. Each company result was subsequently aggregated and the mean value of each particular category was calculated. The results of the responses are shown in the report as mean values however the variance within the actual responses is documented as Appendix 4.

In the case of Part 1 of the study, namely the evaluation of the cost of new product discovery and development, where a company response contained incomplete information on sub categories, the mean values were calculated on a pro rata basis to ensure that the mean category totals agreed with the sub category values.

Study results – Part 1

Cost of New Product Discovery and Development - 1995

Of the ten companies surveyed, data on six companies with respect to the 1995 situation for the cost of discovering and developing a new crop protection product were received. In some cases the company responses did not contain information on all sub categories and as a result sub category mean values were calculated on a pro rata basis according to the number of responses received.

The actual number of responses and the mean values of the company responses are shown in the table below :

Discovery and Development Costs of a New Crop Protection Product (1995)

Category	Sub category	Cost ($m.)	Number of Responses
Research	Chemistry	32	5
	Biology	30	5
	Toxicology/Environmental Chemistry	10	5
Research total		**72**	**6**
Development	Chemistry	18	6
	Field Trials	18	6
	Toxicology	18	6
	Environmental Chemistry	13	6
Development total		**67**	**6**
Registration		**13**	**5**
Total		**152**	**6**

In terms of total costs of new product discovery and development, the results of the survey were essentially identical to the previous investigation (see Appendix 1) where the costs were shown to be DM 250m. ($157m.)

Overall in 1995 the highest costs associated with new crop protection product R&D were in the research process leading to the discovery of a new product, with an overall cost of $72m. Within this chemical synthesis was the most costly stage in the discovery process with an average value of $32m. followed by biological research screening with a mean cost of $30m.

Total development costs in 1995 were found to be $67m. and these were relatively equally split amongst the various sub categories. The remaining expenditure deemed necessary for new product discovery and development comprised $13m. for product registration.

Cost of New Product Discovery and Development - 2000

In total ten companies were surveyed. All companies responded to the questionnaire with nine companies returning responses containing quantitative data.

As with the 1995 data, some company responses were incomplete in that they did not contain information on all sub categories and as a result sub category mean values were calculated on a pro rata basis.

The actual number of responses for each category and sub category, and the mean values of the company responses are shown in the following table:

Discovery and Development Costs of a New Crop Protection Product (2000)

Category	Sub Category	Cost ($m.)	Number of Responses
Research	Chemistry	41	6
	Biology	44	6
	Toxicology/Environmental Chemistry	9	6
Research total		**94**	**9**
Development	Chemistry	20	8
	Field Trials	25	8
	Toxicology	18	8
	Environmental Chemistry	16	8
Development total		**79**	**9**
Registration		**11**	**7**
Total		**184**	**9**

The above results demonstrated that the overall costs for the discovery and development of a new agrochemical product in 2000 had risen to $184m. (Euro 140 m.).

As with the 1995 results, product research or discovery remained the most significant category in new agrochemical R&D with an expenditure of $94m., equivalent to 51.1% of the total. Within this, biological screening was the most significant sub category representing an expenditure of $44m. followed by new product chemistry which accounted for a further $41m. during 2000. Early stage toxicology and environmental chemistry, similar to the 1995 situation, remained a relatively minor component of the research process.

Product development costs in 2000 represented a total expenditure of $79m., equivalent to 42.9% of the overall total. Within this category, field trails were the most significant costs with a value of $25m., followed by developmental chemistry which accounted for a further $20m. and toxicology which was valued at $18m. The remaining expenditure in product development was environmental chemistry at $16m.

Registration costs in 2000 were assessed at $11m., equivalent to 6.0% of the total discovery and development expenditure.

Cost of New Product Discovery and Development – 2005-8

In total six companies were surveyed, responses from five have so far been received and are included in this report.

As with the 1995 data, some company responses were incomplete in that they did not contain information on all sub categories and as a result sub category mean values were calculated on a pro rata basis.

The actual number of responses for each category and sub category, and the mean values of the company responses are shown in the following table:

Discovery and Development Costs of a New Crop Protection Product (2005-8)

Category	Sub Category	Cost ($m.)	Cost (Euro m.)	Number of Responses
Research	Chemistry	42	32	5
	Biology	32	24	5
	Toxicology/Environmental Chemistry	11	8	5
Research total		**85**	**64**	**5**
Development	Chemistry	36	26	5
	Field Trials	54	40	5
	Toxicology	32	23	5
	Environmental Chemistry	24	17	5
Development total		**146**	**107**	**5**
Registration		**25**	**18**	**5**
Total		**256**	**189**	**5**

The above results demonstrated that the overall costs for the discovery and development of a new agrochemical product in 2005-8 period had risen to $256m. (Euro 189 m.).

Unlike the 1995 and 2000 results, product development has now exceeded research or discovery as the most significant category in new agrochemical R&D with an expenditure of $146m., equivalent to 57% of the total. Within this category, field trials were the most significant costs with a value of $54m., followed by developmental chemistry which accounted for a further $36m. and toxicology which was valued at $32m. The remaining expenditure in product development was environmental chemistry at $24m.

Product research costs in 2005-8 represented a total expenditure of $85m., equivalent to 33.2% of the overall total. Within this, new product chemistry was the most significant sub category representing an expenditure of $42m. followed by biological screening which accounted for a further $32m. Early stage toxicology and environmental chemistry, similar to the 2000 situation, remained a relatively minor component of the research process.

Registration costs in bringing a new product to market in the 2005-8 period were assessed at $25m., equivalent to 9.8% of the total discovery and development expenditure.

Comparison between 1995, 2000 and 2005-8 Costs

The following table summarises the overall survey results for 1995, 2000 and 2005-8.

New Crop Protection Product Discovery and Development Costs

(2005-8 versus 2000 and 1995)

Category	Sub Category	Cost ($m.)			Change
		1995	2000	2005-8	2005-8/2000 (%)
	Chemistry	32	41	42	+2.4
	Biology	30	44	32	-27.3
	Toxicology/ Environmental Chemistry	10	9	11	+22.2
Research	**Total**	**72**	**94**	**85**	**-9.6**
	Chemistry	18	20	36	+80.0
	Field Trials	18	25	54	+116.0
	Toxicology	18	18	32	+77.7
	Environmental Chemistry	13	16	24	+50.0
Development	**Total**	**67**	**79**	**146**	**+84.8**
Registration		**13**	**11**	**25**	**+127.3**
Total		**152**	**184**	**256**	**+39.1**

The above results demonstrate that the overall costs of discovery and development for a new crop protection product for the market in the EU and the USA have risen by 39.1% from 2000 to reach $256m. in 2005-8.

As shown above, the total cost of research has declined between 2000 and 2005-8 but the cost of development processes has increased significantly, whilst the survey has shown that the expenditure required for the actual product registration process has more than doubled to $25m. by 2005-8. Statutory registration fees are believed to represent only a small proportion of the overall registration process, with the largest element of this increase being the internal costs for preparing dossiers and managing these operations.

The table above indicates that between 2000 and 2005-8, Research costs have declined, principally due to a fall off in biology (or product screening) costs, whilst chemistry (synthesis and formulation) costs have only increased marginally. This may be due to savings associated with the adoption of combinatorial chemistry and rapid throughput screening/genomics. However, it should be noted that in the Development process both Chemistry and Field Trial costs have increased significantly, possibly indicating a shift in focus in where the expenditure is made from the Research process into the Development procedure.

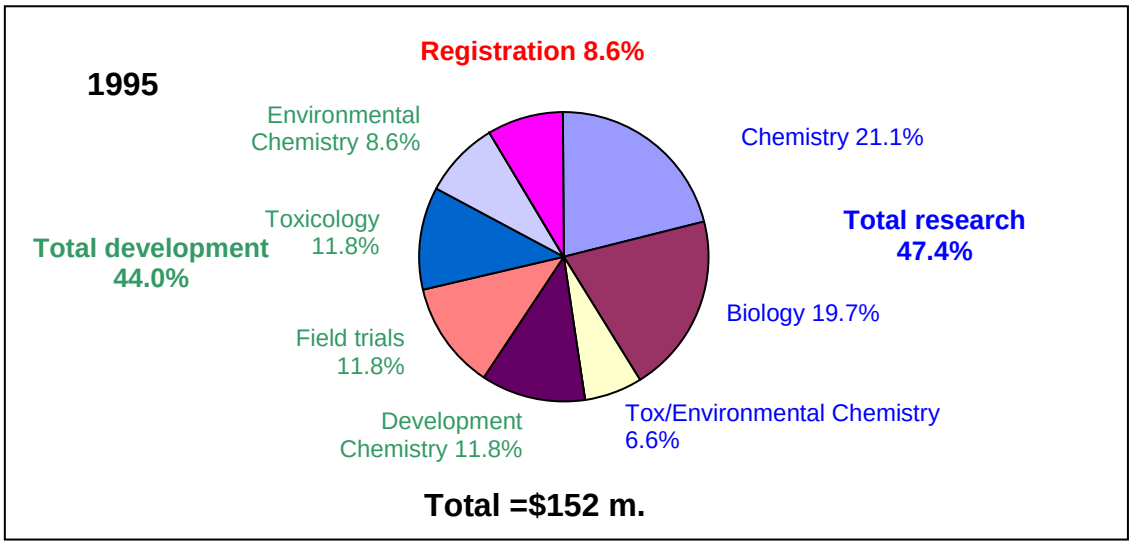
The use of combinatorial chemistry, by definition, significantly increases the number of products available for biological screening; however it is noteworthy that the cost of toxicology and environmental testing at the research stage is relatively unchanged in dollar terms in the 1995 to 2005-8 period. Conversely it can be seen that the cost of environmental chemistry in the development phase has increased. It is possible that with a substantial increase in the number of products being screened it is not viable to undertake the same degree of early stage environmental and toxicology assessment and as a result the focus of this testing may have shifted to the development stage when significantly fewer products are in the pipeline.

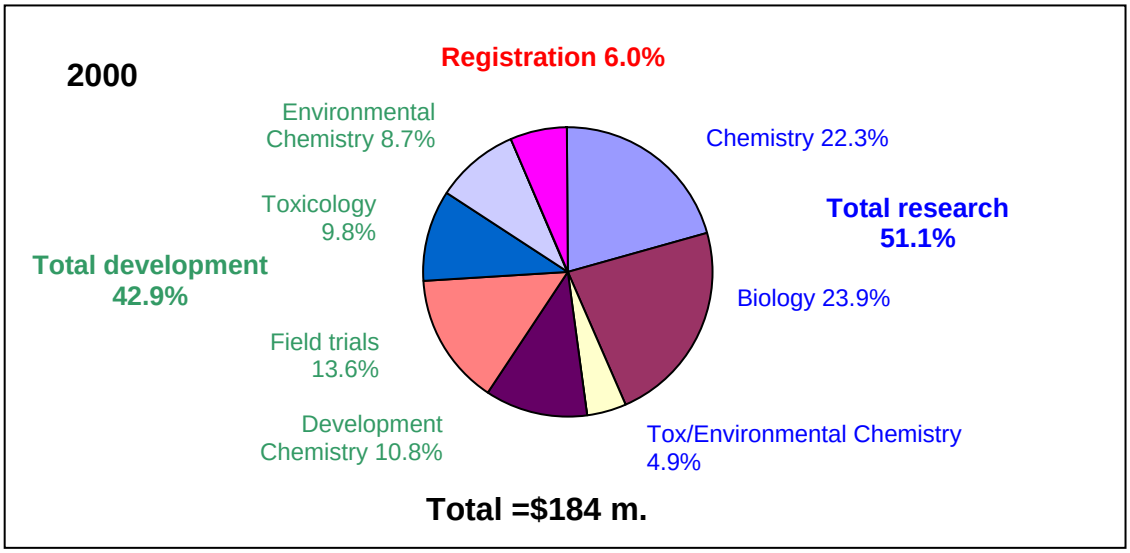
Total product development costs increased by 84.8% from 2000 to 2005-8, with increased costs reported in all sectors, but led by a 116% rise in expenditure on field trails, followed by developmental chemistry with an increase of 80%, toxicology costs up by 77.7% and environmental chemistry whose costs rose by 50%.

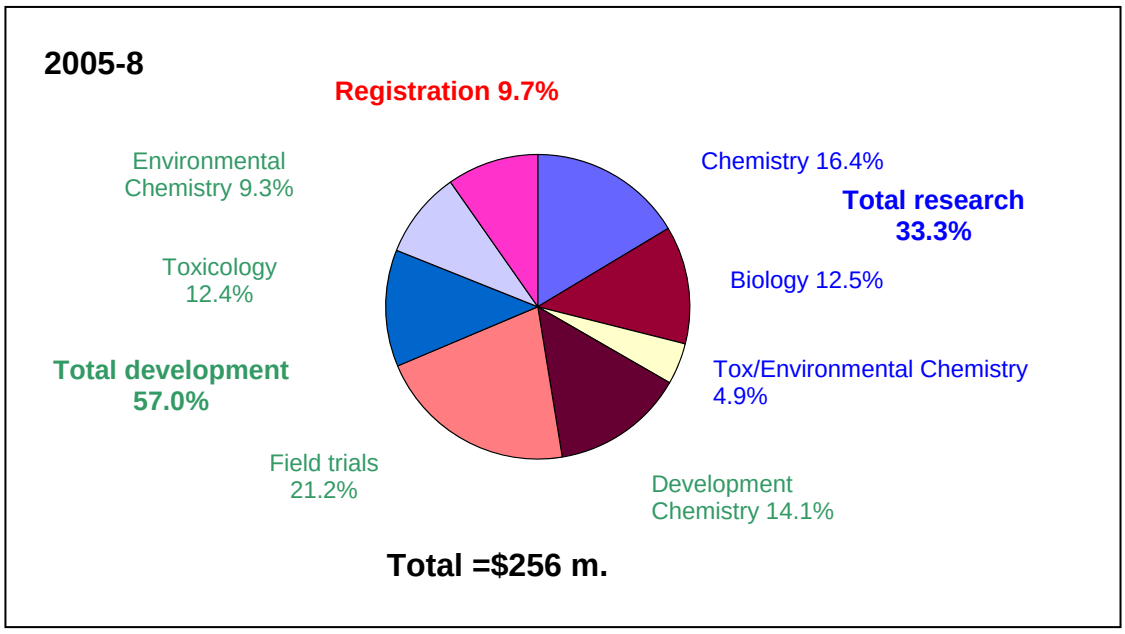
The substantial rise in the costs of field trials in product development could arise from a need to increase efficacy data both for regulatory bodies and for companies as they set increasingly stringent commercial hurdles in the development process. For example some companies set potential sales thresholds that are expected to be achieved by development products when commercialised. In order to satisfy these targets products may well have to have an application in multiple crop and pest situations. If this is the case it could potentially increase the number of field trails that have to be undertaken.

The fact that the costs of chemical development have also increased is noteworthy in that it could well reflect the adoption of more advanced formulation chemistry and an increase in chemical complexity of the new crop protection active ingredient. This latter factor could significantly increase process development costs.

New Crop Protection Product Discovery and Development Costs







Study results – Parts 2 to 4

Part 2: Additional R&D Costs

This part of the questionnaire focussed on the quantification of any additional R&D costs associated with the discovery and development of a new crop protection product that were not identified in Part 1 of the study.

A number of companies identified additional expenses, however all responses highlighted very different costs. For the majority of respondents these additional costs did not exceed $10million

Part 3: Number of Products Processed Leading to a Successful Product Launch

This section of the questionnaire which asked each company to identify the number of products synthesised that would result in the development and launch of a new crop protection product: The responses received showed huge variability. The following table outlines both means and medians of results of this survey section:

Number of Products Processed leading to a Successful Product launch

		1995	2000	2005-8
Research	Synthesis	52500	139429	140000
	Post Synthesis	**	**	**
Development		4	2	1.3
Registration		1	1	1

Note: ** - insufficient data

It is apparent from the above that the number of products that are synthesised and screened to lead to a successful product launch has remained relatively stable on average since 2000.

Despite the high number of products entering the agrochemical R&D chain, it is notable that the average number of products which make it through to the developmental stage has declined from an average of 4 in 1995 to only 2 in 2000 and 1.3 on average in 2005-8. In essence this reflects a greater certainty in the decision making process in product development as the majority of products in development in 2005-8 reach commercialisation.

Although this result may also reflect an increasing level of difficulty in finding new product leads it will also reflect the caution and financial screening of product candidates coming out of research before acceptance for development. This study has shown the increasing costs of bringing a product through development stages, companies need to satisfy themselves that potential commercial return can justify this expenditure. It is believed that a significant number of product leads do not pass into development stages as the potential returns may not justify these costs.

Part 4: Product Development Lead Time

The final section of the questionnaire asked each company to provide details of the time from the first synthesis of a new crop protection product until the first sales of the product. Five companies included these details and the mean values of the responses are outlined in the following table:

Crop Protection Product Discovery and Development Lead Time

	1995	2000	2005-8
Number of years between the first synthesis and the first sale of the product	8.3	9.1	9.8

Based on the results of the survey, over the five year period from 2000 to 2005-8, the lead time between the first synthesis of a new crop protection product and its commercialisation has increased from an average of 9.1 years to 9.8 years. This has occurred despite the adoption of rapid throughput techniques and enhanced fast track registration procedures for selected products. It is possible that the rise is due to an increase in the complexity and volume of data required by regulatory bodies and the time taken to develop this data. Another potential contributory factor could be the increase in workload on development staff within companies due to the need to support existing commercialised products through re-registration programmes.

Discussion : Section 1

This study was designed to determine the relative cost of new crop protection product discovery, development and registration in 2005-2008. During this time frame several important factors have impacted the industry and led to significant changes in the sector:

- Between 1995 and 2008, consolidation within companies has significantly increased, leading to a reduction in the number of companies with comprehensive R&D capabilities.
- The global value of the conventional chemical crop protection market has shown a modest decline.
- The adoption of GM technology has resulted in the increased use of herbicide tolerant and insect resistant crops.
- All the major companies in the agrochemical industry now also support an R&D effort in the seeds and traits area.
- A substantial increase in regulatory activity primarily through the adoption of re-registration programmes in the USA and the EU.
- Technology changes have brought rapid changes to the R&D process.

All of these factors have significantly affected the outlook for the conventional crop protection sector and importantly how companies view their future in the industry. Crop protection research is clearly one of the most important factors in determining the relative competitive position of the companies within the industry especially from a growth prospect viewpoint.

The results of this study in comparison with previous work have clearly shown the increasing cost to Crop Protection Companies to bring new active ingredients to the market. In 1975-80 the cost of bringing a new product through research, development and registration averaged $23.1 million; this study has shown that this figure has increased to $152 million in 1995, $184 million in 2000 and $256 million in the 2005-2008 timeframe.

A number of new technologies have been adopted with the aim of increasing the breadth and rate of new product discovery and screening, notably genomics and rapid throughput screening that assist biological research for new products and their assessment, and combinatorial chemistry that increases the number of new product leads from chemical sources. It is evident that the number of new products in research stages has increased significantly, possibly as a consequence of adopting these technologies, however on average costs have also increased.

In 1995, the average cost of the research phase amounted to 47% of the total cost of bringing a new product to market; in 2000 this share of expenditure had increased to 48%. However in the 2005-2008 timeframe this share fell to 33.3%. Between 1995 and 2000, the most significant factor contributing to this was the substantial increase in the costs of biology research, in part a consequence of the adoption of high throughput screening and new discovery techniques. However between 2000 and 2005-8, the focus of expense now appears to have shifted toward the development stage of the cycle.

As a result the share accountable to development stages which declined from 44% to 43% between 1995 and 2000, increased to 57% by the 2005-8 period. One notable factor is increasing costs in the field trials area, and also in developmental chemistry, possibly associated with a move to more advanced formulations.

With the share of expenditure on the development phase increasing, the move to take a product from research into development remains a key financial decision for any company, the study clearly showing that the number of potential products that approach this stage has been maintained.

An interesting factor is a significant increase in the costs of registration between 2000 and 2005-8. The study identified internal company costs as being the major reason for this increase, potentially due to the increasing complexity of putting registration dossiers together, the people required to do this and the management of the operation.

Section 2: R&D Expenditure 2007 and Expectations for 2012

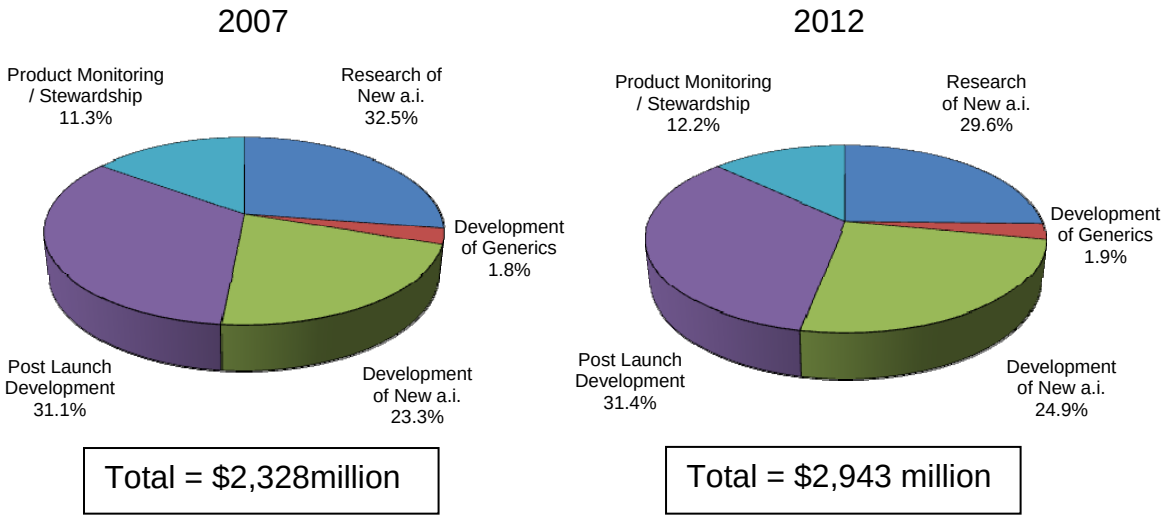
Executive Summary

This study presents the results of a survey of the leading crop protection companies in order to determine:

- The overall level of expenditure devoted by the agrochemical industry to the research and development process.
- The proportion of R&D budget that is targeted at new product discovery, development and managing the existing business including product stewardship and monitoring.
- Expectations for change in R&D expenditure between 2007 and 2012

Responses to the survey were received from fourteen companies. The total cost of agrochemical R&D expenditure in 2007 for these fourteen companies was $2328 m., a value equivalent to 6.7% of their agrochemical sales. These companies also provided expectations of R&D expenditure in 2012; overall the expectation was for a 26.4% increase in expenditure over this five year timeframe, at an average rate of increase of 4.8% p.a.

Agrochemical Industry R&D Expenditure by Function
(Fourteen reporting companies only)



Whilst there was large inter-company variability in the expected growth in R&D expenditure between 2007 and 2012, overall all sectors within R&D expenditure are expected to increase, with the largest growth in expenditure expected in the area of development of generics, followed by product stewardship and monitoring and post launch development of active ingredients.

Background

In 2002 Phillips McDougall undertook a study on behalf of the European Crop Protection Association (ECPA) and CropLife America that was designed to determine the level of expenditure involved in the discovery, development and registration of a new conventional chemical crop protection product. This study has now been repeated as reported in Section 1 of this report. Whilst this study provides information on the costs involved in bringing a new agrochemical active ingredient from the initial discovery process to the market place, it does not provide information on the overall level of R&D expenditure or expectation for the future. A further study was undertaken on behalf of CropLife International regarding company R&D expenditure in 2004, the second section of this study is a repeat of part of this investigation, but for 2007 and expectations for 2012.

This survey undertaken and reported in this second section is designed to provide a greater understanding of the level of annual overall expenditure made by the agrochemical industry on research and development, and also its expectations for the future.

Study Scope

As outlined above, this current study was designed to measure the overall level of expenditure devoted by the agrochemical industry to the research and development process.

- The proportion of R&D budget that is targeted at new product discovery, development and managing the existing business including product stewardship and monitoring.
- Expectations for change in R&D expenditure between 2007 and 2012.

Methodology

The results of this study are based on the responses to a questionnaire, which was sent to the following group of companies that were considered to be representative of the industry:

The questionnaire that was sent to the companies is outlined in Appendix 4 of this report.

The companies included in the survey were:

BASF	Bayer CropScience	Dow AgroSciences
DuPont	Syngenta	Monsanto
Makhteshim Agan	Nufarm	Isagro
Chemtura	Sipcam	Arysta
Gowan	Amvac	

The responses of each company were added to a database, with each company allocated a code number. For companies reporting in non-US dollar terms, the values were converted to US dollar using average year exchange rates:

Average Year Exchange Rates to the US Dollar (2007):
Euro: 0.731
Australian Dollar: 1.1948

The results of each company, in US dollar terms, were subsequently aggregated so that a collective total was produced to represent the overall agrochemical industry.

Study Definitions

The overall scope of the R&D process within the agrochemical industry encompasses both the discovery of new agrochemical products and the research, developmental and regulatory processes associated in managing and maintaining the commercial and regulatory status of the products of each company following their introduction.

Typically the R&D process for new products can be split between the discovery process and product development. Both these stages involve a number of related scientific and regulatory disciplines that are designed to determine the relative efficacy of the product, whilst ensuring that the new active ingredient satisfies the various tests established by regulatory bodies to demonstrate that the product is safe from both a human and environmental viewpoint.

In addition to the various studies associated with new product discovery, the agrochemical industry undertakes a significant amount of research and development aimed at maintaining and developing the existing product portfolio. Some of these studies will be undertaken to extend the application and use of the product following launch to other crop pest situations or to other country markets. Increasingly a number of studies are also being undertaken to satisfy the re-registration requirements of regulatory bodies such as the EU and the US EPA.

The definition of R&D Expenditure and the main R&D phases that were included as categories in the questionnaire were:

R&D Expenditure (scope): The total 2007 expenditure on all research and development activities relating to agrochemicals for both crop protection and non-agricultural uses. This covers R&D related to conventional crop protection in agriculture, pest control, industrial and consumer applications, public health and lawn and garden use. It also includes salaries and all other staff-related costs, as well as costs related to R&D administration, rent, supplies, equipment, materials, etc. Activities carried out (for the purpose of agrochemical development) within the corporation but outside the crop protection organization (for those companies having R&D centres/capacities outside of crop protection divisions) were also included. Corporate research programs, expenditure on joint ventures, alliances, and research agreements with third parties was included. Depreciation costs related to R&D assets are also included. Capital expenditure on R&D is excluded.

Research of New Active Ingredients: All of the R&D activities associated with the discovery of new agrochemical active ingredients up to the start of new product development.

Development of new active ingredients: Starts at the point when a company commits a new active ingredient to full development, generally marked by the decision to commence long-term toxicity tests. It ends with the registration and launch of a product in a major crop market (generally an OECD country).

Post launch development: All product development activities following the launch of a new active ingredient into a major market.

- Re-registration/registration maintenance: refers to any activities or studies that must be undertaken in response to the requirements of registration authorities in order to maintain a product's registration.

- Other: includes activities required to satisfy regulatory requirements for registration in non-OECD countries, and line extensions of existing products.

Development of Off Patent products new to your company: The above sections predominately relate to the research and development of new active ingredients, however a significant level of investment is made by generic companies in the development of off patent products for introduction.

Product Monitoring and Stewardship: This relates to the costs associated with undertaking the requirements of the regulatory authorities' post-introduction.

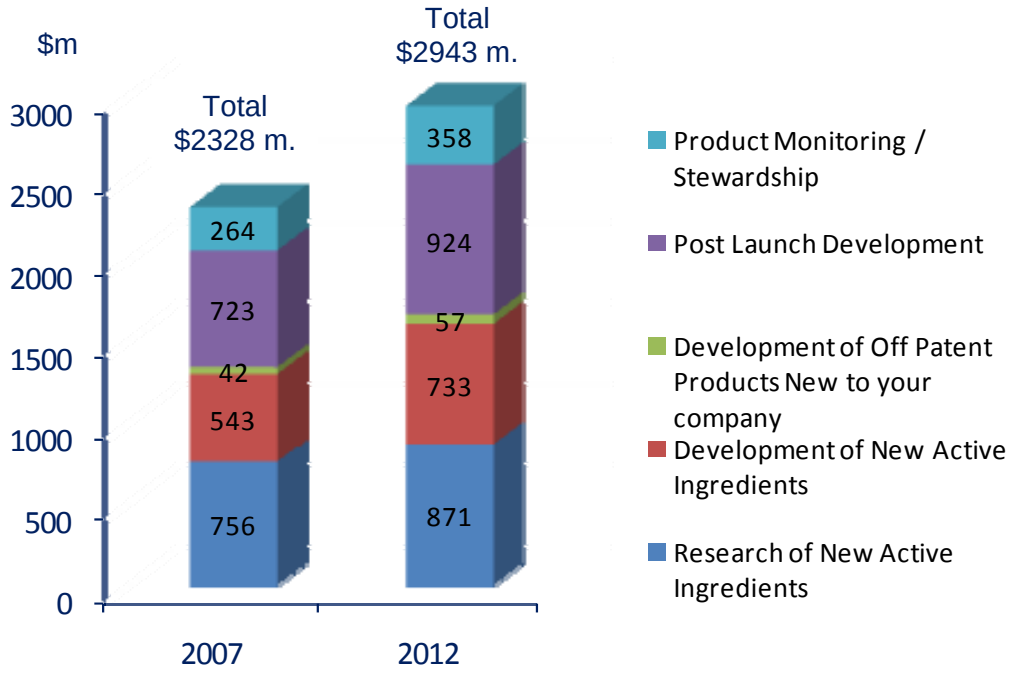
Study results – Part 2

R&D Expenditure 2007 and Expectations for 2012

Responses to the survey were received from fourteen companies. The total cost of agrochemical R&D expenditure in 2007 for these fourteen companies was $2328 m., a value equivalent to 6.7% of the agrochemical sales of these companies. This level of expenditure, 6.7% of sales, is below the level ascertained in the previous study undertaken of R&D expenditures in 2004, which was 7.5%. Unfortunately there is no comparison between the level of total expenditure as the audience of reporting companies has changed.

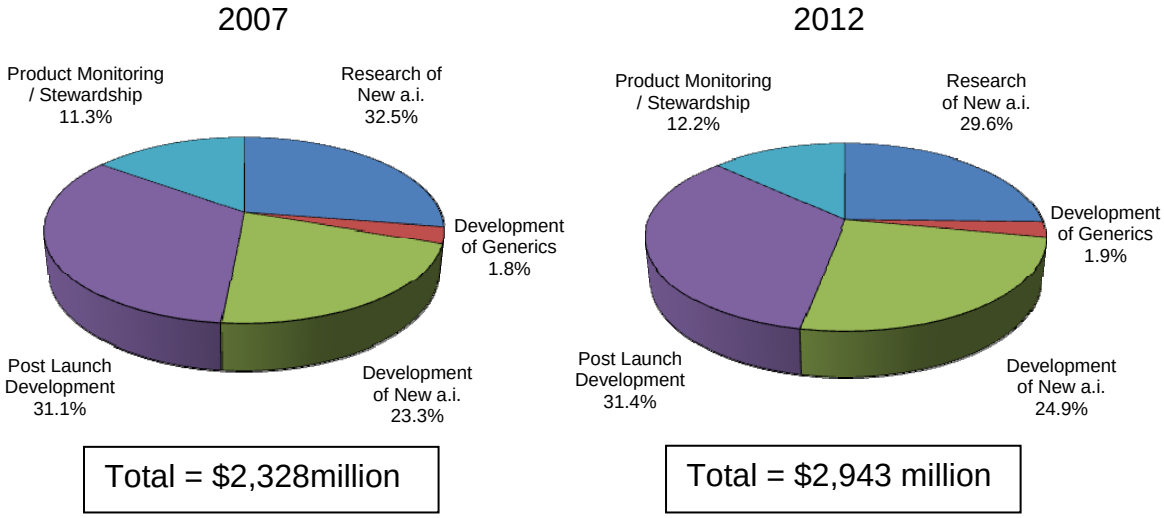
The fourteen responding companies also provided expectations of R&D expenditure in 2012; overall the expectation was for a 26.4% increase in expenditure over this five year timeframe, at an average rate of increase of 4.8% p.a.

R&D Expenditure Breakdown of the Fourteen Responding Companies



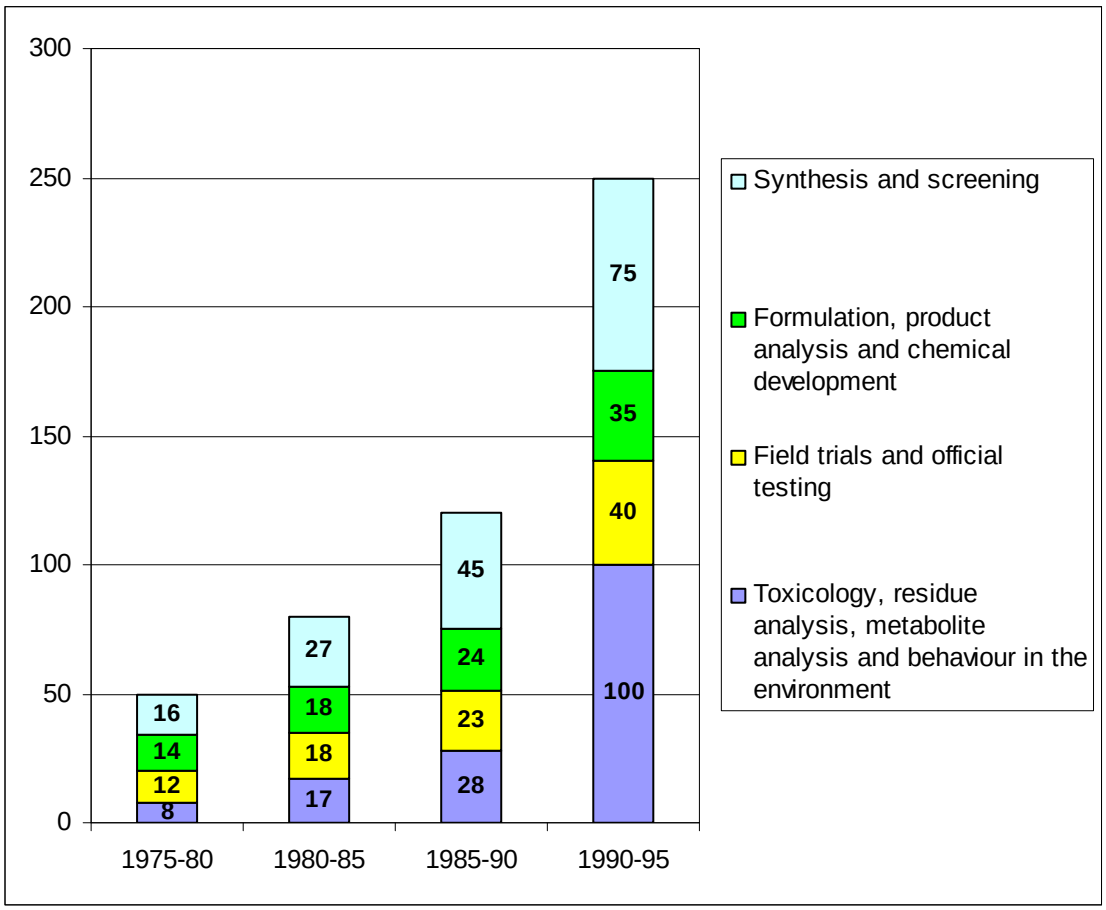
As can be seen in the graph above, the expectations of the fourteen responding companies is that expenditure will increase between 2007 and 2012 in each of the sectors which comprise overall R&D expenditure. The greatest increase being expected in the development of new generics where overall expenditure is expected to rise by 36.3% to $57 m. (albeit the lowest level of expenditure overall) followed by product stewardship and monitoring, up by 35.9% to $358 m. and then development of new active ingredients, where overall expenditure is expected to rise by 34.9% to $733 million. In terms of expenditure, by 2012 post launch product development is expected to account for the largest share, although expected growth is not as great as the other sectors. As stated, the overall rate of growth in expenditure is expected to be 26.4%, the only sector expected to grow beneath this rate being research of new active ingredients at 15.1%.

Agrochemical Industry R&D Expenditure by Function (Fourteen reporting companies only)



Whilst there was large inter-company variability in the expected growth in R&D expenditure between 2007 and 2012, overall all sectors within R&D expenditure are expected to increase, with the largest growth in expenditure expected in the area of development of generics, followed by product stewardship and monitoring and post launch development of active ingredients.

Appendix 1: Development Costs for a Crop Protection Product



Appendix 2: Study Plan

1st March 2009

Private and Confidential

Study Sponsored by ECPA and CropLife America

The cost of bringing a new crop protection product through R&D to introduction and the current breakdown of R&D expenditure and expectations for the future.

Phillips McDougall has been appointed by the European Crop Protection Association (ECPA) and Crop Life America to determine the level of R&D expenditure required to discover and develop a new crop protection product. As part of this study we are undertaking a survey of the leading agrochemical companies to determine what they believe was the level of expenditure necessary to bring a major product candidate through the various stages of R&D and to commercialization in a major market. This element of the study is to examine the cost of bringing a single active ingredient to the market. All major R&D driven companies are being surveyed and mean results will be compared with those calculated from similar studies covering 1995 and 2000. It is anticipated that your return will be a case study for a single major active ingredient introduced in the 2005 to 2008 time frame (it is believed that all major R&D companies have brought to introduction a major new active ingredient within this period). It is understood that these costs will not include product failures etc. or necessarily reflect the breakdown of your current R&D budget. These will be covered in the second more limited questionnaire.

The second questionnaire is being sent to a far wider audience of companies. The aim of this survey is to calculate overall industry R&D spend, both in 2007 and expectations for 2012. This data should include all R&D costs, including post launch development and support even if these are not accounted for in your R&D budget, and should reflect agrochemical products only, and not include any expenditure in the seeds and traits area.

Two questionnaires have been attached, which we would be grateful if you could arrange to complete and return to Phillips McDougall. In order to assist you in the completion of the questionnaire we have included guidelines for completing the questionnaires. We hope that the various questions are self explanatory, however if you are uncertain how to complete any part of the form please do not hesitate to contact us directly.

The results from each company will be held in absolute confidence with only mean results and statistical analysis shown in the final report which will be sent to ECPA and Crop Life America. The study will be conducted under a secrecy agreement, a copy of which is enclosed in this protocol. It would be helpful if you were able to return the completed questionnaire by May 15th 2009.

Study Protocol

(1) Introduction

The aim of the study is to determine:

1. The cost of bringing a new crop protection product through R&D to introduction.
2. Industry R&D spend and breakdown and expectations for the future.

(2) Methods, Confidentiality and Non-Use

This study is being undertaken on behalf of the European Crop Protection Association (ECPA) and CropLife America. These two organizations together are referred to as the **"Client"**.

This Study will be carried out so that any and all data submitted by any Company as well as the results of each Company (hereinafter referred to jointly and separately as "**Confidential Information**") shall remain confidential and shall only be used by us in order to undertake the Study and to prepare the Report (as defined hereinafter) according to the Purpose in a neutralized, aggregated and weighted manner. In order to achieve this, the results of each Company's questionnaire will be assigned a code. Each Company's result will subsequently be neutralized, aggregated and mean values calculated. Only neutralized, aggregated and mean data will be presented.

We undertake to treat all Confidential Information received from any Company

a) as confidential and not to disclose it to third parties (including any other Company as well as Client).

b) only to use it for the Study and within the scope of the Purpose and, in particular, not to exploit it commercially, although we will be able to exploit our authorship of the study commercially.

c) make it available only to those employees who need to have access to such Confidential Information for the Study according to the Purpose and who are contractually or otherwise obligated to keep it confidential.

The above obligations shall not apply to Confidential Information of which we can prove, that such Confidential Information

a) was known to us prior to receipt thereof or

b) was publicly known prior to receipt thereof or

c) became publicly known after receipt thereof without breach of this agreement

d) was disclosed to us by a third party which to the best of its knowledge was authorised to make such disclosure.

The study will also be undertaken under Phillips McDougall standard terms and conditions, a copy of which is attached.

(3) The Survey

There are two questionnaires attached, both have been designed with, and approved by, ECPA and CropLife America for the purpose of the study.

Questionnaire 1

The aim of this survey is to determine the level of expenditure necessary to bring a single, major product candidate through the various stages of R&D and to commercialization in a major market in the 2005 to 2008 time frame. The data returned should only reflect the costs associated with this product, and not include any capital expenditure, the cost of failures etc. and as such may not reflect the breakdown of your current R&D budget.

Questionnaire 2

The aim of this questionnaire is to determine overall industry R&D spend, both in 2007 and expectations for 2012. The data return should include all R&D costs, including post launch development and support even if these are not accounted for in your R&D budget, and should reflect agrochemical products only, and not include any expenditure in the seeds and traits area.

(4) Study Results

The results of the Study will be presented in the form of a written report (the "**Report**") which will be transmitted to the Client in PDF format for subsequent viewing or printing. The Report as well as any rights resulting from or related to the Study and/or the Report shall exclusively belong to ECPA and CropLife America, and Phillips McDougall shall not retain any rights with respect thereto.

(5) Timing

The Study will commence at the start of March with the presentation of this document to the companies to be surveyed. Responses to the survey are requested to be returned to Phillips McDougall, either by E-Mail, fax or post, by May 15th. It is anticipated that the final report will be available for release in September, following approval by ECPA and CropLife America.

If any aspects of the questionnaires are unclear, please do not hesitate to contact Matthew Phillips at Phillips McDougall directly.

Please send the completed forms to:
Dr Matthew Phillips,
Phillips McDougall
Suite 2
Vineyard Business Centre,
Pathhead,
Midlothian EH 37 5XP
UK

Telephone: +44 1875 320611
Fax: +44 1875 320613
E-mail: phillipsmcdougall@dial.pipex.com

Guidelines for Completing the R&D Questionnaire

Please complete all parts of the questionnaire with the relevant data. Also please indicate the reporting currency.

It is recognised that the various cost allocation sectors outlined in the attached questionnaire are somewhat idealised and will depend to on the individual approach of each company to product research and development. However please complete each section according to what you believe best fits your company development programme. If you are able to identify a particular R&D cost that is not shown on the table we would be grateful if you could indicate this in the final section.

The object of the overall exercise is however to identify the average costs for the industry that are incurred in:

- Firstly, discovering a new crop protection active ingredient
- Secondly, in the whole process involved in product development through to product registration

In addition the study will look at identifying any costs that arise because of additional data or study requirements necessary for registration in the EU versus the USA and vice-versa. For this reason it would be helpful if the development costs reflect those associated with a crop protection product that has applications in major food crops in the EU and the USA.

In completing the questionnaire please bear in mind that the cost of the various studies associated with the research phase are those that are necessary to discover and register **one new active ingredient**. Hence research costs should reflect the total cost incurred in synthesising, screening and testing of the appropriate number of products that you consider will lead to one successful product launch. For example if your experience is that it is necessary to synthesise 40,000 molecules to discover one new crop protection product, then the research costs should reflect the total incurred for the synthesis and testing of 40,000 molecules. Similarly if your company believes that for every new molecule registered there has to be X molecules going into the development process then the development costs should reflect the total expenditure on X.

Appendix 3: Company Questionnaire, Section 1

Questionnaire on behalf of ECPA / Crop Life America

Part 1: Breakdown of R&D Expenditure for bringing a single New Active Ingredient to a major market

Please provide indicative data for a product introduced around the 2005-8 timeframe

Company:_____ **Currency :**_____

			Cost
Research	Chemistry	Synthesis	
		Formulation	
	Biology	Efficacy Testing (Glasshouse)	
		Small plot trials	
		Field trials	
	Toxicology	Mammalian acute	
		Mammalian sub chronic	
		Environmental	
	Environmental Chemistry	Metabolism	
		Residue analysis	
Development	Chemistry	Scale up of Manufacture	
		Formulation	
	Biology	Large Scale Field trials	
		Registration Field trials	
	Toxicology	Chronic Mammalian	
		Environmental	
	Environmental Chemistry	Metabolism	
		Residues	
Additional Costs – EU		Registration fees	
		Internal Registration Costs	
		Additional studies **	
Additional Costs - US		Registration fees	
		Internal Registration Costs	
		Additional studies **	

**** Additional studies refer to specific studies that are only requested in the EU or US and have no use in any other country or registrations region**

Questionnaire on behalf of ECPA / Crop Life America (Continued)

Company:_____ **Currency :**_____

Part 2

Any Additional R&D Costs Associated with New Product Development Not Identified in Part 1?

Item	**2005-8**

Part 3

Number of Products Processed to Lead to Successful Product Launch

		2005-2008
Research	Synthesis	
	Post Synthesis	
Development		
Registration		1

Part 4

Development Lead Time

	2005-2008
In your opinion please indicate the number of years between the first synthesis and the first sale of the product	

Appendix 4: Company Questionnaire, Section 2

Questionnaire on behalf of ECPA / Crop Life America

Breakdown of R&D Budget in 2007 and expectation for 2012

Company: **Currency:**

	2007	2012
Currency (millions)		
Research of New Active Ingredients		
Development of Off Patent Products New to your company		
Development of New Active Ingredients		
Post Launch Development*		
Product Monitoring / Stewardship**		

* product defense, label expansions (countries, crops, mixtures) etc
** as required by terms of registration