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THE ROLE AND CONTRIBUTION OF FEDERALLY FUNDED BASIC RESEARCH IN PHARMACEUTICAL INNOVATION

By

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ABSTRACT

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Research and development investment is an important factor in technical progress and productivity growth. Recent theoretical research has suggested that the stock of knowledge created through cumulative research and development feeds new innovation and economic growth. When knowledge creation is funded by public institutions, the research results are both non-rival and non-excludable. Non-rivalry means that the use of public research by one agent does not preclude its use by another while non-excludability guarantees that the results from public research are accessible to all agents. Because of these characteristics, the public stock of knowledge can feed innovation across different sectors and industries in the economy.

This dissertation analyzes the role and contribution of publicly funded basic research in pharmaceutical innovation. Drawing on conversations with industry scientists, it is argued that public funding of biomedical research facilitates advances in public scientific understanding and thereby creates new avenues to therapeutic outcomes and research opportunities for new drug discovery. As new opportunities emerge, private firms use this information in the pharmaceutical innovative process to develop new drug concepts and define

therapeutic outcomes. It is in this manner that public basic research contributes to the discovery of new therapeutic compounds.

The discovery of new compounds is modeled using the economic production framework. In this framework, basic research can make both a direct contribution to the discovery of new therapeutic compounds and an indirect contribution by stimulating private research and development (R&D) investment. The sum of these individual effects leads to an estimate of the total impact of public basic research on pharmaceutical innovation.

The quantitative analysis explores the timing, magnitude, and significance of the impact that public basic research has on pharmaceutical innovation and investment. A new panel data set is constructed using medical therapeutic classes over time. Detailed data on Public Health Service awards between 1955 and 1985 are matched by therapeutic class and year with measures of pharmaceutical innovation, industry R&D investment, Food and Drug Administration regulatory stringency, and pharmaceutical demand.

The analysis finds strong evidence for an economically and statistically significant impact of public basic research on pharmaceutical innovation and investment. The total marginal impact indicates that a $1 million investment in the stock of public basic research produces 0.07 new chemical entities in each therapeutic class after an average of seventeen years. This would yield an average discounted cash flow of $14.2 million in each therapeutic class at the time of introduction.

To Karen, Brittni, Kevin and my parents.

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First and foremost I would like to thank Karen for her incredible patience and understanding during the completion of this research. Brittni and Kevin were also supportive. Everyone helped in one way or another to bring this project to a successful close and I am very thankful and blessed to have them in my life.

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Introduction

> ...the most important aspect of research management is the ability to access the scientific information emanating from academic and industrial laboratories throughout the world, to discern its importance, and to integrate it rapidly into our research.
>
> Edward M. Scolnick, M.D.
> President of Human Health
> at Merck & Co., Inc.

1.1 Overview

Following World War II, the United States Government established itself as the leading financial supporter of basic research. Fueled by the belief that a strong basic research foundation would lead to productivity increases and greater national welfare, federal funding of basic research grew at a real annual rate of 11.8% through the 1960s. However, beginning with the economic challenges of the 1970s and the concomitant pressures on the Federal budget, policy debates resulted in the reduction in the growth rate of federal funding for basic research. For the 1970-1989 period, the real annual growth rate dropped to 2.8% (NSF (1992)).

It is evident from current and past debates that competing demands for federal funds have caused policy makers to re-evaluate national research policy. The traditional belief in basic research as a means to increase national and industrial production has been questioned. At least in part, this policy

debate is perpetuated by a shortage of economic analyses describing and quantifying the impact of federally funded basic research. Since basic research is that research which builds fundamental knowledge within a scientific discipline, its connection and contribution to industrial innovation is less obvious than applied research and development. Nevertheless, the impact of basic research can be examined using the standard production relation described in the economics literature.

The production framework identifies two related channels through which federally funded basic research can influence industry innovation. First, basic research can contribute directly to private industry's product innovation. In this case, basic knowledge is used as a direct input to create the new product introduced by private industry. For example, pharmaceutical firms use the basic research results on biological and chemical processes to conceive therapeutic outcomes and synthesize new therapeutic compounds. Second, federally funded basic research can contribute indirectly to private industry's product innovation. This indirect contribution recognizes the role that basic knowledge plays in stimulating additional private R&D investment. Often times additional private R&D is needed to strengthen and extend the foundation of knowledge created by public financing. Accounting for both the direct and indirect effects leads to an estimate of the overall impact of federally funded basic research on industrial product innovation.

In general, U.S. support for basic research has gone to universities and colleges to fund academic research. A recent survey by Mansfield (1995)

reports that federal funds constitute two-thirds of the total research dollars used by academic researchers. Outside of the agricultural sector, econometric analyses of basic research have focused primarily on the link between academic research and manufacturing innovation and productivity. In this vein, several probing multi-industry studies have been done in recent years. Jaffe (1989) uses the production framework to estimate the elasticity of corporate patents with respect to the stock of academic research spending. Grouping industries and academic departments into "technological areas," Jaffe finds that academic research makes a significant contribution to commercial innovation. Using Jaffe's model and a measure of new business innovation, Acs et al. (1991) also find that academic research contributes to industry innovation. Adams (1990), using knowledge stocks constructed with weighted counts of journal articles, finds that fundamental knowledge either increases or decreases manufacturing productivity depending on the lag specified.

Although the generality of the multi-industry approach is one of its strengths, it is also one of its weaknesses. It is difficult to infer from these studies how basic research has impacted an individual industry. The best we can do is acknowledge the general importance of this research to the various technological areas studied. As will be seen below, our focus on an individual industry motivates the mapping of research between sectors and allows us to control for industry specific characteristics. Moreover, previous studies do not distinguish between federal and non-federal funding sources. In order to gauge the impact of federally supported basic research on industrial innovation and

gather information for policy evaluation and formulation, we must explicitly analyze the impact of this research.

This dissertation provides an estimate of the "total impact" of U.S. Government funded basic research on pharmaceutical innovation by combining separate estimates of the direct and indirect effects. Using insights gained from interviews with industry scientists, the analysis begins by describing the role of basic biomedical research in the pharmaceutical innovative process. This qualitative discussion provides the basis of the four primary hypotheses tested in the empirical analysis: first, public basic research has a positive and significant direct impact on pharmaceutical innovation; second, public basic research has its greatest impact in the formulation of "drug concepts" which come in the earliest stage of drug discovery; third, the distinctive contributions of public basic research and private industry R&D to the pharmaceutical innovative process suggest limited substitution possibilities between these two types of research; and fourth, public basic research indirectly impacts pharmaceutical product innovation through its affect on industry R&D investment. Furthermore, the potential for increasing returns to scale in pharmaceutical innovation and the effects of product quality regulation by Food and Drug Administration (FDA) are also explored.

This study introduces basic research by therapeutic class into the economic model of pharmaceutical innovation. The data used to measure basic biomedical research consists of all extramural grant and contract awards given by the Public Health Service (PHS) between 1955 and 1985. The PHS funds the

largest portion of all basic biomedical research, whether one considers public, private, or both sectors. In 1985, the PHS financed 80% of all U.S. Government obligations for national health R&D, covering 66% of all non-industry funding (NIH data book (1989)). Further, this study incorporates two key characteristics of basic research. First, basic research is allowed to be cumulative over time. This captures the important quality of learning that builds on previous research knowledge. Second, basic research is lagged so that its hypothesized timing can be tested and explored statistically.

The federal awards data are combined with standard measures of pharmaceutical innovation, industry R&D expenditure, and regulatory stringency. Approved new chemical entities (NCEs), a measure of important patents, are used to represent pharmaceutical innovative success. Industry R&D expenditure figures were obtained from the Pharmaceutical Research and Manufacturers Association (PhRMA). The FDA supplied the necessary data to calculate measures of regulatory stringency.

1.2 Plan of the Dissertation

Chapter two describes the role of public basic research in the pharmaceutical innovative process and outlines the main hypotheses to be tested. Chapter three presents the general modeling framework, describes the data and discusses the estimation techniques. Chapter four describes the empirical specification and results of the direct impact of public basic research

on pharmaceutical innovation. Chapter five presents the empirical specification and results of the indirect impact of public research on pharmaceutical innovation. Chapter six concludes the analysis and calculates the total impact of publicly funded basic research.

1.3 A Primer on Public Basic Research

An important part of understanding the relationship between federally funded basic research and industry innovation is understanding the institutional base from which this research is created. In general, the stock of public basic research is the output of the U.S. national research enterprise. The U.S. national research enterprise is the set of government, industrial and academic institutions that conduct research in the United States. With respect to basic research, the U.S. national research enterprise essentially refers to the aggregate of U.S. academic institutions. Under federal sponsorship, the academic research enterprise has grown into a tremendously diversified institutional base supplying the largest portion of the stock of public basic research.

The National Science Foundation defines basic research as that which is directed toward "a fuller knowledge or understanding of the subject under study, rather than a practical application thereof" (NSF, 1985, P. 221). It is the research which builds fundamental knowledge within a scientific discipline. The definition of basic research used in this study encompasses the NSF definition

but also adds that the research must be non-clinical and relevant to the pharmaceutical industry. Figure 1.1 plots overall federal basic research expenditures and the PHS basic research awards (across all classes) used in this study for the years 1960 - 1985. For comparative purposes, both series are presented in real 1987 dollars using the implicit GDP deflator. It is worth noting that the PHS awards trend is not characterized by the rapid increases and decreases that are evident in the trend of overall federal basic research funding.

The Public Health Service is the key governmental body in charge of the allocation of federal research money for biomedical and pubic health projects. This is accomplished through the use of "study sections" or peer review groups which recommend approval of grant applications. Each recommended grant will have an activity code which describes the nature of the proposal in broad terms such as research, fellowship, training, etc. The set of recommended applications are sent on to get final committee approval from the particular institute that will fund the study. Figure 1.2 plots the total number of PHS activity codes, the number of institutes and the number of study sections from 1955 to 1985. There are two interesting points with regard to this plot. First, the rapid expansion of PHS funding through the 1960s is evident in the growth of the number of study sections, activity codes and institutes during this period. Likewise, the steady-state which characterized the 1970s is also evident.

Finally, it is important to remember the public goods aspect of federally financed basic research. Projects funded with federal monies are part of the

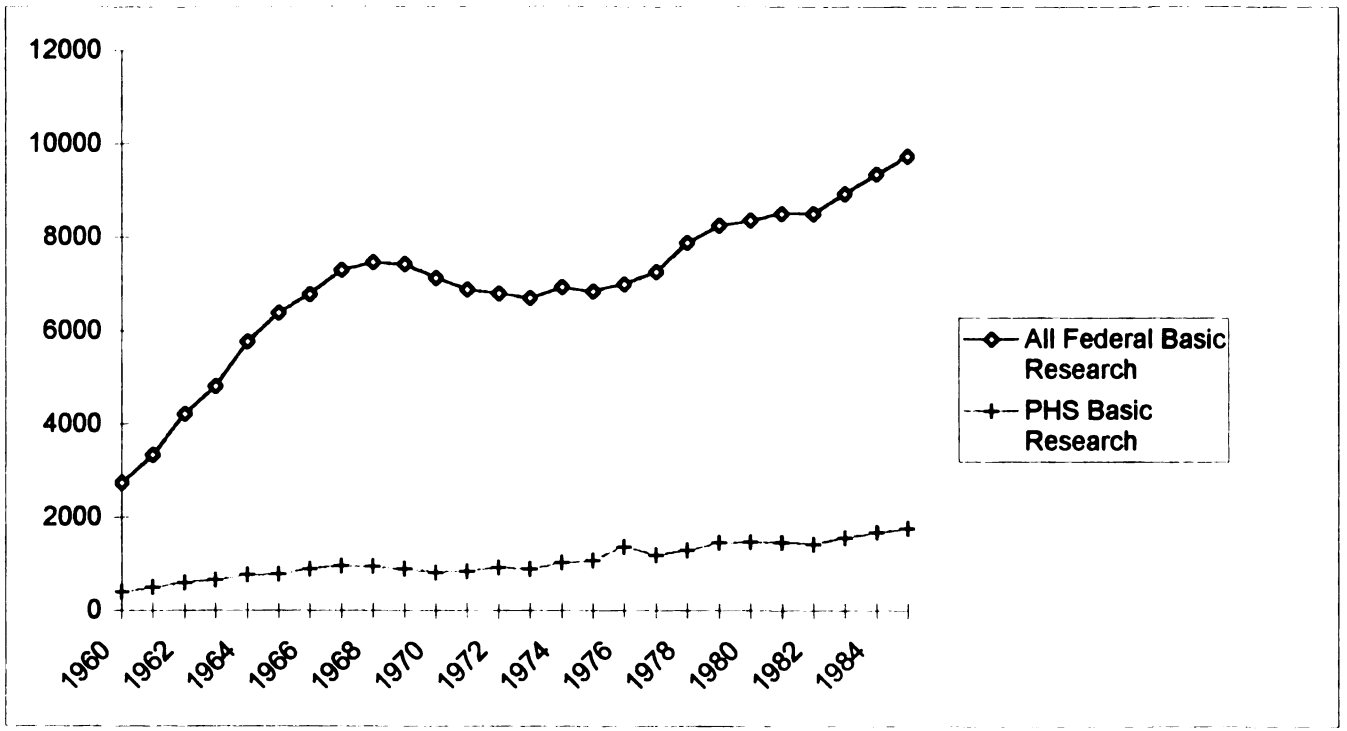

Figure 1.1 - Basic Research Funding (real 1987 $)

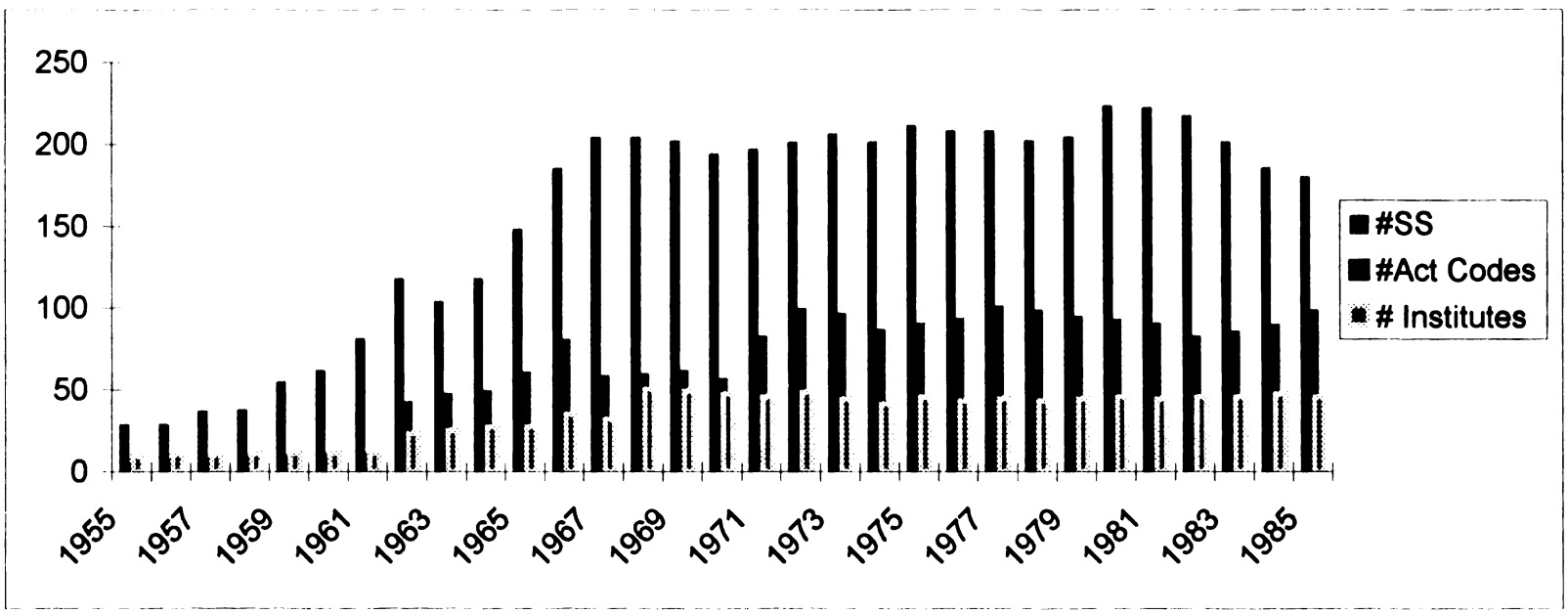

Figure 1.2 - Public Health Service Study Sections, Activity Codes and Institutes

public domain. As such, the results of this research add to the public stock of knowledge and possess two key characteristics: non-rivalry and non-excludability. Non-rivalry means that the use of public research by one agent does not preclude its use by another while non-excludability guarantees that the results from public research are accessible to all agents. Because of these characteristics, the public stock of knowledge can feed innovation across different sectors and industries in the economy.

1.4 Literature Review: Multi-Industry Studies

The focus of this dissertation draws on two lines of research in the economics literature. The first is the literature regarding the measurement of spillovers from government and academic research to industry research and development. In this vein, the central focus has been on studying multi-industry flows.

Mansfield (1991) uses survey data from 76 firms in seven manufacturing industries, one of which is the ethical drug industry, to look at the extent to which technological innovations have been based on recent academic research; the time lags between academic research discoveries and commercial utilization; and the social rate of return from academic research. Mansfield finds that the drug industry has the highest percentage of new products and processes that could not have been developed (without substantial delay) in the absence of recent academic research. However, his study was not designed to produce an

estimate of the extent of these spillovers. A second study directed by Mansfield appears in his book, Research and Innovation in the Modern Corporation, published in the early 1970s. In the chapter on the ethical pharmaceutical industry, Jerome Schnee identifies the discoverer of sixty-eight drug innovations spanning two separate time periods, 1935-1949 and 1950-1962, and presents some descriptive statistics. One of the major conclusions of this exercise is that academe, as a source of drug innovations, has accounted for fewer drug discoveries relative to industry sources over time. He defines discovery as the first identification of a drug's biological activity. That is, he considers the first identification of the therapeutic action of the drug.

Link (1981) appears to be the first study to analyze the impact of government financed basic research on industry productivity. The analysis separates both company financed and government financed research into applied and basic portions. Using data from fifty-four manufacturing firms, Link finds that government financed basic research has a positive and significant effect on total factor productivity. His elasticity estimate for government financed basic research is 1.17. However, it is important to note that Link measures direct government payments to the firms themselves and not the stock of public research available outside of the firms.

Jaffe (1989), in an important study relating academic research to industrial research, looks at the spatial relationship between academic and industrial research and development. It belongs to a class of R&D spillover models that use some measure of "technological distance" separating the origin and

destination (the receiving industry) of the innovation. He estimates a three dimensional simultaneous equation panel data model in which observations are indexed by state, "technological area," and time. The innovative output measure is corporate patent counts and the innovative inputs are measures of industry and academic R&D expenditure aggregated to the level of the technological area.

Importantly, Jaffe distinguishes between basic and applied R&D in his analysis. He finds significant spillovers from university R&D to industrial R&D. While the multi-industry character of his study is both a strength and weakness, his work serves as an important step in understanding the relationship between external knowledge and commercial innovation.

Adams (1990) is a multi-industry study of the relationship between manufacturing total factor productivity and academic research. There are three unique elements to his analysis: first, he uses a labor weighted count of journal articles to measure the stock of "fundamental" knowledge; second, he analyzes the lag between the research and its impact on productivity; and third, he includes knowledge stock measures of within industry knowledge and external knowledge. Although he finds that fundamental knowledge either increases of decreases manufacturing productivity depending on the lag specified, the data reveal that the "science only" spillover lag is about thirty years.

1.5 Literature Review: Studies of the Pharmaceutical Industry

The second line of research consists of those studies which focus exclusively on the pharmaceutical industry. This research falls mainly into two camps: studies of FDA regulatory stringency and studies of research investment and productivity. With regard to the studies of FDA regulation, Martin Baily (1972) and Grabowski et al. (1978) (GVT) estimate the direct effect of regulation using [new chemical entities/R&D] as their measure of pharmaceutical productivity. Having a continuous dependent variable, they use OLS to estimate their models. The only difference in their approaches is that GVT use the United Kingdom as a control for non-regulatory factors.

There are three important non-regulatory factors identified: the thalidomide disaster; advances in pharmacologic science; and the depletion of research opportunities. The idea of the depletion of research opportunities is of direct interest. Baily attempts to capture this using a moving average of past NCE introductions; however, GVT show that this measure is insignificant when a larger sample period is used. GVT prefer to use the U.K. as a control for the relationship between basic biomedical research and pharmaceutical research by assuming that advances in basic research affect both the U.S. and U.K pharmaceutical industries the same. The final important point regarding the GVT analysis is their method of measuring the regulatory stringency. GVT use the mean time from submission of the new drug application to approval in each year of their sample. Their sample covered 1954-1974.

Wiggins (1979) expands on this work in two ways: (1) he estimates the relationship for each therapeutic class;[1] and (2) he estimates the total effect not just the direct effect. Wiggins notes the importance of "scientific knowledge" in the pharmaceutical firms' decision process. In fact, he states, "In conclusion, it must be reemphasized that the most important consideration [in choosing a research project] is still the scientific one." (Wiggins, 1979, p. 69) This being said, Wiggins has no way to account for changing scientific knowledge nor can he estimate its relationship to pharmaceutical drug innovation. Similar to GVT, Wiggins uses the mean time from NDA submission to approval for each class for each year. Finally, because Wiggins uses NCEs as his dependent variable, he uses a Tobit estimation technique in an attempt to account for the truncation at zero.

Using firm level data, Jenson (1987) improves on the estimation technique for the model by using a Poisson specification along the lines of Hausman, Hall, and Griliches (1984). She uses the same measure of regulatory stringency as GVT and includes a time trend and other interacted variables in an attempt to account for scale economies in pharmaceutical R&D. Econometrically, Jenson maintains the nominal variance assumption of the Poisson model (that is the mean = variance property of the Poisson distribution). Jenson does inspect the off diagonal elements of the covariance matrix formed using the standardized residuals for evidence of serial correlation and concludes

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[1] A therapeutic class is a grouping of compounds based on their treatment indication.

that it "does not appear to be a serious problem." Her results indicate that regulatory stringency decreases the expected number of new chemical entities while firm size has no significant affect on the marginal productivity of research expenditure.

There are two existing studies that focus on pharmaceutical research effort and productivity: Ward and Dranove (1995) and Henderson and Cockburn (1996). Ward and Dranove measure R&D spillovers from government-funded basic research to pharmaceutical applied research. The authors are interested in the magnitude and lag structure characterizing R&D spillovers between basic research and applied research. They construct a panel data set of therapeutic classes covering the period 1966-1988.

They measure spillovers in two ways. First, by regressing industry R&D expenditure on a count of journal articles and other variables, they find that a 1% increase in journal articles results in a 0.22%-0.36% increase in industry R&D expenditure. Second, the authors regress industry R&D expenditure on the National Institutes of Health (NIH) obligations broken-down by institute and aggregated, as closely as possible, into therapeutic classes. Within the same therapeutic class, a 1% increase in NIH obligations leads to an increase in industry R&D expenditure by 0.57%-0.76% (cumulative over all lags). Further, an "indirect" spillover is associated with NIH obligations in other therapeutic classes. This effect has industry R&D expenditure increasing 1.26%-1.71% in response to a 1% increase in NIH obligations.

Two things are important to note about the Ward and Dranove analysis.

First, their study explores the determinants of R&D inputs not outputs. Consequently, while this study is interesting and informative, the role of R&D spillovers in the successful development of usable output remains an open question. Presumably, the spillovers of inputs contribute to individual firm success in drug development by either reducing cost or increasing the likelihood of success by providing better leads in drug discovery. Second, the NIH funding data that they use consists of the total obligations of the NIH for a particular institute in a given year. Research obligations correspond to present and future funding commitments while awards measure the actual financial outlays in a given year. Although there is not much difference between the two, using obligations might affect the timing of the relationship since obligations typically lead awards by one year.

Henderson and Cockburn (1996) look at firm specific economies of scope and scale as well as inter-firm spillovers in the drug discovery stage of pharmaceutical R&D.[2] They use disaggregated proprietary firm data at the level of the research program. It is organized as a panel data set which contains detailed R&D input (investment) data from ten pharmaceutical firms spanning a period of twenty years. Innovative output is measured by a count of "important" Composition of Matter patents. This is defined as a patent granted after the discovery stage of research in two of three major markets.

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[2] In the Henderson and Cockburn analysis, economies of scope exist within the firm if physical assets or personnel can be used in more than one application at no extra cost. Economies of scale exist if fixed costs can be distributed over a

Their analysis incorporates both direct and indirect inter-firm spillovers. Direct spillovers occur between firms that are involved in research in the same therapeutic class. For instance, this is the case when two firms both conduct R&D on drugs for the cardiovascular system. Indirect spillovers between firms are those which occur across related therapeutic classes. In this case, research on blood and blood forming organs may uncover a result useful in cardiovascular drug R&D. Both measures were found to have positive and significant coefficients indicating the presence of inter-firm spillovers.

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larger research effort or if the firm can hire specialized researchers as their total research effort grows.

Chapter 2

Basic Research and The Process of Pharmaceutical Innovation

2.1 Overview

This chapter develops the qualitative basis for the hypotheses that are tested in the empirical section of the dissertation. The chapter begins with a description of the standard schematic of the pharmaceutical innovative process. As will become clear, this schematic does not explicitly describe the role and contribution of public basic research in the discovery and development of new therapeutic compounds. To gain an understanding of where basic research fits in the pharmaceutical innovative process, previous research is supplemented by interviews with industry scientists and administrative personnel. Following a description of the interview responses, a new schematic showing the role of basic research is presented and the four main hypotheses regarding public basic research are described. The chapter ends with a description of the discovery of captopril, an example of how public basic research can contribute to pharmaceutical innovation.

2.2 The Pharmaceutical Innovative Process: Standard View

Figure 2.1 gives a detailed breakdown of the pharmaceutical innovative process. This process is divided into two broad stages: drug discovery and

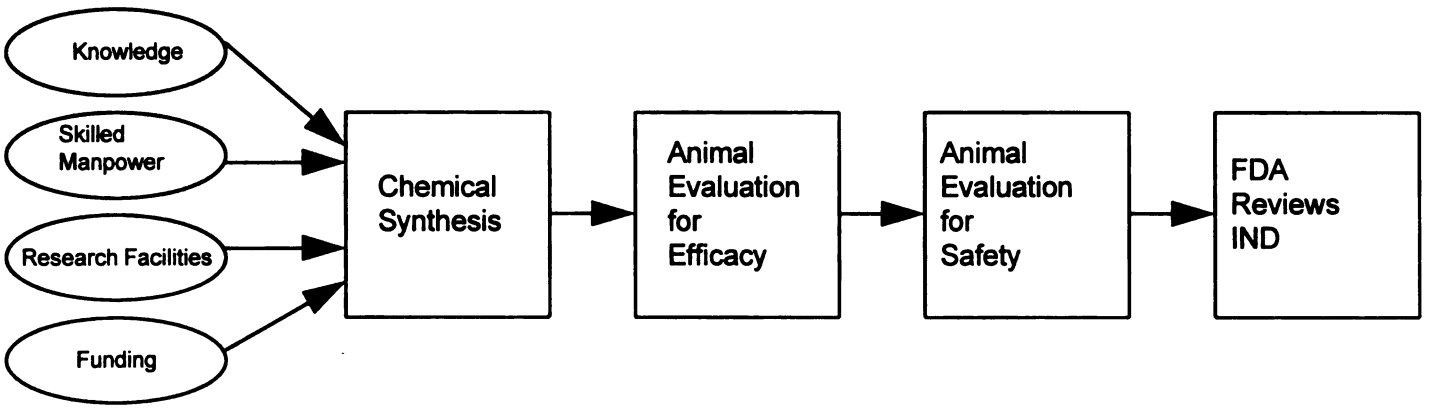

Figure 2.1 - The Pharmaceutical Innovative Process (Source: Bloom (1976))

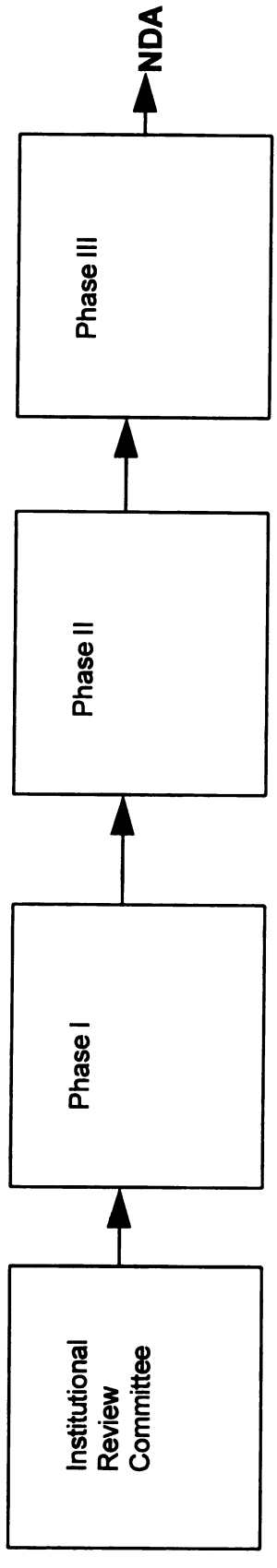

Figure 2.1 - (cont'd)

drug development. Discovery is represented by the first page of Figure 2.1 while development is shown on the following page of Figure 2.1. The diagram indicates that pharmaceutical firms need a set of inputs - knowledge, skilled manpower, research facilities and funding - in order to begin the innovative process. Having these resources, firms begin drug discovery by defining a therapeutic outcome and synthesizing potential compounds that may lead to the desired outcome. After testing or "screening" different chemical combinations, a candidate compound, or group of compounds, is identified. Following chemical analysis to establish certain stability and reproduction properties necessary for mass production, the firm begins animal tests for efficacy and safety.

The two indicators of success in the drug discovery stage are patents and investigational new drug applications (INDs). Patent applications are filed following proof of efficacy in animals. It is commonplace for firms to patent large groups of related compounds, referred to as a "patent estate." This is done both as a strategic move to block out potential competitors and because of the uncertainty regarding which of the compounds will be best suited for the development stage of research. As soon as safety requirements are satisfied, the firm must submit an IND to obtain FDA permission for human testing.

The three pre-marketing clinical development phases appear in the continued portion of Figure 2.1. The initial phase (phase I) provides the first information in human subjects on the tolerance, absorption, and elimination of the compound. Phase II are the first investigations into the drug's dose-response relationship to efficacy in human patients. The final pre-marketing

phase, phase III, uses large-scale clinical trials to establish efficacy and safety in the target patient population. If all phases are successful, the firm will file a new drug application (NDA) while continuing long-term clinical trials during the FDA approval period. Once the firm receives the approved NDA, market sales are legal (DiMasi et al. (1991), OTA (1993)).

It is fundamental to recognize that the pharmaceutical innovative process is highly knowledge intensive. The standard schematic shows the progression from chemical synthesis to NDA submission. Along this progression, knowledge describing the characteristics of both the candidate compound and its close chemical relatives is continuously accumulated. This additional knowledge is used to revise expectations concerning a project's scientific feasibility and ultimate market importance (see Wiggins (1981) for a detailed discussion of the decision-making process).

Given the highly knowledge-intensive nature of the innovative process, it is hardly surprising that pharmaceutical innovation requires long periods of time. In a comprehensive analysis on the cost of new drug development, DiMasi et al. (1991) find that the average time from synthesis to FDA approval is nearly twelve years for the 1979-1989 period. The Pharmaceutical Research and Manufacturers Association also report a twelve year lag between synthesis and approval. Further, in a study looking at the relationship between drug importance and time to market, Dranove and Meltzer (1994) suggest the period from patent application to FDA approval is twelve to fourteen years.

It is further evident that the FDA, a component of the Public Health Service,

has imposed several regulatory requirements at various stages of the process. The two most obvious requirements are the investigational new drug application (IND) and the new drug application (NDA). Although broad guidelines exist, these applications require specific types of data and procedures depending on the compound involved. Moreover, within the application, each claim must be supported by extensive documentation. There has been a fair amount of research investigating the impact of FDA product quality regulation on pharmaceutical innovation (Baily (1972), Peltzman (1973), Grabowski et al. (1978), Wiggins (1981, 1983), Jensen (1987), Thomas (1990)). Although opinions on timing and magnitude differ among the studies, all conclude that regulation has lowered pharmaceutical innovation.

2.3 Basic Research and FDA Regulation: Industry Interviews

Within the standard schematic of the pharmaceutical innovative process (Figure 2.1), the role of basic research is not explicit. Interviews with industry scientists revealed that the primary role and contribution of basic research comes in the drug discovery stage of industry research. In fact, they identify basic research as feeding an independent step in the discovery stage called the "rock turning" or "drug concept" period. This is the very first point in the pharmaceutical innovative process and necessarily precedes chemical synthesis. By providing greater understanding of biological and chemical processes and structures, basic research creates a foundation of knowledge

which opens up new avenues to therapeutic outcomes.

In the typical case, the basic research that leads to the discovery of new therapeutic compounds is a combination of publicly available biomedical knowledge and a firm's own basic research. In a recent paper, Henderson and Cockburn (1997) point out that drug discovery is characterized by a high degree of public and private interaction in research. While this is undoubtedly true, our analysis suggests that the "net flow" of ideas is from publicly funded basic research to pharmaceutical industry research. This not the "simple waterfall model" of innovation. There is a high degree of complexity and creativity in the process of drug discovery. Nevertheless, there is a progression in research and learning. To the extent that firms monitor and use the advance of public medical understanding in their research, they can begin the process of drug innovation with something other than a "blank chalkboard."

Industry scientists point out that the continually expanding stock of public basic research knowledge creates both new opportunities for therapeutic outcomes and new approaches to chemical screening. The new opportunities stem mainly from advances in our understanding of metabolic processes in normal and disease states while, in the chemical screening step, more clearly defined therapeutic outcomes are combined with structural design methods that utilize computer and electronic equipment. By monitoring the advances in public basic science, the pharmaceutical industry absorbs and extends this "core knowledge" with an eye toward the ultimate commercial products that may be produced.

Since the structure and objectives of the pharmaceutical innovative process are determined in part by the regulatory requirements of the Food and Drug Administration, industry regulatory personnel were asked to comment on the impact of this regulation. In particular, given that NDA review times are the traditional measure of FDA regulation used in the economics literature, they were asked to comment on the strengths and weaknesses of the review time measure.

Interviews revealed that there are some real limitations with the average review time measure of FDA regulatory stringency. First, pharmaceutical firms must keep FDA requirements in mind beginning with the animal tests early in the drug discovery stage of the innovative process. The results and procedures used in animal efficacy and safety tests are reviewed by the FDA before clinical (human) tests can begin. Moreover, the clinical testing protocols used in the three development phases are closely reviewed. This supports the standard argument that FDA regulation has, over time, contributed to longer delays in the overall pharmaceutical innovative process. Since the early 1960s, synthesis to approval times have increased from about 3 to 14 years (DiMasi et al. (1991)).

Second, and perhaps more importantly, industry regulatory personnel point out that, since at least the late 1970s, the industry has followed a broad regulatory strategy to minimize expected review times. This strategy is designed to achieve shorter NDA review times by establishing a relationship with the FDA very early in the innovative process and consulting with the FDA about a particular compound. The strategy is intended to lower overall costs by

eliminating some uncertainty regarding the FDA approval criteria as well as to increase revenues by realizing sales more quickly for these completed therapeutic compounds. Overall, this seems to indicate that a large proportion of regulatory cost is borne by pharmaceutical firms before the NDA review period.

Third, the regulatory impact is not only occurring earlier but it appears that pharmaceutical firms have internalized much of the cost of FDA regulation. The creation and growth of the "government affairs" departments, which are intended to specialize in regulatory affairs, illustrate the increasing internal resources devoted to regulation. Although these resource costs could be measured with detailed proprietary firm data, public data include some portion of the regulatory resource costs as part of the overall research and development expenditure figures. This highlights the problems with the composite public numbers used in the subsequent empirical analysis and should be kept in mind when interpreting the magnitudes of both industry R&D and FDA regulation coefficients.

All of these limitations notwithstanding, average NDA review times do provide some measure of FDA regulatory stringency. This period still represents the largest regulatory hurdle confronting pharmaceutical firms trying to bring new compounds to the market. Moreover, to the extent that firms are either unsuccessful with their minimizing strategies or do not anticipate changes in regulatory requirements, NDA delay times capture part of the burden of regulation.

2.4 Development of the Hypotheses

Figure 2.2 presents the basic research augmented schematic of the pharmaceutical innovative process. The essential change to the standard schematic is the addition of a drug concept stage or step which precedes chemical synthesis in drug discovery. Although this step is implicit in the standard view, making this step explicit is important for two reasons: first, it is absolutely fundamental in that it defines the therapeutic outcomes which determine the goals of the entire innovative process; and second, it moves away from the danger of seeing drug discovery as the mechanistic application of physical and financial capital and toward the view that human capital or knowledge capital drives the innovative process. Within the drug concept step, public basic research is combined with proprietary basic research and creative thinking to develop a set of potentially valuable therapeutic outcomes. Along with the underlying biomedical and chemical basic research, these drug concepts are fed into the chemical synthesis step where computer design, chemical engineering and screening technologies are applied.

Figure 2.2 shows that the stock of public basic research, which is produced mainly by academic researchers, is made possible through the financing from four primary sources: Public Health Service (the major component of the Department of Health and Human Services), other federal agencies, state and

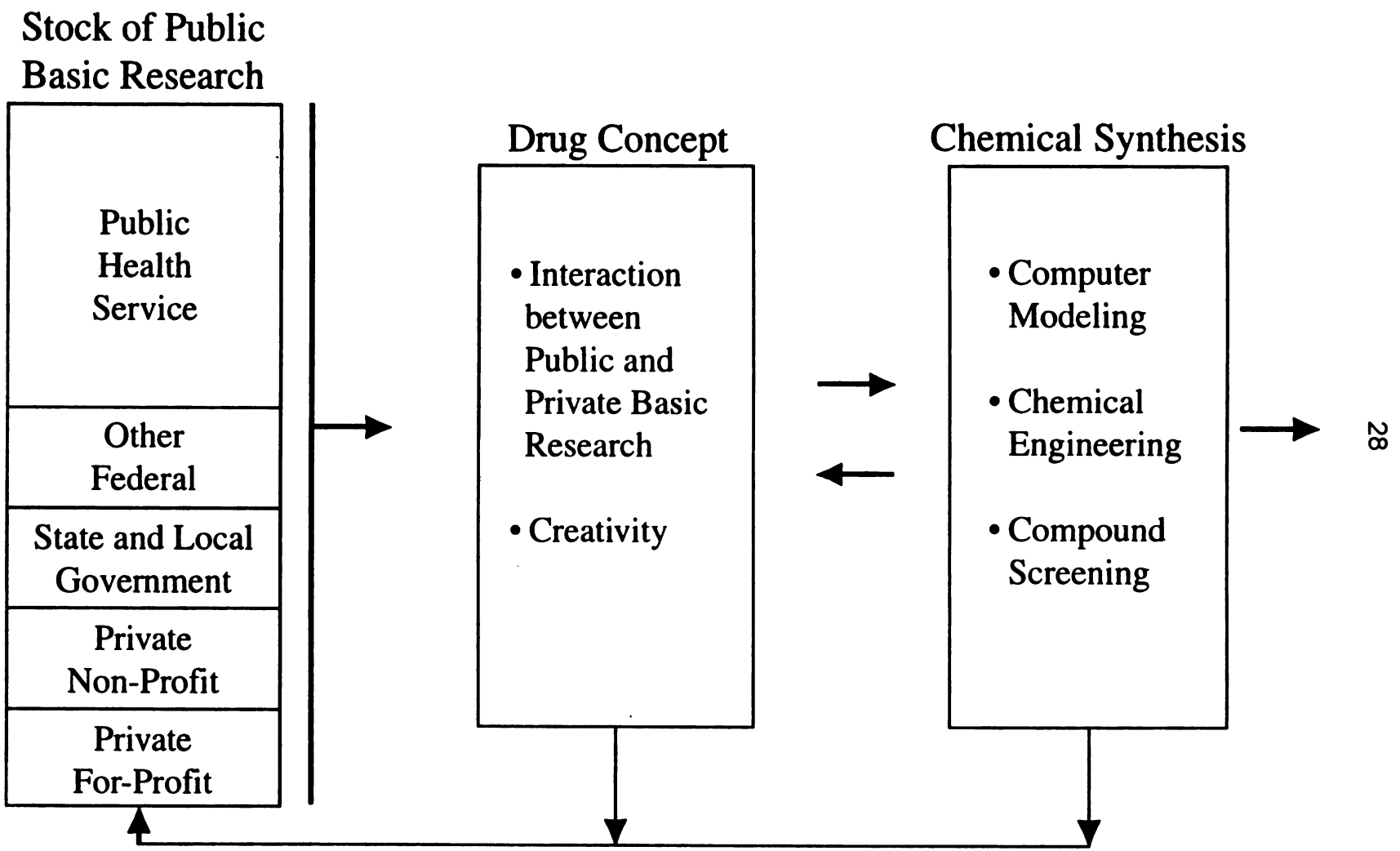

Figure 2.2 - Where Basic Research Fits into the Pharmaceutical Innovative Process

locate government, and private nonprofit institutions.[1] This analysis focuses on PHS funded extramural basic research. The PHS accounted for 80% of U.S. Government funds for national health R&D in 1985, which is 66% of all non-industry funding (NIH data book (1989)). Of the remaining 34% of non-industry health R&D, other federal institutions account for 17%, state and local government account for 11% and private nonprofit institutions make up 6%. In terms of basic research, the NIH (a component of the PHS) accounts for 39% of all federal basic research obligations with 67% going to colleges and universities.

Economic analysts have just recently begun to investigate the relationship between advances in medical science and the pharmaceutical industry (Henderson(1994), Grabowski and Vernon (1994), Henderson and Cockburn (1996), and Gambardella (1992, 1995)). Using a detailed example drawn from cardiovascular drug discovery, Henderson (1994) argues that those pharmaceutical firms which possess a greater ability to integrate research information have a competitive advantage in the industry. Grabowski and Vernon (1994) note its importance in the rise of biotechnology firms. Henderson and Cockburn (1996) and Gambardella (1992) analyze research spillovers between firms and describe how public medical research has improved the screening process used in drug discovery.

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[1] To a much lesser degree, publicly available basic research results also come from firms within the industry and foreign sources. Intra-industry sources are small and subject to long lags due to the high degree of secrecy regarding research opportunities while little is known about foreign sources.

Unlike previous analyses, this study focuses on the empirical relationship between the stock of *publicly funded* biomedical research and drug discovery. Since this is the dominant funding source creating the research that feeds drug concept development, public basic research serves as a core driver of industry innovation. Although specifying the mechanisms through which public research is monitored, integrated and utilized by pharmaceutical firms is a high research priority, the first step toward understanding begins with identifying, measuring, and testing the broader empirical importance of this relationship. Our objective is to test the timing, magnitude and significance of the impact that public research has on pharmaceutical innovation and industry R&D investment. When combined with the qualitative evidence, this objective leads to the following testable hypotheses concerning core knowledge created by publicly funded basic research:

Hypothesis 1: Core knowledge produced by public basic research funding has an economically and statistically significant *direct effect* on pharmaceutical innovation.

Hypothesis 2: Core knowledge produced by public basic research funding feeds the drug concept stage of industry research and, therefore, has its greatest impact in the earliest stages of drug discovery.

Hypothesis 3: The distinctive contributions of public basic research and private industry R&D to the pharmaceutical innovative process suggest limited substitution possibilities between these two types of research.

Hypothesis 4: Core knowledge produced by public basic research funding has an economically and statistically significant *indirect effect* on pharmaceutical innovation by inducing industry R&D investment.

Like public basic research, FDA regulation can have a direct effect on pharmaceutical innovation and an indirect effect on innovation through its impact on industry R&D expenditure. In studying each of these effects much of the previous economic research has used average NDA review times as a proxy to measure the impact of regulatory stringency on pharmaceutical innovation (Grabowski and Thomas (1978), Wiggins (1981,1983) and Jensen (1987)). Using lags of review times to account for changing expectations concerning FDA review criteria, these studies find that regulation has a negative and significant impact on pharmaceutical innovation up to five years prior to NDA submission. However, these studies also focused on FDA review data covering the 1960s and 1970s. In light of the interview results that claim the industry is adjusting to FDA regulation earlier in the innovative process, one would expect that the direct impact of FDA review times on innovation would show up in lags greater than five. To account for this, the cumulative direct impact of FDA regulatory stringency is allow to extent nine years prior to an approved NDA.

The indirect effect of regulation is more problematic. Some studies, Wiggins (1981,1983) and Jensen (1987), find NDA review times reduce industry R&D investment while a more recent study, Ward and Dranove (1995), finds that NDA review times increase industry R&D investment. In the former studies, longer FDA review is interpreted as reducing the number of candidate compounds entering the innovative process while, in the later study, longer FDA review times are interpreted as leading to increased expenditure on those projects already in process. Aside from covering different sample periods, there is one

notable methodological difference: Instead of using observed average review times, Ward and Dranove (1995) use the predicted review times from a first stage regression. By reducing the random variation in the review times measure, it seems the Ward and Dranove approach should lead to a more precise estimate rather than a change in the sign of the estimate. Nevertheless, each of these findings is theoretically possible.

2.5 The Captopril Example

There is a growing case study literature describing the successful interaction between public biomedical research and private industry R&D (see Maxwell et al. (1990), Gambardella (1992, 1995), Henderson (1994), and Henderson and Cockburn (1996, 1997). Although each story is unique in its details, there are two major themes that emerge. First, public research knowledge develops or matures into a body of knowledge that can be extended and utilized by the pharmaceutical industry. Second, private industry is in a position to transform public basic research into new compounds. The story of captopril illustrates these themes.

Captopril is an important drug for regulating blood pressure. Figure 2.3 illustrates that captopril inhibits the conversion of angiotensin I to angiotensin II. It is referred to as an ACE inhibitor because it blocks the conversion to angiotensin II and thereby prevents high blood pressure. The scientists at Squibb synthesized captopril in the early 1970s. The patent was granted in

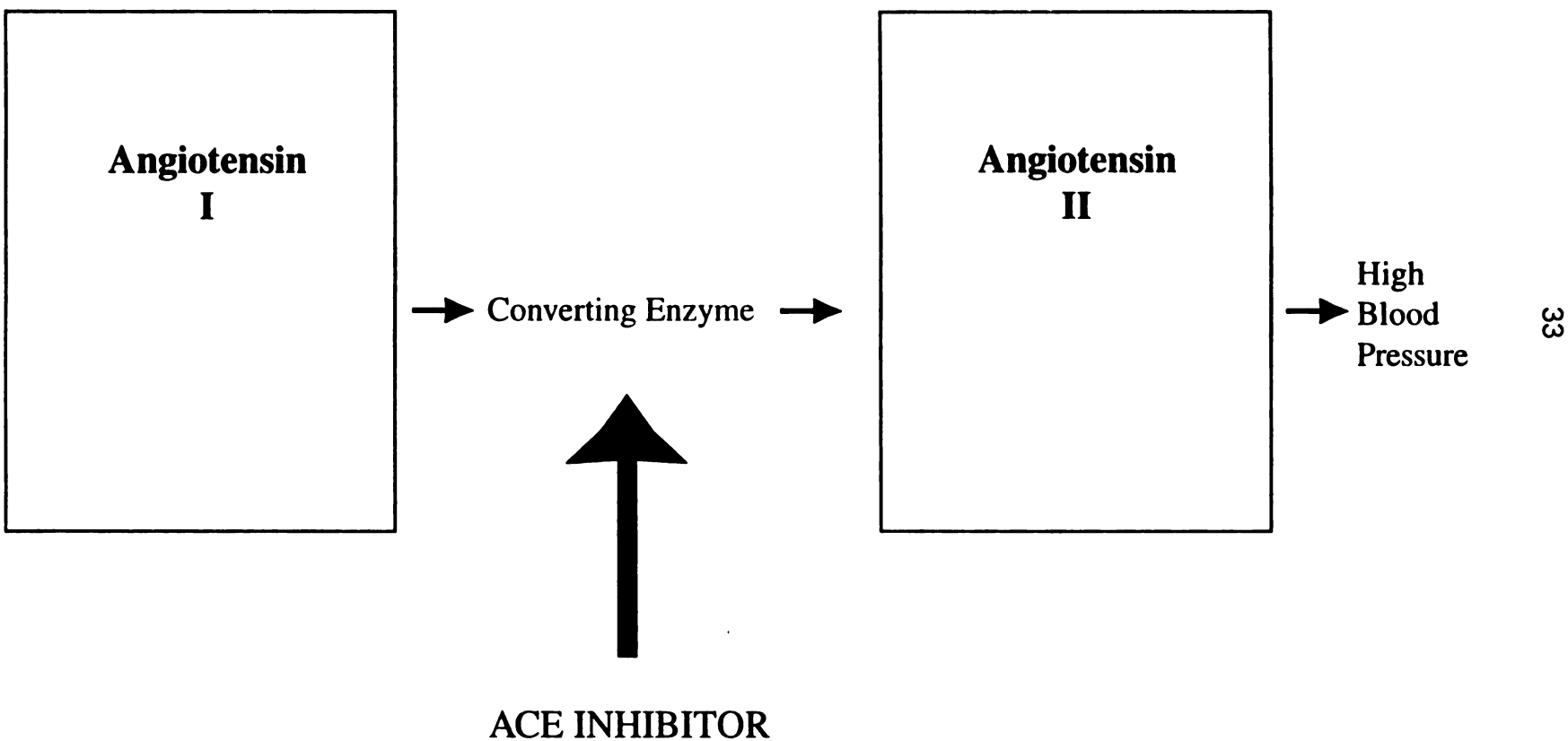

Figure 2.3 - Captopril Example

1977, which is the same date as the publication of their research underlying its discovery. In 1981, the FDA approved captopril for market sales.

Notwithstanding the creative work of the Squibb scientists, their discovery is built on two lines of public research. The first line involved the identification and description of the renin-angiotensin system. While this public research dates back to at least 1934, it was the late 1950s when the key scientific papers which identified angiotensin I and angiotensin II were published. The second line of important public research originated in Brazil. Research into the cause of death from snake venom identified a natural substance which acts on its victim by fatally lowering blood pressure. In 1965, it was shown that this natural substance blocks the conversion of angiotensin I to angiotensin II. Thus, armed with this public knowledge, the scientists as Squibb were able to discover and develop a drug for human consumption that lowers blood pressure.

The discovery of captopril illustrates several points. First, the advance of public basic research knowledge can open up new avenues to therapeutic outcomes. This knowledge can be used directly in the discovery of new compounds. Second, basic research is cumulative and reaches some maturity point as which private firms can usefully apply their skills. There is a lag between this "critical point" and the ultimate FDA approval of a new compound. If one were to describe the study published in 1965 as the critical point, then the lag between the key public research discoveries and FDA approval of captopril would be sixteen years. Third, it was the combination of public basic research and private industry R&D that created this new therapeutic compound.

Chapter 3

The Analytical Framework, Data, and Estimation Method

3.1 The Analytical Framework

This analysis uses the production framework to model pharmaceutical technology and new drug innovation. This framework has been used to study the impact of research and development on innovation by Pakes and Griliches (1984). Their "knowledge production function" (KPF) model has also been used to study knowledge spillovers from academic research to corporate patents (Jaffe (1989)) and manufacturing innovation (Acs et al.(1991)). While these models take patent counts as their metric of innovation, this analysis uses a measure of important patents as its metric of innovation. Important patents in the pharmaceutical industry are defined as the number of approved new chemical entities. Recent research by Henderson and Cockburn (1996) use the KPF to analyze a measure of important pharmaceutical patents.

The KPF is particularly well suited for an investigation of pharmaceutical innovation due to the industry's research intensive character. It focuses on the relationship between research expenditures and innovation. One limitation of this framework, however, is its reduced-form approach. Many of the complex interactions and details of the pharmaceutical innovative process are not explicitly modeled. The lack of sufficiently detailed public data prevents the specification of a more sophisticated structural model. Nevertheless, the KPF

provides a useful framework to extend our understanding of pharmaceutical innovation and to provide evidence on the impact of government funded research.

The KPF is used to estimate the direction and magnitude of knowledge spillovers or transfer from public medical research to pharmaceutical innovative output. This type of productivity relationship is not embodied in a purchased product but instead in the free communication of useful research results. The model utilizes the "therapeutic class" as its map between federally funded research and industry research and output.[1] The therapeutic class is a grouping of compounds based on their treatment indication and has been used by the Pharmaceutical Research and Manufacturers Association to group industry R&D since the early 1960s. For example, cancer basic research is grouped and related to industry cancer drug research and not to industry cardiovascular drug research. To capture the differences across therapeutic classes, an individual intercept (indexed by the subscript i) is specified for each of seven therapeutic classes.[2]

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[1] Although federally funded basic research can be usefully grouped into therapeutic classes, these classes are not always mutually independent. Occasionally, basic research from one class will feed the discovery of compounds in another class.

[2] The classes considered in this study are: endocrine/neoplasm, central nervous system, cardiovascular, anti-infective, gastrointestinal/genitourinary, dermatologic, and respiratory. These classes cover over 80% of the industry R&D investment.

The general form of the direct relationship determining pharmaceutical innovation is represented as:

(3.1) $Y_{it} = q\,(I_{it}, B_{it}, R_{it})$

where i represents the medical therapeutic class, t represents time, Y_{it} is a count of pharmaceutical innovative output, I_{it} is industry R&D, B_{it} is the stock of Public Health Service funded basic research, R_{it} is FDA product quality regulation. The empirical specification of the functional form, q, will be discussed in chapter four.

Based on the qualitative discussion in chapter two, the expected signs of the partial direct effects (marginal productivities) are:

$$q_1 > 0,\ q_2 > 0,\ q_3 < 0$$

The first relation, $q_1 > 0$, is the expectation that industry R&D increases pharmaceutical innovation. The second relation, $q_2 > 0$, is the statement of hypothesis one discussed in chapter two. That is, public basic research contributes to pharmaceutical innovation by providing new avenues to therapeutic outcomes and facilitating the chemical screening step of drug discovery. The third relation, $q_3 < 0$, is consistent with previous research on FDA regulation that shows increased regulatory stringency reduces pharmaceutical innovation.

In addition to the direct production relationship, basic research and regulation have an indirect effect acting through their influence on industry R&D investment. The pharmaceutical investment decision is modeled using a net present value (NPV) framework. While the details of this model are discussed in chapter five, the structural investment relation can be summarized as follows:

(3.2) $I_{it} = g\ (B_{it}, R_{it}, \text{Expected Demand}_{it}, \text{Cost of Capital}_t)$

where subscripts i and t represent therapeutic class and time, respectively; B_{it} and R_{it} are defined as in equation (3.1); Expected Demand_{it} are other explanatory variables affecting the rate of return to pharmaceutical investment by influencing the expected revenue stream, and the cost of capital variable(s) account for the influence of the opportunity cost of capital. The NPV model and each of the explanatory variables will be discussed fully in chapter five.

Here, the expected partial effects are:

$$g_1 > 0,\ g_2 < 0,\ g_3 > 0,\ g_4 <> 0$$

The first relation, $g_1 > 0$, corresponds to hypothesis four of chapter two. This is the inducement effect of public basic research on pharmaceutical R&D. The second relation, $g_2 < 0$, follows previous research on FDA regulation that shows increased regulatory stringency reduces pharmaceutical investment. The third relation, $g_3 > 0$, states that increased expected demand for pharmaceutical compounds in a therapeutic class will lead to greater industry R&D investment. The final relation, $g_4 <> 0$, indicates that the cost of capital can either increase

or decrease investment. Generally speaking, a fall in the cost of capital implies greater investment since more projects become profitable.

The estimate of the total effect of basic research is calculated by estimating the direct effect (chapter four) and the indirect effect (chapter five) separately and combining the results to calculate the total effect (chapter six). The overall or total effects of government funded basic research and FDA regulation on pharmaceutical innovation are given by:

$$(dY_{it} / dB_{it}) = q_2 + q_1 * g_1$$

$$(dY_{it} / dR_{it}) = q_3 + q_2 * g_2$$

where the subscripts represent partial derivatives of the indicated functions. Combining the expected signs of the partial effects discussed above implies the following signs on the overall impact of public basic research and FDA review times:

$$(dY_{it} / dB_{it}) > 0$$

$$(dY_{it} / dR_{it}) < 0$$

3.11 Issues Regarding Possible Endogeneity

The theoretical production function model embodied in equation (3.1) defines the direction of causation as running from the inputs to outputs. This

means that industry R&D, government funded basic research and FDA regulation all combine to cause the flow of pharmaceutical innovative output, Y_{it}. Yet it is reasonable to believe that innovative output may spur or cause changes in any three of the defined inputs. For example, a newly approved drug by one firm may cause other firms to undertake related research and, hence, stimulate industry R&D. For basic research, a new FDA approved drug may spur greater academic interest in exploring some biological process and, consequently, cause some academic researchers to write up and submit grant proposals for federal support. For regulation, a previously approved drug may begin to show negative long-term side-effects that cause the FDA to review and possibly change its approval criteria. In all of these cases there is feedback from the pharmaceutical innovative output to future values of the input variables. Econometrically, we are saying that the input variables are not strictly exogenous. Failure of strict exogeneity can be the cause of inconsistent estimators (see Wooldridge(1994) and Blundell et al. (1995)) . However, this analysis does not impose strict exogeneity. The pooled estimation technique used to calculate the direct effect allows for feedback of an arbitrary nature from current realizations of the dependent variable to future values of the explanatory variables.

The direction of causation postulated between industry R&D investment and government funded basic research in equation (3.2) has been subject to some debate among researchers. The current research literature on spillovers points out the possibility that a bias may arise due to changes in "scientific

opportunity." That is, researchers have noted that a promising development in a particular scientific discipline may lead to correlation between industry and public R&D funding that is not correctly characterized as spillovers. It arises when research funding agents respond to the same "scientific break-through" information when making their funding decisions. Further, if scientific opportunity is a problem , then estimates of the relationship between public and private funding of research are biased by the endogenous response of funding agents. One way to conceptualize the scientific opportunity problem is as an omitted variable bias. In this scenario, equation (3.2) has an omitted "scientific opportunity" variable and, consequently, the basic research variable is endogenous. This would lead to bias and inconsistent estimates of the parameters.

As a practical matter, any bias due to scientific opportunity will always be a possibility in models of research spillovers. In our context, the issue rests on three basic questions. First, how fine a line can be drawn between basic research and applied research? The National Science Foundation definition provides a broad guide to follow when delineating between the two; however, it does not allow one to construct mutually exclusive sets of research. To the extent that public and industry research overlap, the possibility of a scientific opportunity bias remains. As with the present study, researchers must use great care when breaking research projects into separate categories.

Second, at what stage of research "maturity" is the promising development in the scientific discipline? A fundamental assumption in models of

R&D capital is that R&D is effective over many periods and has an evolutionary character; learning and research are cumulative processes that are best measured as stocks. One idea underlying the model of equation (3.2) is that there exists some level of research maturity at which point basic biomedical research becomes useful to pharmaceutical drug discovery. A scientific opportunity bias is less likely when the academic researcher and the industry researcher focus on different areas of research.

Third, what proportion of pharmaceutical research effort is devoted solely to the exploration of basic science? Although an exact figure is not publicly available, pharmaceutical firms do conduct basic research. By all accounts it is a small but growing element of the industry's research strategy. Again, to the extent that research overlaps, a scientific opportunity bias is possible. Although it is expected that any bias related to scientific opportunity would be minimal in this analysis, chapter five explores the endogeneity issue between industry R&D and public basic research.

3.2 Data Sources and Construction

The well known difficulties of measuring the spillover or transfer of knowledge across sectors has made the data collection and preparation a very important aspect of this project. The three primary sources of data, the Public Health Service, Food and Drug Administration, and the Pharmaceutical Research and Manufacturers Association, are matched by year and therapeutic

class.[3] Together these sources represent the most recent and comprehensive public data available to address the hypotheses in this paper.

3.21 Productivity Measure

The measure of innovative output, Y_{it}, is a count of new chemical entities (NCEs) approved by the FDA. These are defined as new molecular compounds that have never before been tested or used in humans. The FDA supplied the data on approved NCEs for the years 1960-1994. As used here, the counts of NCEs exclude diagnostic and certain biological agents, new dosage formulations, surgical and other materials such as contact lens and devices.

To construct the counts of NCEs, the FDA data were grouped by year of approval and therapeutic class. Although the year of approval was supplied by the FDA, the compounds had to be assigned to the various therapeutic classes. This was accomplished by using the clinical pharmacology and treatment indication descriptions from the Physician's Desk Reference, Merck Index, and Martindale The Extra Pharmacopoeia. These sources were also used to eliminate any compounds not fitting the definition of NCEs used in this project.

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[3] Each measure used in this analysis has been grouped according to the therapeutic classification scheme used by the U.S. Department of Commerce Current Industrial Reports, Pharmaceutical Preparations except Biologicals.

Both the tabulation of counted NCE and some descriptive statistics by therapeutic class are presented in Table 3.1 and Table 3.2, respectively. Figure 3.1 graphs the number of counted NCEs against time for the cardiovascular, anti-infective and gastro/genito-urinary classes.

Although NCEs are only one possible productivity measure of pharmaceutical innovation, DiMasi et al. identify NCEs as the "most therapeutically and economically significant" (DiMasi et al. (1991), p. 108). Of course, patents are the traditional indicator of economically productive knowledge in KPF types of studies. It should be kept in mind that even though simple patent counts are an alternative, approved NCEs are a measure of economically important patents because they have proven therapeutic value. "Important" patent measures address one of the key criticisms of patent measures as an indicator of innovative output--the wide variation in the economic value of individual patents (Griliches (1984)). Trajtenberg (1990) provides an informative discussion on this issue.

3.22 Industry R&D Measure

The public data on pharmaceutical industry R&D expenditure, I_{it}, come from the Pharmaceutical Research and Manufacturers Association's Annual Survey Report. Domestic U.S. company-financed R&D expenditures for human-use (dosage form) ethical drugs were obtained for the period 1963-1994. Table 3.3 presents summary statistics for industry R&D for 1963-1994 while Figure 3.2

Table 3.1 - Tabulation of Counted NCEs

Year	Total Approved NCEs	Number of Material and Device NCEs	Number of Diagnositc NCEs	Number of Repeat Dosage NCEs	Other Excluded NCEs	Number of Counted NCEs
1964	24	1	0	0	1	22
1965	12	0	0	0	0	12
1966	18	0	0	4	1	13
1967	22	0	0	3	0	19
1968	9	0	1	0	0	8
1969	17	0	2	1	0	14
1970	20	0	0	0	0	20
1971	16	2	1	0	0	13
1972	11	0	2	1	0	8
1973	28	1	11	2	0	14
1974	36	3	3	0	0	30
1975	20	0	1	5	0	14
1976	26	1	9	0	0	16
1977	21	3	1	0	0	17
1978	20	2	2	0	0	16
1979	14	1	0	0	0	13
1980	12	0	0	0	0	12
1981	25	0	3	0	0	22
1982	28	0	5	0	0	23
1983	14	0	1	0	0	13
1984	20	0	1	0	0	19
1985	28	0	3	0	0	25
1986	19	0	2	0	0	17
1987	20	0	3	0	0	17
1988	19	0	3	0	0	16
1989	22	0	2	0	0	20
1990	22	0	4	0	0	18
1991	30	0	0	0	0	30
1992	32	0	3	5	0	24
1993	24	0	3	0	0	21
1994	22	0	4	0	0	18
Totals	651	14	70	21	2	544

Table 3.2 - Descriptive Statistics on Counted NCEs by Therapeutic Class

Therapeutic Class	1964-1977			1978-1994			1964-1994		
	MIN	MAX	MEAN	MIN	MAX	MEAN	MIN	MAX	MEAN
Endocrine/Neoplasm	1.00	8.00	4.50	1.00	7.00	3.18	1.00	8.00	3.77
Central Nervous System	2.00	8.00	5.14	1.00	8.00	4.53	1.00	8.00	4.81
Cardiovascular	0.00	4.00	1.14	0.00	7.00	3.65	0.00	7.00	2.52
Anti-Infectives	0.00	7.00	2.00	2.00	9.00	4.53	0.00	9.00	3.39
Gastrointentinal/Genitourinary	0.00	4.00	1.71	0.00	5.00	2.18	0.00	5.00	1.97
Dermatologic	0.00	3.00	0.50	0.00	1.00	0.29	0.00	3.00	0.39
Respiratory	0.00	3.00	0.71	0.00	2.00	0.71	0.00	3.00	0.71
All Classes/All Years	8	30	15.71	12.00	30	19.06	8.00	30.00	17.55

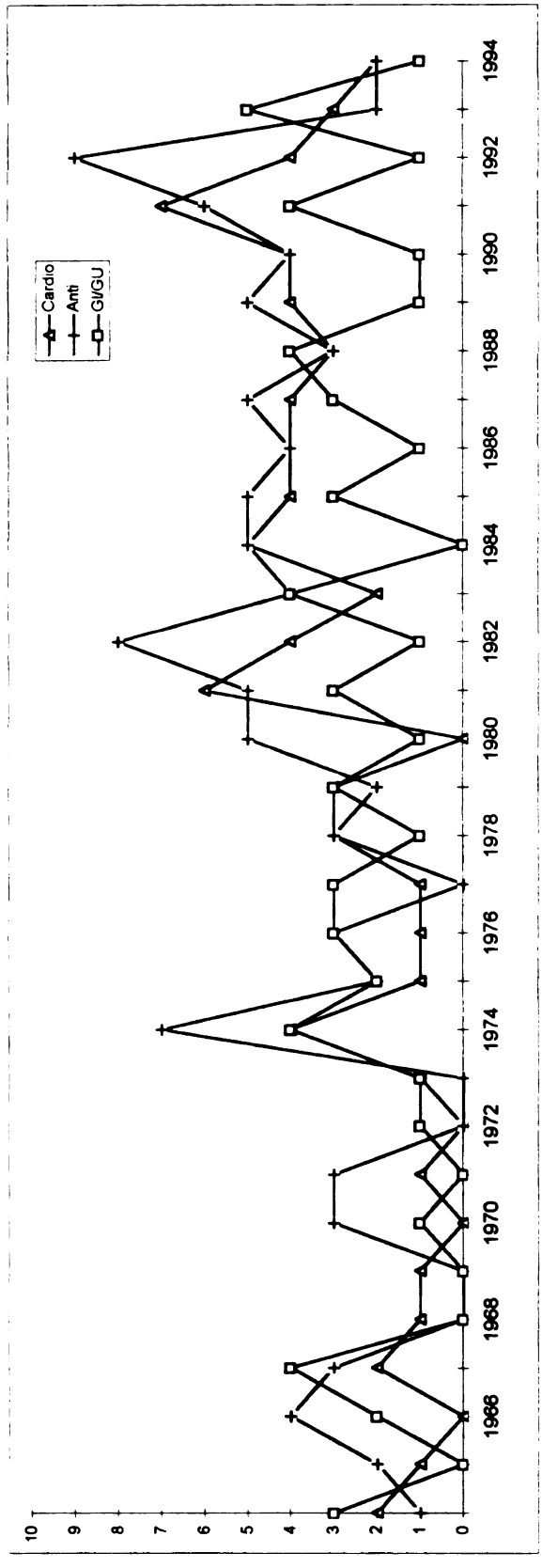

Figure 3.1 - Cardiovascular, Anti-infective and Gastro/Genito-urinary Counted NCEs

Table 3.3 - Pharmaceutical Industry R&D (millions of 1986 $)

Therapeutic Class	1963-1975		1975-1985		1985-1994		1963-1994	
	Mean R&D	Growth Rate	Mean R&D	Growth Rate	Mean R&D	Growth Rate	Mean R&D	Growth Rate
Endocrine/Neoplasm	241.65	4.33%	405.21	7.82%	1019.33	12.21%	526.78	7.69%
Central Nervous System	263.56	3.72%	369.40	2.68%	948.06	13.83%	505.30	6.21%
Cardiovascular	177.42	9.74%	496.43	12.15%	1171.48	4.63%	571.51	8.99%
Anti-Infectives	276.60	7.07%	430.34	3.03%	827.97	8.22%	490.56	6.08%
Gastrointensinal/Genitourinary	97.72	0.09%	145.09	7.53%	250.63	2.50%	158.45	3.14%
Dermatologic	41.78	15.53%	63.12	0.99%	111.90	10.83%	70.08	9.30%
Respiratory	55.07	12.23%	121.05	6.54%	326.07	9.80%	156.31	9.66%
All Classes	1153.80	5.81%	2030.63	6.54%	4655.43	9.12%	2478.98	7.00%

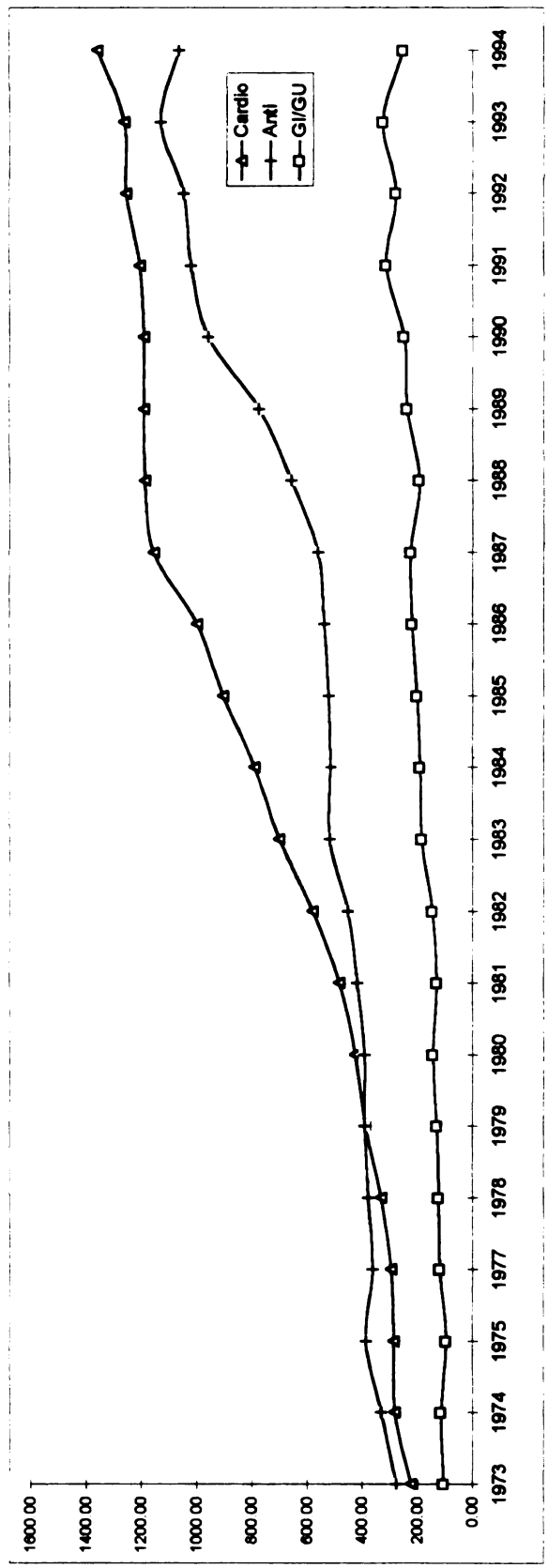

Figure 3.2 - Cardiovascular, Anti-infective and Gastro/Genito-urinary Industry R&D (millions of 1986 $)

graphs industry R&D against time for the cardiovascular, anti-infective and gastro/genito-urinary therapeutic classes.

Perhaps the biggest problem with the PhRMA data is its level of aggregation. Firms are aggregated into industry figures to protect the strategic position of individual firms. Moreover, the R&D investment totals are a composite measure of industry resources used in drug discovery and development (the cost of manufacturing appears to be in these figures as well). The PhRMA definition of R&D investment is as follows:

> The total cost incurred for all pharmaceutical research and development activity, including cost of salaries, other direct costs, service, routine supplies, and supporting costs, plus a fair share of overhead (administration, depreciation, space charges, etc.). Cost of drugs or medical research and development conducted on grant or contract for other companies are excluded. Conversely, total outlays for all research and development work contracted to others (manufacturers, independent research laboratories, academic institutions, etc.) are included.
>
> (PhRMA, Annual Survey Report)

Consequently, due to the nature of the industry data, nothing can be said about the relative productivity of individual components of industry R&D expenditure.

Therapeutic class totals were computable for most years in the data. Although yearly totals were always available, some therapeutic class totals had to be imputed (this amounted to five individual years of data). All figures include expenditure on research failures as well as expenditures in both discovery and development. Further, these figures were adjusted for inflation using the Biomedical Research and Development Price Index (BRDPI) supplied by the National Institutes of Health.

3.23 Measure of Government Funded Basic Research

The annual federally funded basic research flows were constructed from a comprehensive data set which includes all extramural grant and contract awards by the U.S. Public Health Service since 1955. For each grant and contract award, the data includes: the title, the identification number (activity code, institute code, and grant or contract number), the fiscal year of award, the award amount, and the scientific review group that recommended its approval. The individual grant level data allow the construction of annual flow and stock measures of PHS research awards by therapeutic class. The final set of research projects, called "core" research, consists of all those scientific studies that represent basic research relevant to the pharmaceutical industry. Of the PHS research grants, basic research excludes non-medical, instrumentation and clinical (human) studies.[4]

Beginning with the total set of grants and awards for an individual year, the annual basic research flow series are constructed using several data filters. Four main filter levels are defined and used. The first eliminates awards based on activity code. Generally speaking, this filter purged activities such as training, education, construction, demonstration, and institutional block grants from the data. The second filter eliminates awards based on institute code.

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[4] Industry scientists helped with the data construction process due to the complexity of medical scientific terminology.

There are several institutes or divisions that contribute nothing or only a negligible amount to core research. Examples of eliminated institutes include the National Institute on Dental Research, the National Institute on Environmental Health Sciences, the National Library of Medicine, the Food and Drug Administration, and several others. The third filter eliminates scientific review groups that consider research outside the definition of core basic research. These groups are reviewed in every year and the filter is modified to be year specific. (This was necessary due to the splitting, adding, and discontinuance of scientific review groups over time.) The fourth filter level, which is really a group of filters, analyze awards based on keywords contained in the title of the grant or contract. This group consisted of seven keyword "inclusion" filters that help identify awards belonging to specific therapeutic classes as well as an "exclusion" filter designed to further sift out inappropriate awards missed in the earlier levels. The primary sources of information in the construction of the class filters are the Department of Commerce Current Industrial Reports and medicine's scientific vocabulary. Table 3.4 shows the mean expenditure and growth rate by therapeutic class over the sample period (all figures are in millions of 1986 dollars). Figure 3.3 plots PHS basic research flows against time for the cardiovascular, anti-infective and gastro/genito-urinary classes. Appendix A contains an explanation and copies of worksheets and filter programs used in the data construction effort.

The filter levels separate the total universe of PHS grants into seven therapeutic classes of core research and a group of all other research. For a

Table 3.4 - PHS Biomedical Basic Research (millions of 1986 $)

Therapeutic Class	1955-1965		1965-1975		1975-1985		1955-1985	
	Mean Basic	Growth Rate	Mean Basic	Growth Rate	Mean Basic	Growth Rate	Mean Basic	Growth Rate
Endocrine/Neoplasm	142.89	21.84%	323.13	4.20%	506.27	3.15%	323.01	9.40%
Central Nervous System	81.87	22.16%	162.00	2.80%	265.12	5.65%	169.55	9.89%
Cardiovascular	84.26	22.02%	160.66	2.19%	240.34	4.52%	161.78	9.23%
Anti-Infectives	78.02	28.83%	156.40	1.70%	209.84	5.78%	148.28	11.49%
Gastrointestinal/Genitourinary	62.85	25.75%	121.77	0.19%	178.86	5.40%	120.89	9.91%
Dermatologic	4.89	24.19%	6.84	-2.81%	8.76	4.78%	6.80	8.14%
Respiratory	9.02	59.81%	23.16	7.70%	55.44	4.58%	29.41	21.65%
All Classes	463.80	23.61%	953.96	2.75%	1464.64	4.55%	959.72	9.91%

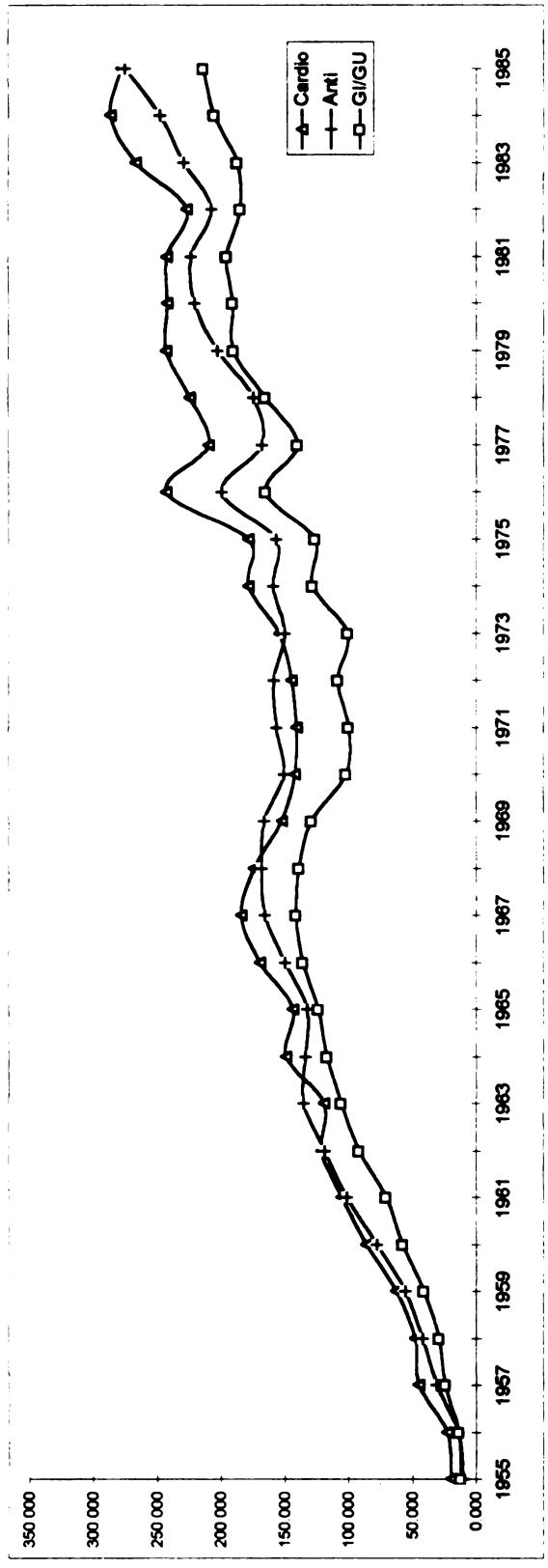

Figure 3.3 - Cardiovascular, Anti-infective and Gastro/Genito-urinary PHS Basic Research (millions 1986 $)

class total, the awards are summed across all grants. This is a simple method that does not attempt to apply different weights to individual research projects based on "importance" or scientific discipline.

Having completed the construction of the annual basic research series the next step is to construct the cumulative stock measure, B_{it}, used in the analysis. The government funded basic research stock is created using the standard perpetual inventory model described by Hall et al. (1988). For each therapeutic class, the stock of basic research is given by:

$$(3.3) \qquad B_{it} = (\text{Annual Flow})_{it} + (1-\delta)*(B_{it-1})$$

where B_{it} is the stock of PHS funded basic research in class i and year t, $(\text{Annual Flow})_{it}$ is the annual flow of PHS funded basic research in class i and year t, and δ is the depreciation rate of "knowledge capital". With δ constant over time we are assuming a geometric form of depreciation. In this case, a given year's flow of basic research losses its "productive capacity" at a constant percentage rate each year. Using a 15% rate of depreciation we see a 48% decline in the productivity of basic research over four years. In the literature, Hall et al. (1988) assume a 15% depreciation rate of R&D capital and Henderson and Cockburn (1996) use a 20% rate. The sensitivity of the estimated coefficient to changes in the rate of depreciation is explored in chapter four. The geometric form has the additional property that assets never "retire." Unlike the case of physical capital, this makes sense when applied to research

capital (it avoids the issue of having to estimate the useful life of research results--which we expect are long anyway).

To implement the perpetual inventory model the stock measure must begin at a benchmark. The benchmark for the B_{it} variable is the year 1944. This is the year Congress passed the Public Health Service Act authorizing the surgeon general to award research grants. Using the 1955-1985 sample growth rate by therapeutic class, the annual flow series were projected back to 1944. These nominal flows were also adjusted for inflation using BRDPI. Finally, equation (3.3) is used to construct the stock series.

3.24 Measure of FDA Regulatory Stringency

Since the passage of the 1962 Kefauver-Harris amendments to the Federal Food, Drug and Cosmetic Act of 1934 economists have been interested in the relationship between regulation and pharmaceutical innovation. The two most popular approaches are: first, to use a proxy variable for FDA regulation (Ward and Dranove (1995) and Wiggins (1979, 1981)), and second, to use the international residual from comparing the U.S. experience with that of the United Kingdom. The studies in the second group assume that U.S. firms and U.K. firms differ only in their regulatory environment (Grabowski et al. (1978)) or that they differ in their regulatory environment after controlling for firm size (Thomas (1990)). They ignore the possibility of that public knowledge can affect pharmaceutical innovation. While the technical determinants of pharmaceutical

innovation are just beginning to be understood, it is clear that the public stock of basic biomedical research is one such factor. The contention that U.K. pharmaceutical firms have the same access as U.S. firms to U.S. Government funded biomedical research is unsubstantiated. In fact, there is some interesting research on the role of geography in mediating knowledge spillovers (see Jaffe (1989) and Trajtenberg et al. (1993)). Moreover, Gambardella (1992) presents some initial evidence that public research results may be utilized with different degrees of effectiveness depending on firm human capital.

This paper follows the first approach by specifying a proxy variable for FDA regulation. In particular, it uses the same method of measuring regulatory stringency as Wiggins (1981). In his method, firms are assumed to form expectations of regulatory stringency based on current and past observed delays between the submission of a new drug application and its final FDA approval. These average review times are calculated by year and therapeutic class. The therapeutic class distinction is appropriate since it corresponds fairly well with the review structure of the FDA.

Using the new chemical entity data supplied by the FDA the review times are calculated for each approved NDA in months. The appropriate therapeutic class for each compound was determined in the process of constructing the NCE productivity measure. For those years in which no approved NDA is observed in a particular therapeutic class it is assumed that firms adjusted their expectations by increasing or decreasing the last observation in that class by the change in the **overall** average review time across all classes. The resulting regulatory

measures capture the cost associated with NDA review segment of FDA regulation. Table 3.5 shows the minimum, maximum and mean delay times by therapeutic class over the period 1973-1994. Figure 3.4 plots average FDA delay times by year for the cardiovascular, anti-infective and gastro/genito-urinary classes.

3.25 Measures of Pharmaceutical Demand and Medical Need

The expected demand for a therapeutic compound in an important component of the investment decision for pharmaceutical firms. It is the firm's forecast of actual sales over the life cycle of the therapeutic compound. Informal interviews reveal that many firms purchase expensive market information that is specific to individual market segments within therapeutic classes. Purchased market data is combined with firm specific information on product characteristics and sales infrastructure to estimate the revenue stream.

The main variable used in this analysis to proxy for expected demand is actual industry sales by therapeutic class and year. Wiggins (1983) and Henderson and Cockburn (1996) also use industry sales to proxy for demand. Sales by therapeutic class convey information on current market size, including demand from chronic medical conditions, as well as the distribution of industry sales resources (human and physical). This makes actual sales an important variable for conveying information about the market. Human-use, dosage-form ethical pharmaceutical industry sales figures broken down by therapeutic class

Table 3.5 - Statistics on FDA Regulatory Delay Times (months)

Therapeutic Class	1964-1977			1978-1994			1964-1994		
	Minimum	Maximum	Mean	Minimum	Maximum	Mean	Minimum	Maximum	Mean
Endocrine/Neoplasm	10.00	61.69	34.27	11.00	90.50	30.78	10.00	90.50	32.36
Central Nervous System	19.33	111.75	53.98	8.50	74.00	40.50	8.50	111.75	46.59
Cardiovascular	13.00	129.50	66.09	21.08	56.25	36.03	13.00	129.50	49.61
Anti-Infectives	12.88	140.38	38.80	9.00	46.25	23.59	9.00	140.38	30.46
Gastrointensinal/Genitourinary	15.00	182.75	51.98	9.00	46.55	26.98	9.00	182.75	38.27
Dermatologic	18.75	98.50	47.10	9.75	41.00	24.03	9.75	98.50	34.45
Respiratory	28.77	158.71	88.02	20.50	88.00	47.32	20.50	158.71	65.70

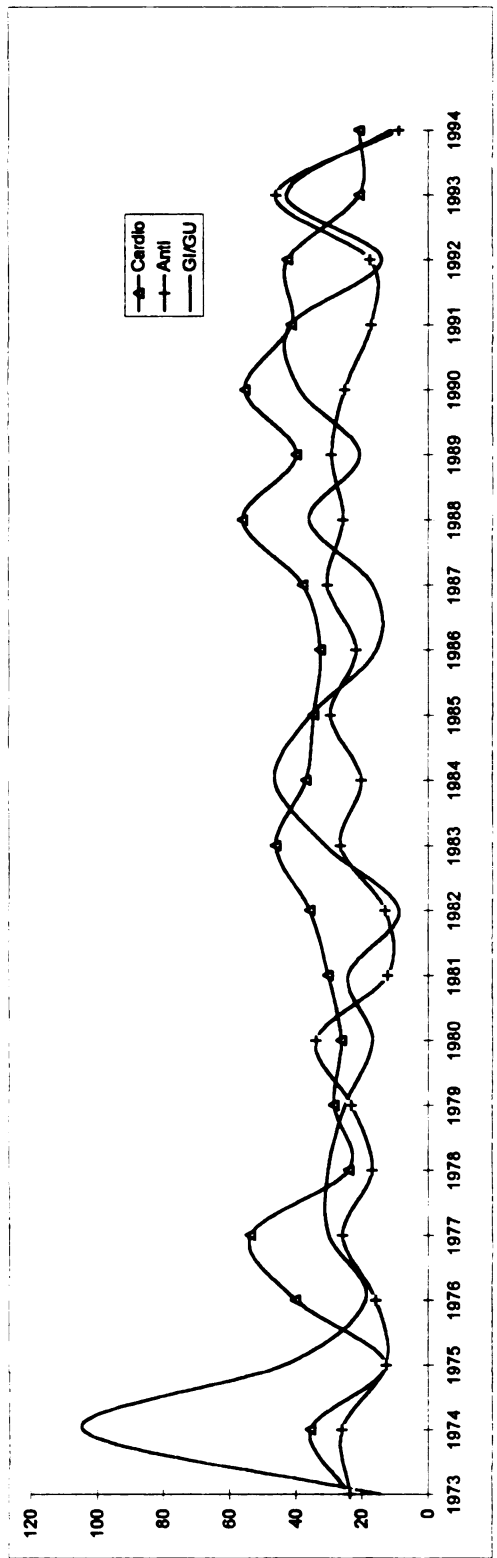

Figure 3.4 - Cardiovascular, Anit-infective and Gastro/Genito-urinary FDA Review Times (months)

are available from PhRMA.[5] Table 3.6 shows the mean and growth rate of industry sales from 1971 to 1985. Figure 3.5 graphs the series for the cardiovascular, anti-infective and gastro/genito-urinary classes.

In addition to industry sales, disease incidence and "severity" measures are developed. Data on the incidence and "severity" of disease are supplied by the National Discharge Survey. This survey covers non-Federal short-stay hospitals and is collected from a national sample of hospital records of discharged inpatients. Although the survey dates back to 1965, a fairly consistent time series is only available since 1971. It should be noted, however, that a new classification scheme was introduced in 1979. The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) replaced the earlier edition. This change caused a small shift in some of the therapeutic class totals.

A simple count of first-listed diagnoses, which are equivalent to the number of discharges, are grouped by therapeutic class and year. These counts represent the incidence of disease requiring short-stay hospital visits for the civilian non-institutionalized U.S. population. "Severity" is measured by a count of the number of hospital inpatient days. The basic notion is that more severe illness requires longer hospital stays. Because the hospital sample is inflated to estimates for the civilian non-institutionalized U.S. population, each of these

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5 Industry sales to Federal hospitals were purged from the annual sales totals prior to computing therapeutic class totals. As an empirical matter, this correction had no effect on the results discussed in chapter five.

counts cover most of the U.S. population. The measures are less accurate for the older segment of the population since many senior citizens move to nursing homes. Tables 3.7 and 3.8 present the mean and growth rate of disease incidence and severity by class for 1971-1985, respectively. Figures 3.6 and 3.7 plot disease incidence and severity against time for the cardiovascular, anti-infective and genito-urinary therapeutic classes.

Before turning to the estimation methodology for the analysis, it is important to note a few limitations with these measures. First, disease incidence is measured not disease prevalence. Since incidence measures the number of new cases over a period of time, it is not equivalent to prevalence, which measures the number of disease cases at a point in time. Although these concepts differ, incidence may be a good substitute for disease prevalence. Second, measuring severity by the length of hospital stays is fairly crude. In fact, the length of stay may be more related to the recovery period of illness or surgery.

3.26 Time Effects and Therapeutic Class Effects

Time effects have been treated inconsistently in the current research on pharmaceutical innovation. Some researchers, such as Ward and Dranove (1995), do not include a time trend in their model while other researchers, such as Henderson and Cockburn (1996) and Thomas (1990), do not specify a full set of year dummies in their analyses. Dating back to Bailey's analysis, all

Table 3.6 - Pharmaceutical Industry Sales (millions of 1986 $)

Therapeutic Class	1971-1985	
	Mean Sales	Growth Rate
Endocrine/Neoplasm	1,968.18	4.28%
Central Nervous System	4,202.18	3.20%
Cardiovascular	2,134.65	9.13%
Anti-Infectives	2,622.88	4.21%
Gastrointensinal/Genitourinary	1,704.13	2.26%
Dermatologic	523.24	-1.78%
Respiratory	1,044.98	2.90%
All Classes	14,200.24	4.04%

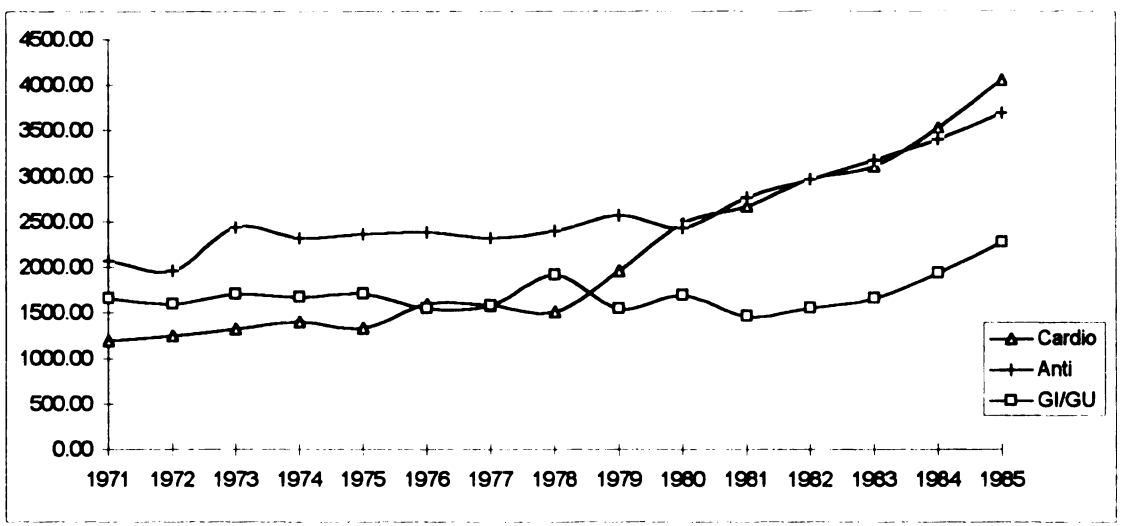

Figure 3.5 - Cardiovascular, Anti-infective and Gastro/Genito-urinary Industry Sales (millions of 1986 $)

Table 3.7 - Incidence of Disease (hospital discharges in thousands)

Therapeutic Class	1971-1985	
	Mean	Growth Rate
Endocrine/Neoplasm	3,589	2.13%
Central Nervous System	4,284	2.57%
Cardiovascular	4,906	3.10%
Anti-Infectives	1,901	0.92%
Gastrointensinal/Genitourinary	3,853	-0.38%
Dermatologic	280	-1.74%
Respiratory	1,923	2.17%
All Classes	20,736	1.83%

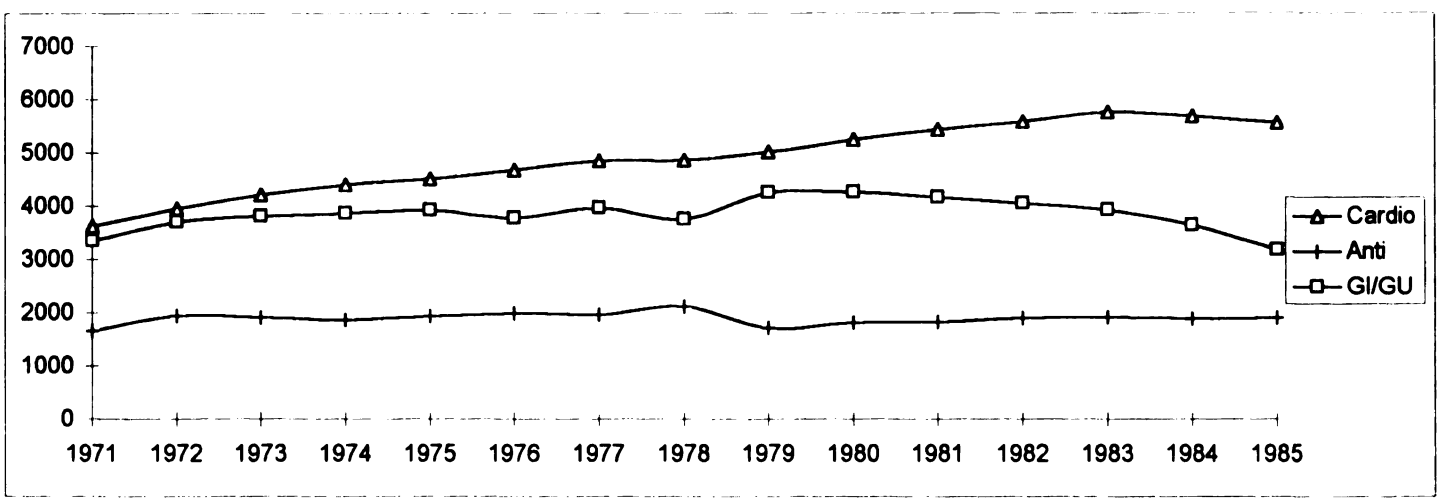

Figure 3.6 - Cardiovascular, Anti-infectives and Gastro/Genito-urinary Hospital Discharges

Table 3.8 - "Severity" of Disease (hospital days in thousands)

Therapeutic Class	1971-1985	
	Mean	Growth Rate
Endocrine/Neoplasm	35,227	-0.30%
Central Nervous System	35,849	1.03%
Cardiovascular	48,666	0.15%
Anti-Infectives	14,034	0.77%
Gastrointensinal/Genitourinary	22,968	-2.07%
Dermatologic	2,231	-0.82%
Respiratory	12,541	1.36%
All Classes	171,517	0.08%

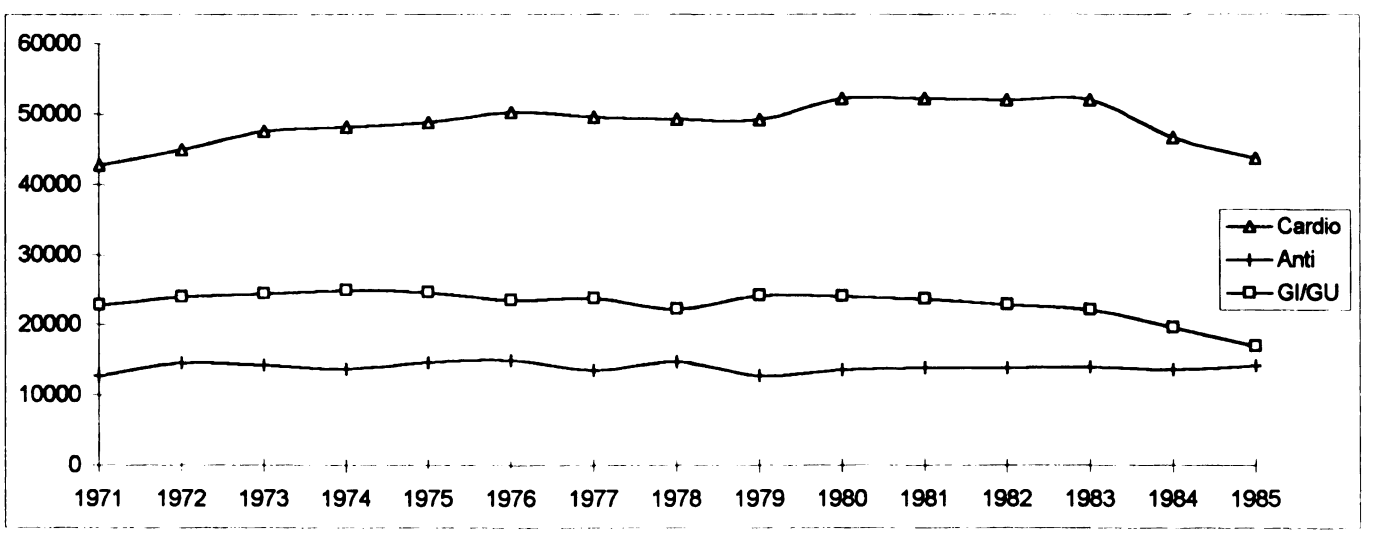

Figure 3.7 - Cardiovascular, Anti-infectives and Gastro/Genito-urinary Disease Inpatient Days

indications are that time has an important and somewhat unexplainable impact on pharmaceutical innovation. In light of this fact, the current analysis specifies individual year dummy variables. Allowing each year to have its own intercept is the most general way to account for variation over time due to inflation, industry shocks, and other unobserved changes.

As discussed above, the therapeutic classes provide the mapping of research knowledge used in this paper. Each of these classes encompasses the research from a cross-section of medical disciplines. Depending on the distribution of industry research investment as well as scientific and managerial skill, one class may feed into drug discovery more easily than another. For this reason, it is important to include some control for therapeutic class effects. This has been done using fixed-effect dummy variables for each class.

3.3 The Estimation Technique

3.31 The Direct Effect

Since approved NCEs only take on non-negative integer values, a discrete dependent variable model is appropriate. In this analysis the conditional expectation of approved NCEs, $E[NCE_{it}| \mathbf{X}_{it}]$, is assumed to be generated by a Poisson process for each therapeutic class, i, and each year, t. The Poisson distribution has been the workhorse of the empirical literature studying innovation counts. Due to advances in the econometrics literature on count

variable estimation, the actual conditional distribution of approved NCEs is not restricted to the Poisson form. In particular, the model can be estimated without imposing any restriction on the conditional variance of approved NCEs. The robustness properties of the estimation method are discussed below.

The Poisson parameter, λ_{it}, is represented as a exponential function of all explanatory variables, **X**, and the parameters, b, as follows:

$$(3.4) \qquad E[NCE_{it}|\ \mathbf{X}_{it}] = \lambda_{it} = \exp(\mathbf{X}_{it}b)$$

where i indexes therapeutic class, t indexes time, an **X** are the explanatory variables.

There are two important time series characteristics that must be considered when estimating models for panel data. The first is the strict exogeneity assumption discussed in section 3.11. Once again, the estimation technique used in this analysis does not impose this assumption. Second, dynamic models that do not include lagged dependent variables are not necessarily "dynamically complete." The dynamic completeness assumption says that the model specifies the lag structure correctly so that further lags add no new information:

$$(3.5) \qquad E(NCE_{it}|\ \mathbf{x}_{it}, y_{it-1}, \mathbf{x}_{it-1}, \ldots) = E(NCE_{it}|\ \mathbf{x}_{it}, \mathbf{x}_{it-1}, \ldots, \mathbf{x}_{it-k})$$

where $y_{it-1}, \ldots$ are lagged dependent variables, $\mathbf{x}_{it}$ are the explanatory variables and, possibly, lags of other variables. Since there is no guarantee that dynamic

completeness holds, serial correlation is not ruled out. A Lagrange multiplier test is used to identify serial correlation in the model that may arise due to neglected dynamics in the conditional mean. Based on the results of this test, the heteroscedasticity and serial correlation robust asymptotic standard errors are calculated following Wooldridge (1991).

A pooled quasi-maximum likelihood estimation technique (QMLE) is used to estimate equation (3.1). The technique is quasi-likelihood because the specified likelihood function, a Poisson likelihood function in this case, is not required to correspond to the actual distribution of the explained variable (NCEs) conditional on the explanatory variables, **X**. This leads to certain robustness properties. For instance, the actual distribution need not have the exact properties of the Poisson distribution, such as the mean equals the variance. In fact, Gourieroux, Monfort, Trognon (1984) show that an entire class of quasi-likelihoods in the linear exponential family (LEF) produce consistent estimates for the parameters of a correctly specified conditional mean. It is important to note that the Poisson QMLE produces consistent estimates under any variance assumption and arbitrary serial correlation in the observations.

Under reasonable assumptions, the Poisson QMLE is relatively efficient. The asymptotic variance was estimated under three alternative assumptions about the conditional variance of $E[NCE_{it}| \mathbf{X}_{it}]$. The first method is "fully robust" in that it is valid under any conditional variance (or distributional) assumption (Wooldridge (1996)). The second method, the Generalized Linear Model (GLM) assumption, requires that the conditional mean and variance be proportional.

This requirement is represented as follows:

(3.6) $\text{Var}[NCE_{it} | \mathbf{X}_{it}] = \sigma^2 E[NCE_{it} | \mathbf{X}_{it}]$ Where $\sigma^2 > 0$

The assumption implies that the ratio $\text{Var}[NCE_{it} | \mathbf{X}_{it}] / E[NCE_{it} | \mathbf{X}_{it}]$ is constant but allows them to be different from each other by some positive number. The case where $\sigma^2 > 1$ is referred to as overdispersion whereas the case when $\sigma^2 < 1$ is called underdispersion. If there is overdispersion in the model, then the GLM standard error will be larger than the MLE and the resulting test statistic will show lower significance levels.

The third method is the most restrictive because it requires the Poisson nominal variance assumption to hold.

(3.7) $\text{Var}[NCE_{it} | \mathbf{X}_{it}] = E[NCE_{it} | \mathbf{X}_{it}]$

This assumption imposes a standard property of the Poisson distribution, namely that the first and second moments of the distribution are equal. In most cases, Poisson models that do not relax the nominal variance assumption find spuriously high levels of significance.

In the standard cross-sectional problem, calculating the standard errors under these three alternative conditional variance assumptions would be all that is needed for correct inference. However, models that incorporate a time dimension need to account for possible failure of the dynamic completeness

assumption. Under the GLM variance assumption, a Lagrange Multiplier statistic was computed to test for serial correlation. For equation (3.1), the test statistic is computed by estimating the model under the null hypothesis of dynamic completeness; calculating weighted residuals and weighted explanatory variables; running an auxiliary regression of these weighted residuals on the weighted explanatory variables and lagged weighted residuals. If k lags of residuals are included in the auxiliary regression, then this is equivalent to testing for kth order serial correlation. The sample size multiplied by the uncentered r-squared from this regression is distributed chi-squared with k degrees of freedom. Further, the significance of the individual coefficients on the lagged residuals can be tested using the standard t-statistic (for details on this test see Wooldridge (1996)). If the null hypothesis of dynamic completeness can not be accepted, the heteroscedasticity/serial-correlation (H/SC) robust standard errors should be used for inference (Wooldridge (1991)).

3.32 The Indirect Effect

The estimation of equation (3.2) is carried out using pooled ordinary least squares (OLS). As with the pooled Poisson QMLE, the asymptotic properties of this estimator do not impose the strict exogeneity assumption. This allows current industry R&D expenditures to influence future values of public basic research, FDA regulation and pharmaceutical demand.

Robust inference requires that the standard errors be adjusted to account for the possible failure of the dynamic completeness assumption. Once again, a Lagrange multiplier statistic is used to test for serial correlation. It is the same procedure as used for the direct effect except the residuals and explanatory variables are not weighted. If serial correlation is detected, then the heteroscedasticity/serial correlation (H/SC) robust standard errors will be computed following Wooldridge (1989) and used for inference.

Chapter 4

The Direct Impact of Public Basic Research on Pharmaceutical Innovation

4.1 Overview

This chapter explores the direct determinants of pharmaceutical innovation. It is postulated that pharmaceutical product innovation is a function of publicly funded basic research, industry R&D and FDA regulatory stringency. Previous empirical research has failed to link public basic research with pharmaceutical innovation. This link, however, is quite important. The extent to which economic agents can exploit productive external information has fundamental implications for theories of productivity and growth. Consider, for instance, that knowledge externalities are one key to unbounded growth in endogenous growth theory. This chapter will describe how knowledge externalities from publicly funded biomedical research impact pharmaceutical innovation.

Strong evidence is found for an economically and statistically significant impact of public research on pharmaceutical innovation (hypothesis one). Public research "capital" is intended to mimic the creation of scientific knowledge by using a cumulative stock form of measurement. The elasticity of the number of new chemical entities with respect to the stock of public basic research is found to lie in the range of 2.2 to 2.5. These point estimates are large and imply

increasing returns to scale in the pharmaceutical innovative process due to publicly funded basic research.

If public basic research is used to formulate new drug concepts, then the impact of this research should come early in the drug discovery stage of the pharmaceutical innovative process (hypothesis two). In fact, the data show that public research has its most significant impact on pharmaceutical innovation seventeen years before an approved NCE. This finding implies that an average of seventeen years elapse between federal award and new product approval. Because basic research is cumulative and measured as a stock variable, this result is perhaps best interpreted as a seventeen year lag between the time basic research reaches a "maturity" point or "critical mass" and the approval of a new chemical entity.

When one looks at the nature of the research that is supported by the federal government and private industry, it is clear that these two types of research are quite distinct. While pharmaceutical firms invest in basic research, by far the largest portion of their R&D investment is "applied." The bulk of this money is spent on testing specific drugs and documenting their findings. Publicly supported basic research, on the other hand, is more diverse and general. The analysis finds that both these types of research are important in the pharmaceutical innovative process. Their distinctive contributions suggest limited substitution possibilities in the production technology (hypothesis three). Using a constant elasticity of substitution production function, the elasticity of substitution (E_s) between industry R&D and public basic research is found to be

0.29. Since the substitution possibilities between two inputs approach the fixed proportions Leontief technology as values of E_s approach zero, it can be inferred that public basic and private industry research do not easily substitute for each other in the pharmaceutical innovative process.

Using the results from Grabowski and Vernon (GV) (1996) regarding the average discounted stream of revenues for a NCE, the marginal contribution of the public research stock can be given an explicit present value. The estimated marginal productivity of federally funded basic research on the number of approved new chemical entities is 0.07 per $1 million in each therapeutic class. This marginal product has a present discounted value of $13 million in real 1986 dollars at the time of introduction. In fact, the marginal contribution of public research is greater that the marginal contribution of private R&D, which has a marginal product of 0.05 per $1 million. Using the GV data and the seventeen year lag between research award and product approval, the net present value of publicly funded basic research at the time of introduction is $5582.368 million in real 1986 dollars.

Further, the results hold up to robust statistical inference. Using the heteroscedasticity and serial correlation robust standard errors, the public research stock variable becomes more statistically significant. In addition to calculating the robust standard errors, the analysis allows for alternative lags describing the pharmaceutical innovative process as well as for lagged effects from FDA regulatory stringency. In both of these cases, using a finite distributed

lag is a robust specification since it does not restrict the coefficient values over time.

4.2 Model Specification

Two empirical specifications of the KPF described by equation (3.1) are implemented. The first is the Cobb-Douglas. This formulation has been used in most studies of R&D and productivity. Besides assuming that inputs are strictly separable, the major limitation of the Cobb-Douglas functional form is that the elasticity of substitution between inputs is restricted to unity. This restriction implies that a percentage increase in the relative price of private R&D will induce the same percentage decrease in the industry's relative quantity of private R&D input without any loss of productive output. To the extent that a dollar of public basic research buys something different than a dollar of private R&D investment, the Cobb-Douglas elasticity of substitution is probably too restrictive.

To order to explore the potential substitutability between private and public research, a constant elasticity of substitution (CES) production formulation is used. As its name implies, the CES requires the elasticity of substitution between inputs to be constant; however, it is not restricted to unity. In terms of the estimation, the essential difference is that an additional term, called the "substitution term," is added as an explanatory variable. It is perhaps important to point out that the CES formulation requires a stock measure of

private R&D in order to avoid problems of collinearity between multiple substitution terms. The industry level Cobb-Douglas production function is:

$$(4.1) \qquad Y_{it} = e^{(\lambda t)(\eta i)}(I_{it})^{\alpha 1},\ldots,(I_{it-k})^{\alpha k}(B_{it-m})^{\beta 1}(R_{it})^{\gamma 1},\ldots,(R_{it-h})^{\gamma h}e^{(\mu)}$$

where i represents the medical therapeutic class, t represents time, Y_{it} is a count of pharmaceutical innovative output, λ and η capture the exogenous effects of time and therapeutic class on innovation, $\alpha 1$ - αk are the output elasticities of the industry R&D distributed lag, $I_{it},\ldots,I_{it-k}$; $\beta 1$ is the output elasticity for the stock of Public Health Service funded basic research B_{it-m}; and $\gamma 1$ - γh are the output elasticities for the predetermined distributed lag of FDA regulation (where h= 9), $R_{it},\ldots,R_{it-h}$. The term, μ, is a random error that is assumed to have a zero mean and constant variance. The distributed lag for the pharmaceutical innovative process is specified to be length k (where k = 12 and k = 14 alternatively). The appropriate lag for PHS basic research (m) will be determined empirically.

The production function is assumed to hold across therapeutic class and time. The coefficients estimates are long-run industry elasticities for each of the variables. For instance, the coefficient, $\beta 1$, tells us the percentage change in the number of approved NCEs in each therapeutic class for an exogenous change in the stock of government funded basic research. The industry level results demonstrate the general importance of PHS funded research in pharmaceutical innovation. Other industry level estimates concerning the effectiveness of

industry R&D dollars and the industry average FDA regulatory delay will also be of interest. Since the research parameters (α,β) are not restricted to the constant returns to scale case, these estimates will shed some light on possible industry-wide increasing returns to scale stemming from the contribution of public research.

The dynamics of the R&D and regulatory relationships in pharmaceutical innovation are not known with certainty and have been changing over time. In a comprehensive analysis on the cost of new drug development, DiMasi et al. (1991) find that the average time from synthesis to FDA approval is nearly twelve years for the 1979-1989 period. Moreover, in a study looking at the relationship between drug importance and time to market, Dranove and Meltzer (1994) suggest the period from patent application to FDA approval is twelve to fourteen years. Based on these studies, the analysis allows for both a twelve year and fourteen year industry lag specification.

Following Grabowski et al. (1978), Wiggins (1981) and Jensen (1987), regulatory stringency is measured by the average delay between submission of a new drug application and its approval by the FDA. Both Wiggins (1981) and Jensen (1987) included their annual stringency measures lagged up to five periods prior to pharmaceutical innovation. Since it is common for pharmaceutical firms to anticipate regulatory requirements several years before submitting new drug applications, the specification of equation (4.1) allows

regulatory stringency to have its impact as far back as nine years prior to FDA approval.[1]

Chapter two suggests that PHS basic research feeds the creative conception of new therapeutic compounds with its greatest impact coming in the early stages of drug discovery. Combined with the existing studies on industry lag lengths, this implies that firms draw on the pool of available public knowledge at least thirteen years prior to the drug's approval by the FDA. Further, because research awards are used to measure the public stock of knowledge it is necessary to allow for the lag between research award and research output as well as for the lag between research completion and its utilization by industry. In the case that two years are enough time for these lags to work themselves out, the impact of basic research should occur at least fifteen years prior to an approved NCE. Using this as a starting point, the timing of the effect is explored in the next section.

4.3 The Timing of the Relationship

The average timing of the impact of PHS basic research is established using both non-nested and nested regression criteria. The non-nested criteria

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[1] No structure is imposed on the distributed lag of FDA regulatory stringency variables. As in the case of industry R&D, this is intended to provide a better econometric control by not restricting the annual coefficients.

are appropriate for evaluating those regressions that include a single lag of PHS basic research. One advantage of this approach is that it avoids problems of collinearity between alternative stock variables. The nested regression criteria are applied to an additional set of regressions that include other lagged stocks as control variables. Taken together, these approaches determine the empirical timing of the impact of PHS basic research. Tables 4.1 and 4.2 present the single PHS lag regression results assuming a twelve and fourteen year industry R&D distributed lag, respectively. Each basic research stock is assumed to have a 15% depreciation rate (alternative depreciation rates are explored later in the chapter). Columns (1) through (6) show the results for the fifteenth through the twentieth lags of PHS basic research. The rows of Tables 4.1 and 4.2 show the values of the coefficient estimates and the relevant statistics for each regression. Because of space considerations not all of the regression coefficients are show in the tables. The full regression output can be seen in Appendix B.

In each table, all three non-nested regression criteria , the sum of squared residuals (SSR), the coefficient of determination, and the value of the log likelihood function, indicate that PHS basic research feeds pharmaceutical innovation seventeen years prior to NCE approval. Also note that the values of these criteria are not much different for the eighteenth lag of PHS basic

Table 4.1 - PHS Basic Research (15% Dep.) Non-Nested Regression Results with 12 Year Industry Lag

Dependent Variable: Count of NCEs

	Equations					
Variable or Statistic	1	2	3	4	5	6
Constant	-8.9826	-10.7455	-14.9479	-16.8552	-17.0110	-13.2528
Poisson t-statistic	[-1.2706]	[-1.4607]	[-1.8593]	[-1.8642]	[-1.7178]	[-1.3202]
Sum of Industry R&D Coefficients	0.6976	0.6793	0.6934	0.8248	1.0377	1.1981
Sum of Regulatory Coefficients	-0.7221	-0.6873	-0.5903	-0.4684	-0.3673	-0.4601
PHS Basic Research Stock	**Lag 15**	**Lag 16**	**Lag 17**	**Lag 18**	**Lag 19**	**Lag 20**
Estimated Coefficient	1.2686	1.5773	2.2458	2.4592	2.3222	1.6304
Poisson t-statistic	[1.3405]	[1.5661]	[2.0151]*	[1.9542]*	[1.7513]*	[1.2901]
GLM t-statistic	[1.4694]	[1.7270]*	[2.2501]**	[2.1864]*	[1.9543]*	[1.4296]
Fully Robust t-statistic	[3.6504]**	[3.5933]**	[3.5567]**	[2.8479]**	[2.1214]*	[1.4108]
H/SC Robust t-statistic	[5.6648]**	[7.1332]**	[8.9539]**	[9.5858]**	[8.4166]**	[5.7363]**
SSR	129.2024	128.1536	123.9466	124.2330	127.2843	135.4568
R-Squared	0.7709	0.7727	0.7802	0.7797	0.7743	0.7598
Log Likelihood	90.8615	91.1734	91.9585	91.8617	91.5366	90.7854

Note: All variables are in logs

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

Table 4 2 - PHS Basic Research (15% Dep.) Non-nested Regression Results with 14 Year Industry Lag

Dependent Variable: Count of NCEs

	Equations					
Variable or Statistic	1	2	3	4	5	6
Constant	-8.1476	-10.4326	-15.6360	-17.0365	-16.1177	-13.2528
Poisson t-statistic	[-1.0517]	[-1.2662]	[-1.7288]	[-1.7147]	[-1.5585]	[-1.3202]
Sum of Industry R&D Coefficients	0.6591	0.6653	0.7177	0.8239	0.9810	1.1961
Sum of Regulatory Coefficients	-0.7292	-0.6914	-0.5854	-0.4684	-0.3826	-0.4601
PHS Basic Research Stock	**Lag 15**	**Lag 16**	**Lag 17**	**Lag 18**	**Lag 19**	**Lag 20**
Estimated Coefficient	1.1721	1.5410	2.3369	2.4900	2.2417	1.6304
Poisson t-statistic	[1.1568]	[1.3922]	[1.8964]*	[1.8373]*	[1.6506]*	[1.2901]
GLM t-statistic	[1.2532]	[1.5158]	[2.0880]*	[2.0294]*	[1.8187]*	[1.4296]
Fully Robust t-statistic	[3.9926]**	[4.4701]**	[4.9998]**	[3.6357]**	[2.2324]	[1.4108]
H/SC Robust t-statistic	[4.0037]**	[5.0575]**	[7.1278]**	[8.8831]**	[8.3760]**	[5.7363]**
SSR	129.3799	128.8590	125.0113	125.4553	127.2538	131.5788
R-Squared	0.7705	0.7715	0.7783	0.7775	0.7743	0.7666
Log Likelihood	90.9016	91.1903	91.9928	91.9016	91.6246	90.8343

Note: All variables are in logs

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

research. Further, the timing of the basic research contribution is consistent across both industry lag specifications, either the twelve year or fourteen year.

Tables 4.3 and 4.4 present the alternative PHS stock regression results. Each table shows two alternative regressions in which the seventeenth lag of PHS basic research is set against alternative lags. The first regression includes the twelfth, seventeenth, and twenty-second lags. The second regression expands the range to ninth, seventeenth, and twenty-fifth lags. In each of these specifications only the seventeenth lag of PHS basic research falls within the range hypothesized in chapter two. Although the collinearity of these stock variables lowers the precision of the estimates, the seventeenth lag stands out as the relevant timing. Both the generalized linear model (GLM) and fully robust standard errors show statistical significance at conventional levels. Consequently, both regression approaches support the timing hypothesis outlined in chapter two. Moreover, the results are consistent with previous studies on the lag in pharmaceutical innovation (see DiMasi et al. (1991) and Dranove and Meltzer(1994)). Since an F-test found that the thirteenth and fourteenth lags of industry R&D do not add explanatory value to the equaiton, the remainder of the discussion will focus on the twelve year industry lag results shown in Table 4.1.

Table 4.3 - PHS Basic Research (15% Dep.) Nested Regression Results with 12 Year Industry Lag

Dependent Variable: Count of NCEs

	Equations					
Variable or Statistic	1			2		
Constant		-16.5726			-16.02741	
Poisson t-statistic		[-1.7439]			[-1.5752]	
Sum of Industry R&D Coefficients		0.9147			0.7514	
Sum of Regulatory Coefficients		-0.4708			-0.507	
PHS Basic Research Stock	**Lag 12**	**Lag 17**	**Lag 22**	**Lag 9**	**Lag 17**	**Lag 25**
Estimated Coefficient	-0.4624	2.4084	0.4405	0.0722	2.0720	0.2133
Poisson t-statistic	[-0.3523]	[1.6205]	[0.5382]	[0.0542]	[1.7343]*	[0.5273]
GLM t-statistic	[-0.4319]	[1.9864]*	[0.6596]	[0.0661]	[2.1153]*	[0.6432]
Fully Robust t-statistic	[-0.6830]	[2.6007]**	[0.9243]	[0.1090]	[2.8138]**	[1.0975]
SSR		124.2308			125.4506	
R-Squared		0.7797			0.7775	
Log Likelihood		92.1515			92.1205	

Note: All variables are in logs.

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

Table 4.4 - PHS Basic Research (15% Dep.) Nested Regression Results with 14 Year Industry Lag

Dependent Variable: Count of NCEs

	Equations					
Variable or Statistic	1			2		
Constant	-16.7339			-15.9892		
Poisson t-statistic	[-1.7060]			[-1.5036]		
Sum of Industry R&D Coefficients	0.9255			0.7452		
Sum of Regulatory Coefficients	-0.4751			-0.5095		
PHS Basic Research Stock	**Lag 12**	**Lag 17**	**Lag 22**	**Lag 9**	**Lag 17**	**Lag 25**
Estimated Coefficient	-0.5247	2.5249	0.4109	0.0755	2.0709	0.2106
Poisson t-statistic	[-0.3872]	[1.4641]	[0.4833]	[0.0559]	[1.4889]	[0.5032]
GLM t-statistic	[-0.4621]	[1.7474]*	[0.5767]	[0.0663]	[1.7670]*	[0.5972]
Fully Robust t-statistic	[-0.9058]	[4.8890]**	[0.7190]	[0.1263]	[3.8177]**	[0.9428]
SSR	125.3121			126.2564		
R-Squared	0.7778			0.7761		
Log Likelihood	92.1813			92.1361		

Note: All variables are in logs.

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

4.4 The Magnitude of the Public Research Impact

Given the fact that PHS funded research is an intermediate input into an innovative process that is subject to long lags, it is not surprising that its economic impact has been hotly debated in policy circles. Looking at the estimated coefficients in columns (3) and (4) of Table 4.1, the economic significance of PHS basic research as a determinant of pharmaceutical innovation becomes clear. An estimated constant elasticity ranging between 2.2 and 2.5 implies a 10% increase in the stock of PHS basic research will, on average, lead to a 22% to 25% increase in the number of approved NCEs in each of the seven therapeutic classes.

The following two examples provide a sense of the important impact of PHS basic research on pharmaceutical innovation. First, consider the impact of a 10% increase in the basic research stock in 1976 on the number of approved NCEs in 1993. In 1976 the PHS granted $705 million in awards for basic research across all classes. This is approximately 26% of all PHS extramural awards given in that year. A 10% increase in the stock of basic research available in 1976 would have required an additional $216 million--an 8% reallocation of the total value of PHS awards to basic research. The effect, on average, would have been five additional therapeutic compounds in each class in 1993. It should be noted that this impact will continue to feed pharmaceutical innovation beyond 1993.

Unlike overall federal basic research, PHS funding of basic research relevant to the pharmaceutical industry has not experienced a dramatic decline in real annual growth. This contrast in funding trends allows us to ask what pharmaceutical innovation would have been had PHS basic research followed the overall trend. The counter factual experiment illustrates both the importance of federally funded basic research in pharmaceutical innovation as well as the potential impact of changes in the real growth rate of basic research funding.

Using the estimated model, Figure 4.1 shows the impact of imposing a slower growth rate in PHS basic research funding on pharmaceutical innovation. The solid line represents the observed (and predicted) number of approved NCEs in the sample period 1978-1994. The dotted line represents the predicted number of NCEs with an imposed 0.6% decline in the real growth rate of PHS basic research. Holding all else constant, this decline leads to a drop in the average number of approved NCEs from 19 to 11. Clearly, evidence from the pharmaceutical industry suggests that a decline in the growth rate of federal basic research funds will lead to a significant drop in measured innovation.

4.5 The Statistical Significance of Public Research

The tests for statistical significance involve alternative assumptions on the conditional variance of NCEs as well as accounting for potential serial correlation in the implied disturbances. Until recently, the most common test for

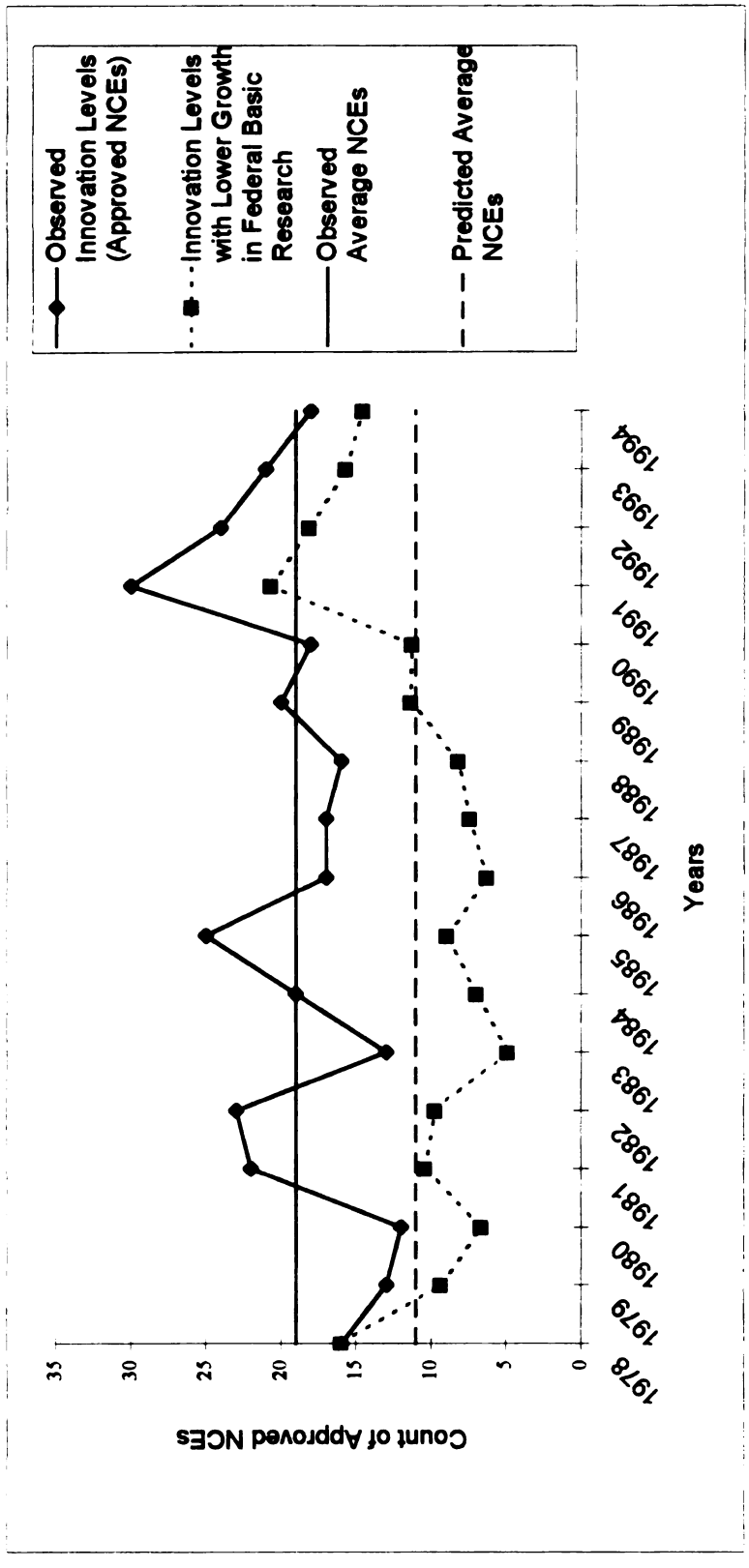

Figure 4.1 - Pharmaceutical Innovation Levels with Slower Real Basic Research Funding Growth (0.06% slower)

statistical significance in count data models assumed the Poisson nominal variance property in which the mean and variance are restricted to equality. Under this assumption, which is shown in column (3) of Table 4.1, the seventeenth lag of PHS basic research has a positive coefficient with a t-statistic equal to 2.02 implying a p-value < 0.025 (one-sided alternative). The weakness of this assumption is that it rarely holds in empirical applications and, consequently, can lead to spuriously high levels of significance.

The next two assumptions generalize the Poisson property. The GLM assumption allows a proportional relationship between the mean and the variance. Since the conditional distribution of NCEs is characterized by underdispersion, estimated $\sigma^2 < 1$, the variance is less than the mean. Accounting for the underdispersion in the conditional distribution of NCEs leads to a smaller standard error. So, PHS basic research has a t-statistic equal to 2.25 implying a p-value < 0.025. The underdispersion finding is consistent with previous research on pharmaceutical innovation. In particular, Thomas (1990) also found underdispersion in his analysis of NCEs and pharmaceutical regulation. Finally, the fully robust standard error does not impose any restriction on the conditional variance of NCEs. The fully robust t-statistic is equal to 3.56 implying a very small p-value, less than 0.0001. Consequently, regardless of which assumption on the conditional variance of NCEs one feels is most appropriate, PHS basic research is strongly statistically significant.

To be completely robust, it is necessary to account for the time dimension of the data.[2] A Lagrange Multiplier test is used to detect serial correlation in the implied disturbances. Both the magnitude and significance of the serial correlation indicator variables show that negative serial correlation is present in the model. The LM statistic for the regression is (T-4) * (uncentered R-Squared) = 35.19. Using the chi-squared distribution with four degrees of freedom, the null hypothesis of no serial correlation is rejected at a 5% level. Based on this finding, the heteroskedasticity-serial correlation (H/SC) robust standard error is calculated accounting for up to fourth order serial correlation. The adjustment for serial correlation reduces the standard error to 0.2508. As seen in column (3) of Table 4.1, the resulting t-statistic on PHS basic research is 8.95 showing a high statistical significance.

4.6 Alternative Depreciation Rates for Public Research

In general, the impact of PHS basic research on pharmaceutical innovation is robust to the assumed depreciation rate of knowledge capital. Up to this point the empirical analysis has assumed a 15% depreciation rate of PHS basic research. Although this is the depreciation rate used Hall et al. (1988), if the effect of federally funded basic research is important, we would expect a

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[2] Adjusting the standard errors for serial correlation ex post has the advantage of not imposing auxiliary assumptions on the model. Using a FGLS AR(1) or higher order model would have introduced common factor restrictions into the statistical model. See Wooldridge (1991) for further discussion.

change in the depreciation rate to only affect the magnitude of the effect and not its timing or statistical significance. The magnitude of the impact will depend on the size of the effective "knowledge stock." To evaluate the sensitivity of the timing, magnitude, and significance of the PHS basic research results to the assumed depreciation rate, the non-nested regression analysis is repeated using both a 10% and a 20% depreciation rate for the basic research stock. The results of the sensitivity analysis can be seen in Tables 4.5 and 4.6. As before, the non-nested criteria point to the seventeenth and eighteenth lags as the relevant timing of the effect. The pattern of statistical significance remains unchanged. The magnitude of the effect, however, does change slightly when alternative depreciation rates are used. Under the 10% rate, the estimated impact is greatest with a coefficient of 2.6 as opposed to a coefficient of 2.0 under a 20% depreciation rate. The pattern implies a slightly smaller impact when the effective stock of basic research "knowledge capital" decays rapidly.

4.7 The Industry Elasticity and Net Present Value of Public Research

The estimated elasticity of industry R&D can be seen in row 3 of Tables 4.1 and 4.2. Focusing on seventeenth lag of basic research in column (3), it can be seen that the magnitude of the cumulative effect of pharmaceutical R&D does not change dramatically between the two lag specifications. Under the twelve year specification, industry R&D has an elasticity estimate of 0.69 while,

Table 4.5 - 10% Depreciation -- PHS Basic Research Non-Nested Regression Results for 12 Year Industry Lag

Dependent Variable: Count of NCEs

	Equations					
Variable or Statistic	1	2	3	4	5	6
Constant	-10.9148	-13.1358	-17.9262	-19.5282	-18.4868	-13.7640
Poisson t-statistic	[-1.3734]	[-1.5715]	[-1.9499]	[-1.9024]	[-1.7048]	[-1.3166]
Sum of Industry R&D Coefficients	0.71032	0.7108	0.7657	0.9260	1.1351	1.2442
Sum of Regulatory Coefficients	-0.6928	-0.6482	-0.5360	-0.4194	-0.3520	-0.4560
PHS Basic Research Stock	**Lag 15**	**Lag 16**	**Lag 17**	**Lag 18**	**Lag 19**	**Lag 20**
Estimated Coefficient	1.5020	1.8601	2.5709	2.7159	2.4088	1.6243
Poisson t-statistic	[1.4075]	[1.6304]	[2.0443]*	[1.9495]*	[1.7136]*	[1.2814]
GLM t-statistic	[1.5447]	[1.8001]*	[2.2833]*	[2.1811]*	[1.9124]*	[1.4199]
Fully Robust t-statistic	[3.7578]**	[3.5855]**	[3.3716]**	[2.6343]**	[2.0439]*	[1.4651]
H/SC Robust t-statistic	[6.0986]**	[7.6226]**	[9.2622]**	[9.4866]**	[8.3557]**	[5.6105]**
SSR	128.9766	127.8379	123.9461	124.8713	128.3145	132.1550
R-Squared	0.7713	0.7733	0.7802	0.7785	0.7724	0.7656
Log Likelihood	90.9509	91.2732	92.0209	91.8694	91.4921	90.8349

Note: All variables are in logs.

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

Table 4.6 - 20% Depreciation -- PHS Basic Research Non-nested Regression Results for 12 Year Industry Lag

Dependent Variable: Count of NCEs

	Equations					
Variable or Statistic	1	2	3	4	5	6
Constant	-7.6651	-9.0893	-12.7848	-14.6253	-15.3277	-12.3073
Poisson t-statistic	[-1.1766]	[-1.3559]	[-1.7646]	[-1.8054]	[-1.7001]	[-1.2979]
Sum of Industry R&D Coefficients	0.6981	0.6665	0.6489	0.7526	0.9517	1.1391
Sum of Regulatory Coefficients	-0.7450	-0.7180	-0.6351	-0.5149	-0.3952	-0.4769
PHS Basic Research Stock	**Lag 15**	**Lag 16**	**Lag 17**	**Lag 18**	**Lag 19**	**Lag 20**
Estimated Coefficient	1.1014	1.3729	2.0015	2.2271	2.1799	1.5673
Poisson t-statistic	[1.2759]	[1.5052]	[1.9872]*	[1.9462]*	[1.7638]*	[1.2732]
GLM t-statistic	[1.3969]	[1.6579]*	[2.2181]*	[2.1778]*	[1.9679]*	[1.4101]
Fully Robust t-statistic	[3.5490]**	[3.5810]**	[3.7434]**	[3.1086]**	[2.2428]*	[1.3658]
H/SC Robust t-statistic	[5.2862]**	[6.7148]**	[8.6875]**	[9.6107]**	[8.4808]**	[5.5912]**
SSR	129.4562	128.5241	124.1313	124.0017	126.7039	131.1788
R-Squared	0.7704	0.7721	0.7799	0.7801	0.7753	0.7674
Log Likelihood	90.7797	91.0837	91.9019	91.8387	91.5430	90.8024

Note: All variables are in logs.

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

under the fourteen year lag, the elasticity is 0.72. These estimates are similar to the findings of Thomas (1990) whose elasticity estimate is 0.66.

The results indicate that the marginal contribution of PHS funded basic research (MP = 0.067 per $1 million) is larger than the marginal contribution of industry R&D (MP = 0.046 per $1 million) leading to approved NCEs. This makes sense given the different nature of public basic research and industry R&D. Whereas public research expands fundamental knowledge about disease processes, the bulk of industry R&D effort is devoted to animal and human testing of specific compounds for safety and efficacy. Basic research has broader applicability and may contribute to the discovery and development of many therapeutic compounds.

An alternative method for evaluating the relative merit of our national investment in basic biomedical research is to calculate the net present value (NPV) of this investment. A recent study by Grabowski and Vernon (1996) uses a sample of new chemical entities and a product life cycle model to estimate the present value of cash flows for an average NCE. Their present value stream of cash flows for an average NCE is $193.1896 million in real 1986 dollars. If we take an initial 10% increase in the stock of PHS basic research, say in 1976, then our investment in basic research will produce an average of five approved NCEs in each therapeutic class by 1993. Across all classes, this gives a total NPV of cash flows of $6761.636 million [(5 NCEs) * (7 classes) *(193.1896 cash flow per NCE)] at the time of drug introduction. To calculate the NPV, we capitalize our initial investment of $216 million at 10.5% (this is the GV (1996)

cost of capital) and subtract this from the present value of cash flows. Doing this calculation indicates that our public investment in basic research has a positive NPV of $5582.368 million in real 1986 dollars at the time of introduction.

4.8 Substitution Possibilities, Returns to Scale, and FDA Regulation

Given that the marginal productivity of public research is greater than that of private R&D, one might suggest that public funding should be substituted for private funding in order to increase the number of new therapeutic compounds available to fight disease. This suggestion is overly simplistic. A closer look at the nature of the research funded with federal monies and the research funded with private industry monies reveals that these separate funding agents are "buying" different types of research. Most obviously, public basic research does not include the uncertain and expensive animal and human testing for safety and efficacy that must be completed to obtain FDA approval. In order to investigate the potential substitutability between publicly funded basic research and private industry R&D, a substitution parameter is introduced into the model based on the CES production function described by Kmenta (1967).

In this extension of the model, industry R&D is specified as a stock variable using the methodology established by Thomas (1990). The results of this regression appear in Table 4.7. The estimated elasticity of substitution (E_s) of industry R&D for public basic research is 0.29. Since this value is near zero,

Table 4.7 - CES Production Function Estimation

Dependent Variable: Count of NCEs	
	Equation
Variable or Statistic	1
Constant	-12.5714
Poisson t-statistic	[-1.7121]
Industry R&D Stock Coefficient	0.3773
Poisson t-statistic	[0.625]
GLM t-statistic	[0.7238]
Fully Robust t-statistic	[4.2677]**
"Substitution" Term: (ln I/B)^2	-0.3996
Poisson t-statistic	[-1.0344]
GLM t-statistic	[-1.1979]
Fully Robust t-statistic	[-2.1903]*
Sum of Regulatory Coefficients	-0.4941
PHS Basic Research Stock (15% dep.)	**Lag 17**
Estimated Coefficient	2.1769
Poisson t-statistic	[2.0306]*
GLM t-statistic	[2.1852]*
Fully Robust t-statistic	[4.2099]**
SSR	157.3997
R-Squared	0.7209
Log Likelihood	85.6068
Elasticity of Substitution	0.2869
Scale Parameter	2.5542

Note: All variables are in logs.

Asymptotic t-statistics are in brackets [].

Years: 1978-1994

*Significance at the 5% level.

**Significance at the 1% level.

public basic and private industry R&D are substitutable, however, they are poor substitutes. In the CES model, the elasticity of substitution can vary between 0 and ∞. When $E_s \rightarrow 0$, the isoquants become L shaped indicating a fixed proportions Leontief technology. The result implies that pharmaceutical technology is characterized by limited substitution possibilities between private R&D and public basic research. A 1% increase in the relative price of private R&D investment, holding output constant, will only allow a 0.29% decease in the relative use of private R&D (its factor share). And, since the relationship is symmetric, a 1% increase in the relative price of public basic research, holding output constant, will only allow a 0.29% decrease in the industry's relative use of this research. This finding is consistent with the development of our national research enterprise following World War II. Our national commitment to financing an expanding institutional foundation producing basic research, largely through universities, has created a profitable and productive opportunity for the pharmaceutical industry to specialize in more applied research. One may argue that what has evolved is more or less an institutional division of labor.

Both the Cobb-Douglas and CES estimation results indicate strong increasing returns to scale in the discovery and development of approved new chemical entities. Under the twelve year industry distributed lag, the sum of the research coefficients (α, β) is 2.89, while the scale parameter in the CES regression is 2.55. Without the contribution of PHS basic research, the estimates indicate that pharmaceutical innovation is characterized by decreasing returns to scale. Most previous studies, including Henderson and Cockburn

(1996), do not find evidence of increasing returns to scale in pharmaceutical innovation in the post-1978 sample period. However, it is important to keep in mind that previous studies have not included a measure of basic biomedical research. If fact, it is the contribution of this research that leads to industry increasing returns to scale.

The cumulative effect of FDA regulatory stringency can be seen in row 4 of Tables 4.1 and 4.2. Regardless of the industry lag specified, the cumulative elasticity is -0.59. In the CES estimation, the elasticity has a value of -0.49. Although there are no other estimates of FDA regulation for the sample period used in this study, the estimate is slightly lower than the estimate reported by Grabowski el al. (1978) in their study of the regulatory impact of the Kefauver-Harris Amendments of 1962. FDA regulation appears to have a fairly strong negative impact on pharmaceutical innovation.

4.9 Conclusion

Strong evidence is found for an economically and statistically significant impact of public research on pharmaceutical innovation (hypothesis one). The elasticity of the number of new chemical entities with respect to the stock of public basic research "capital" is found to lie in the range of 2.2 to 2.5. These point estimates are large and imply increasing returns to scale in the pharmaceutical innovative process due to publicly funded basic research.

The chapter finds that public research has its most significant impact on pharmaceutical innovation seventeen years before an approved NCE. This is consistent with the idea that pharmaceutical scientists monitor public research and use public research results in drug discovery. It is the drug concept stage of the pharmaceutical innovative process in which publicly funded basic research has its impact (hypothesis two). This result is perhaps best interpreted as a seventeen year lag between the time basic research reaches a "maturity" point or "critical mass" and the approval of a new chemical entity.

Publicly funded basic research and the bulk of industry investment are very different in their objectives and results. Public basic research is typically more diverse and general while private industry R&D tends to be directed at testing specific drugs and documenting their findings. Each type of research is important in the pharmaceutical innovative process. Their distinctive contributions imply limited substitution possibilities in the production technology. The estimated elasticity of substitution (E_s) of 0.29 supports this hypothesis.

It is found that the marginal productivity of federally funded basic research is 0.07 per $1 million in each therapeutic class. A $7 million investment in public basic research produces, after a lag of seventeen years, a present discounted value of $91 million in real 1986 dollars at the time of drug introduction. Further, publicly funded basic research has a large net present value. The NPV equals $5582.368 in real 1986 dollars at the time of introduction.

The results hold up to robust statistical inference. As assumptions regarding the conditional variance of NCEs are relaxed, the estimated impact

becomes more significant. The heteroscedasticity and serial correlation robust asymptotic t-statistic is 8.96. Further, the impact is robust to alternative industry lag specifications. A twelve year innovative lag is preferred by the data. Finally, the PHS impact is robust to variation in FDA regulatory stringency. This effect was allowed to reach as far back as nine years prior to FDA approval.

CHAPTER 5

The Indirect Impact of Public Basic Research on Pharmaceutical Innovation: Investment in Response to Research Opportunities

5.1 Overview

This chapter explores the indirect impact of public basic research and FDA regulatory stringency on pharmaceutical innovation. Each of these factors indirectly impacts the number approved new chemical entities by influencing the level of industry R&D investment. Hypothesis four, developed in chapter two, postulates that public funding of basic biomedical research facilitates advances in public scientific understanding and thereby creates research opportunities for new drug discovery. As new avenues to therapeutic outcomes emerge, private industry attempts to exploit these opportunities by investing in research and development. The induced private R&D investment makes some contribution to the successful introduction of new therapeutic compounds. This is the indirect effect of public basic research on pharmaceutical innovation.

Similar to public funding of basic research, FDA regulatory stringency indirectly impacts pharmaceutical innovation by influencing the level of industry R&D investment. In this case, however, one would expect that increases in regulatory stringency reduce industry research and development investment. Empirical support for this hypothesis was provided by Wiggins (1979, 1983).

Because of the parallel approach taken here, it is expected that increases in regulatory delay lower industry R&D investment. Both analyses use the same methodology to construct the regulatory stringency proxy variable and use the same source for industry research and development data. This similarity provides an opportunity to compare results and test the robustness of Wiggins' analysis. Direct comparisons with Wiggins (1983) appears in section 5.5 of the chapter.

The central objective of this chapter is to empirically describe the timing, magnitude, and significance of the indirect impact of public research on pharmaceutical innovation. Of the previous research, no study has linked publicly funded research with pharmaceutical innovation. Ward and Dranove (1995) explore the inducement effect of NIH obligations on pharmaceutical investment but stop short of linking this with innovation. Henderson and Cockburn (1996) and Grabowski and Vernon (1981) have used "research program" and firm level data to look at the determinants of pharmaceutical R&D investment without including any measures of public research. As regards FDA regulation, Wiggins (1979) was the first to use therapeutic class distinctions to show that FDA regulatory stringency depressed pharmaceutical investment and innovation. Ward and Dranove (1995), on the other hand, use a somewhat different approach and find that "expected" approval delays increase pharmaceutical R&D investment.

This chapter advances our understanding of the determinants of pharmaceutical industry investment and the indirect contribution of public

biomedical knowledge to pharmaceutical innovation. Whereas previous analyses have treated public research investment in a broad and somewhat simplistic fashion, this analysis is based on detailed public research awards data that have been carefully classified into meaningful therapeutic categories for each year between 1955 and 1985. Additionally, the contribution of biomedical knowledge is measured as a capitalized stock. This is intended to mimic the cumulative learning process that characterizes the advancement of scientific research. Both of these aspects improve the empirical results by reducing the measurement error and matching limitations found in previous research.

The chapter finds that the elasticity of industry R&D investment with respect to the stock of publicly funded basic research lies in the range of 0.42 to 0.46. Although publicly funded research begins to stimulate industry investment as early as three years following award, the data reveal that its effect is statistically dominant in the seventh year following research award. Using the estimated marginal effect of industry R&D on approved NCEs from chapter four, a $1 million increase in the PHS research stock produces a marginal physical product of 0.01 approved NCEs in each of the seven therapeutic classes. This amounts to a total increase in pharmaceutical innovation of 0.07 additional approved NCEs (across all classes). If this increase in innovative output earns the average discounted revenue, then a discounted present value of $10.3 million in additional revenue will be produced at the time of introduction.

As regards FDA regulatory stringency, the point estimates are statistically insignificant and small in magnitude. These elasticities, one for the current year

through the fourth lag of regulatory stringency, were not found to be statistically different from zero either individually or jointly. Taken literally, this implies that a marginal increase in FDA approval delay time does not affect the level of industry R&D. Although this may be true, collinearity among the included stringency variables is one cause of the imprecise estimates. If we put any faith in the estimated coefficients, then the cumulative impact of FDA regulatory stringency has an overall elasticity value of -0.1023.

The chapter contains several other ancillary results. Perhaps the most interesting of these pertains to industry sales. With an estimated elasticity of 0.24, a 1% increase in pharmaceutical sales in 1985 would have increased industry investment by $7.1 million in that year. Using the estimated impact of industry investment on the production of NCEs found in chapter four, this increase produces 0.08 new therapeutic compounds across all classes after twelve years. Again, if these marginal NCEs each earn the average discounted revenue, then this increase in sales will bring fourth nearly $14.8 million in new revenues at the time of introduction.

It is also found that industry R&D investment increases with disease incidence and falls with disease "severity." A 1% increase in disease incidence in the forty-five to sixty-four year old age group leads to an 0.4% increase in industry investment. The estimated effect of disease "severity," which is measured as the number of hospital days, is negative and significant. Thus, longer hospital stays are associated with lower pharmaceutical investment.

The last section of the chapter presents some exploratory analysis regarding the potential simultaneity bias between publicly funded research and private industry R&D investment. As discussed in chapter three, this is the "scientific opportunity" problem. It arises when research funding agents respond to the same "scientific break-through" information when making their funding decisions and thereby induce a correlation that is not a spillover of knowledge. Using instruments for public research implied by the Ward and Dranove (1995) analysis, no evidence is found that supports an endogeneity bias due to scientific opportunity. The intended instruments, however, are poorly correlated with public funding of basic research. This makes the endogeneity test uninformative as to the presence of a scientific opportunity problem. Nevertheless, scientific opportunity is unlikely to affect lagged public funding. The analysis finds that the relevant public and private funding decisions are separated by a seven year period. In order for scientific opportunity to be causing a simultaneity bias, the relevant scientific opportunities would need to remain constant over the seven year period. This seems unlikely.

5.2 Model Specification

Based on previous research as well as interviews with industry marketing personnel, this section follows the net present value (NPV) methodology for modeling pharmaceutical R&D investment decisions. This method is consistent with the interview responses given to Wiggins (1979) and used in his analysis.

It is also the approach taken by Grabowski and Vernon (1981) in their firm level analysis of the determinants of pharmaceutical R&D investment.

The basic NPV relation is shown in equation (5.1). The calculated NPV is the difference between a project's discounted present value stream of expected revenue and its the discounted present value stream of expected costs. If the NPV is positive, then it is profitable to invest in the R&D project. If the NPV is less than or equal to zero, then it is not profitable to invest.

(5.1) NPV = PV[expected revenues] – PV[expected costs]

To make projects comparable, the discounted present value of cash flows for revenues and costs are calculated using a "discount factor" that adjusts for the time value of money and for risk. Alternatively, the internal rate of return for a proposed R&D project can be calculated. This return is the value of the discount rate that equates the present value of expected revenues and expected costs. Comparing the calculated internal rates of return to the opportunity cost of capital for any project is one way of making an R&D investment decision.[1] If the firm calculates the internal rate of return for all projects and ranks them in descending order, then they can fund projects down to the point where the return on the marginal project just equals the cost of capital. Notice that this assumes pharmaceutical firms are not liquidity constrained.

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[1] The opportunity cost of capital is the expected rate of return to investors offered by all other investments of similar risk.

It is useful to image a downward sloping "marginal return to investment" schedule plotted with the rate of return on the vertical axis and the level of investment on the horizontal axis. Given the distribution of returns, the downward slope of the curve reflects that R&D investment increases as additional R&D projects are funded. Along this curve, all variables influencing the rate of return on new chemical entities are held constant. Because the opportunity cost of capital is assumed to be exogenous, it is represented by a horizontal line emanating from the vertical axis and extending across all levels of investment. The equilibrium level of investment is determined by the intersection of the "marginal return" schedule and the "opportunity cost of capital" schedule.

The empirical analysis will be done on an industry level using the observed level of investment in each medical therapeutic class. It is postulated that public basic research, FDA regulatory stringency, and demand factors influence the rate of return and shift the marginal return schedule for each therapeutic class. Macro changes that shift the opportunity cost of capital schedule are modeled using yearly time dummy variables. Allowing each year to have its own intercept is the most general way to account for variation over time due to inflation, industry shocks and other unobserved "macro" changes. Therapeutic class dummies are included to account for the fixed differences in technological opportunity across medical classes. Depending on the distribution of research investment and scientific skill, one class may feed into drug

discovery more easily than another. The structural investment equation is as follows:

$$(5.2)\quad I_{it} = (B_{it-m})^{\beta 1}(R_{it})^{\gamma 1},\ldots,(R_{it-h})^{\gamma h}(Sales_{it})^{\theta 1}(Inc_{it})^{\theta 2}(Sev_{it})^{\theta 3}e^{(\lambda t)(\eta i)}e^{(\mu)}$$

where i represents the medical therapeutic class, t represents time. I_{it} is the level of industry research and development investment; $\beta 1$ is the long-run investment elasticity with respect to the lagged stock of PHS funded basic biomedical research, B_{it-m} ; $\gamma 1$-γh are the investment elasticities with respect to the distributed lag of regulatory stringency, R_{it} - R_{it-h} (length h = 4); $\theta 1$-$\theta 3$ are the elasticities of investment with respect to industry sales, U.S. disease incidence and severity, respectively. The λt (one for each year) are the semi-elasticities capturing changes in the opportunity cost of capital while the ηi correspond to each therapeutic class. The term, μ, is a random disturbance with mean zero and constant variance. The lag, m, characterizing the stock of PHS basic research will be determined empirically.

It is postulated that increases in the stock of public basic research knowledge, B_{it-m}, lead to increases in the level of pharmaceutical investment. In the present framework, this effect works by increasing the rate of return for all projects in a given therapeutic class. Although research opportunities may affect the rate of return through alternative mechanisms, it is likely that the effect of public research is some combination of lower costs and a higher the probability

of success. Either by lowering expected costs or increasing the expected payoff to private R&D, public research increases the rate of return. This implies $\beta 1 > 0$.

It was noted above that increases in FDA regulatory stringency are expected to lower pharmaceutical R&D investment, $\gamma_j < 0$. FDA regulation can lower the rate of return through two mechanisms. First, changes in regulatory stringency may increase the risk of FDA approval in a therapeutic class. In our framework, an increase in the risk of approval implies a lower probability of approval. With a lower probability of approval, fewer R&D projects will be profitable because the expected revenue stream will be lower. If fewer projects are pursued, then investment will be lower. The second mechanism works through the costs of approval and holds the risk of approval constant. In this case, an increase in the expected stream of costs associated with getting an FDA approved drug lowers the rate of return to all projects. Assuming the opportunity cost of capital remains constant, fewer projects will be pursued and R&D investment will be lower.

In a multi-period setting, FDA product quality regulation may either increase or decrease pharmaceutical research investment. To the extent that increases in regulatory stringency require more testing and documentation, the cost of those compounds already in the pipeline will increase, $\gamma_j > 0$. However, if firms are able to adjust their portfolios of research investment, then increased regulatory stringency would reduce the number of profitable candidate compounds. Fewer profitable compounds, in turn, lead to reduced spending as

these potential new therapies are not pursued, $\gamma_j < 0$. It is this later effect that Wiggins (1983) found to be dominant between 1971 and 1976. However, Ward and Dranove (1995) find the former effect to be dominant.

Industry sales and measures of U.S. disease incidence and severity are included in the structural equation to represent the influence of expected demand on the pharmaceutical investment decision. Increases in industry sales are expected to increase the level of pharmaceutical investment, $\theta 1 > 0$. This effect can work through two alternative channels. First, sales represent an important source of funds for financing R&D projects. To the extent that pharmaceutical firms are liquidity constrained, greater sales allow firms to fund additional projects and increase their level of R&D investment. It should be noted, however, that the rate of return framework used here assumes that firms are not liquidity constrained. The second channel works through the market information provided by drug sales. Here, the level of sales acts as an indicator of market size and the potential for future sales. To the extent that observed sales in a therapeutic class affect the forecasted revenue stream for projects in that therapeutic class, sales will influence the level of R&D investment. It is expected that greater sales signals increasing market demand. This, in turn, shifts the marginal return schedule up and stimulates investment.

This analysis includes two additional measures of expected demand, disease incidence and "severity" for the civilian non-institutionalized U.S. population. Based on the first listed diagnosis on the hospital discharge sheet, the total number of discharges are summed across disease category into

therapeutic classes by year and age group. Disease "severity," which is measured as the total number of nights in the hospital, is constructed using the same methodology. For each variable, four age groupings are used: 0-14 years, 15-44 years, 45-64 years, and 65 and older. It is expected that increases in disease incidence and severity lead to greater demand for therapeutic compounds. As demand increases, the expected revenue streams are increased and the return to all projects in that therapeutic class shift up. Holding all else constant, industry R&D investment will increase, $\theta j > 0$.

5.3 Functional Form

Previous studies of pharmaceutical investment and regulation have used either the linear model (Wiggins (1979, 1983), Grabowski and Vernon (1981), Jensen (1987), Henderson and Cockburn (1996)) or the log-log functional form (Ward and Dranove (1995)). In all cases, the authors did not claim that their choice of functional form was based on a statistical test. In this analysis, however, two alternative econometric tests were used to determine the statistically preferred functional form. The first, developed by Davidson and MacKinnon (1981) (DM), is referred to as the P_E test. The second test was developed by Wooldridge (1991) and is robust to heteroscedasticity and serial correlation.

The results of all tests indicate that the log-log specification is preferred. Two DM tests were performed. The first test takes the linear model as the null

hypothesis and involves evaluating the statistical significance of a nested indicator variable (the indicator is calculated as the difference between predicted values of the alternative models). With the linear model as the null, the indicator variable has a asymptotic t-statistic of 6.0879 (p-value < 0.0005). Thus, the null linear hypothesis is rejected in favor of the alternative log-log hypothesis. In the second DM test, the log-log model served as the null hypothesis. In this case, the indicator was statistically insignificant with a t-statistic of -1.3127. Consequently, the log-log null hypothesis is not rejected.

The limitation of the DM test is that it assumes a correctly specified conditional variance. The test proposed by Wooldridge (1991), however, is robust to conditional variance mis-specification, including both heteroscedasticity and serial correlation.[2] He proposes a Lagrange Multiplier test which produces a chi-squared statistic under the null hypothesis. Taking the log-log model as the null hypothesis, the value of the test statistic is 0071. This is less than the chi-squared critical value at a 1% significance level and one degree of freedom. Thus, the robust test fails the reject the null log-log hypothesis.

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[2] To be completely precise, the correspondence between the linear and log-linear models requires the additional assumption that E(I|X) is proportional to exp(E[log(I)|x]). This, however, is not restrictive and is usually assumed implicitly.

5.4 The Regression Results and Discussion

Table 5.1 presents the regression results for equation (5.2) using alternative lags of the PHS basic research stock. The leftmost column lists the variables and the relevant statistics while columns (1) through (9) of the table show the results for the alternative lags of public research. Notice that the heteroscedasticity (Hetero) and the heteroscedasticity/serial correlation robust (H/SC) standard errors have been calculated for the PHS basic research variable following Wooldridge (1989). The H/SC standard errors were calculated accounting for up to 1st order serial correlation. It should be noted that this is not the same as using a feasible generalized least-squares (FGLS) procedure with an AR(1) model for the errors. Unlike FGLS, the procedure used here does not impose any common factor restrictions on the model (see Wooldridge (1991) for further details).

5.41 Timing of the Relationship

In order to describe the magnitude and significance of the indirect impact of public research, the timing of its relationship with pharmaceutical investment must be considered. This is important because there is a time lag between the financial award to researchers and when this research becomes available to the broader research community. The empirical identification of the appropriate lag

Table 5.1 - Regression Results for the Indirect Effect of PHS Basic Research (15% Dep.)

Dependent Variable: Log Industry R&D Investment

	Equations								
Variable or Statistic	1	2	3	4	5	6	7	8	9
Constant	7.9002	7.7872	7.5153	7.1554	6.9067	6.5958	6.3384	6.0009	5.9795
t-statistic	[3.5169]***	[3.4723]***	[3.3673]***	[3.2448]***	[3.1587]***	[3.0572]***	[2.9620]***	[2.7766]***	[2.6996]***
PHS Basic Research Stock	**Current**	**Lag 1**	**Lag 2**	**Lag 3**	**Lag 4**	**Lag 5**	**Lag 6**	**Lag 7**	**Lag 8**
Estimated Coefficient	0.1744	0.1853	0.2317	0.2976	0.3331	0.3807	0.4204	0.4562	0.4620
OLS t-statistic	[0.9909]	[1.1623]	[1.5804]	[2.1187]**	[2.4779]**	[2.9405]***	[3.2552]***	[3.3179]***	[3.0259]***
Hetero Robust t-statistic	[0.8317]	[0.9606]	[1.2654]	[1.5988]*	[1.7368]**	[2.0545]**	[2.2926]**	[2.3590]**	[2.0060]**
H/SC Robust t-statistic	[0.7133]	[0.8457]	[1.1447]	[1.4684]	[1.6028]*	[1.8984]**	[2.1381]**	[2.2172]**	[1.8966]**
Industry Sales	0.1488	0.1630	0.1862	0.2168	0.2327	0.2442	0.2419	0.2383	0.2191
t-statistic	[1.1896]	[1.2864]	[1.4575]	[1.6982]*	[1.8385]*	[1.9700]**	[1.9941]**	[1.9767]**	[1.8116]*
Incidence (age 45-64)	0.7132	0.6746	0.6050	0.5118	0.4562	0.4093	0.3954	0.4001	0.4484
t-statistic	[3.1475]***	[2.8716]***	[2.5114]**	[2.1026]**	[1.8797]*	[1.7335]*	[1.7261]*	[1.7664]*	[1.9823]**
"Severity" (age 15-44)	-1.0936	-1.0734	-1.0487	-1.0150	-0.9797	-0.9471	-0.9248	-0.9045	-0.9154
t-statistic	[-4.6326]***	[-4.5809]***	[-4.4995]***	[-4.3920]***	[-4.2561]***	[-4.1588]***	[-4.0969]***	[-3.9968]***	[-3.9982]***
Current Regulation	-0.0248	-0.0237	-0.0232	-0.0233	-0.0236	-0.0218	-0.0219	-0.0212	-0.0228
t-statistic	[-0.8492]	[-0.8158]	[-0.8119]	[-0.8338]	[-0.8551]	[-0.8036]	[-0.8158]	[-0.7934]	[-0.8439]
Lag 1 Regulation	-0.0167	-0.0155	-0.0146	-0.0159	-0.0189	-0.0211	-0.0218	-0.0233	-0.0234
t-statistic	[-0.6351]	[-0.5915]	[-0 5639]	[-0.6262]	[-0.7558]	[-0.8571]	[-0.8952]	[-0.9604]	[-0.9533]
Lag 2 Regulation	-0.0031	-0.0021	-0.0003	0.0001	-0.0031	-0.0076	-0.0115	-0.0133	-0.0149
t-statistic	[-0.1159]	[-0.0772]	[-0.0113]	[0.0055]	[-0.1201]	[-0.2975]	[-0.4561]	[-0.5295]	[-0.5867]
Lag 3 Regulation	-0.0223	-0.0211	-0.0189	-0.0162	-0.0166	-0.0199	-0.0248	-0.0286	-0.0299
t-statistic	[-0.8155]	[-0.7695]	[-0.6916]	[-0.6004]	[-0.6258]	[-0.7677]	[-0.9726]	[-1.1238]	[-1.1658]
Lag 4 Regulation	-0.0158	-0.0143	-0.0127	-0.0106	-0.0093	-0.0090	-0.0120	-0.0159	-0.0185
t-statistic	[-0.5483]	[-0.4968]	[-0.4431]	[-0.3747]	[-0.3325]	[-0.3294]	[-0.4460]	[-0.5919]	[-0.6846]
Class Dummies	Most Sig.	Most Sig.	Most Sig.	Some Sig.	Some Sig.	Some Sig.	Some Sig.	Some Sig.	Some Sig.
Time Dummies	Some Sig.	Some Sig.	Some Sig.	Some Sig.	Not Sig.	Not Sig.	Not Sig.	Not Sig.	Not Sig.
Endogeneity Chi-Squared Statistic (1 DF)									
PHS Basic Research	2.3510								
P-value (one-sided)	p-value<0.10								
SSR	1.3240	1.3170	1.2990	1.2650	1.2400	1.2020	1.1750	1.1690	1.1950
R-Squared	0.9790	0.9790	0.9790	0.9800	0.9800	0.9810	0.9810	0.9810	0.9810
Rbar-Squared	0.9700	0.9710	0.9710	0.9720	0.9720	0.9730	0.9740	0.9740	0.9730
Number of Observations	105	105	105	105	105	105	105	105	105

Note: All variables are in logs.
Asymptotic t-statistics are in brackets [].
Years: 1971-1985
*Significance at the 10% level.
**Significance at the 5% level.
***Significance at the 1% level.

is determined by comparing the sum of squared residuals and adjusted coefficient of determination across alternative specifications.

Looking at the non-nested regression criteria, the seventh lag of the stock of PHS funded basic research has the smallest sum of squared residuals and the largest adjusted r-squared. While this is the preferred timing and will be used in all subsequent discussion, it should be noted that the values of the non-nested regression criteria are not much different for the sixth and eighth lags of PHS basic research.

5.42 The Magnitude and Significance of PHS Basic Research

Table 5.1 reveals that the stock of basic research begins to influence pharmaceutical investment as early as three years following research award. The constant elasticity estimate is smallest and insignificant in the concurrent year while, with each passing year, the magnitude and significance of the effect increases until the seventh lag. Given that research awards are used to measure the PHS public knowledge stock, it is sensible that its immediate impact would be small relative to longer lags. Longer lags allow for the process of doing scientific research and the process of communicating results.

Referring to column (8) of Table 5.1, it is clear that the coefficient on the PHS funded stock of basic research is statistically significant. Without correcting for heteroscedasticity or serial correlation in the model, publicly funded research has a t-statistic of 3.32 (p-value < 0.001). Accounting for

heteroscedasticity reduces the t-statistic to 2.29 (p-value < 0.05) while the H/SC robust t-statistic drops further to 2.14 (p-value < 0.05).

The magnitude of the impact indicates that industry R&D investment responds strongly to the stock of PHS basic research. A 1% increase in this stock will result in a 0.46% increase in industry R&D after seven years. At the sample mean, the marginal effect on pharmaceutical investment is about $166 thousand per million of public basic research. Alternatively, a 1% increase in the stock of basic research in 1978 ($70.6 million) would have induced $13.7 million in pharmaceutical investment by 1985.

Using this estimate with the marginal impact of industry R&D on approved NCEs calculated in chapter four, a $1 million increase in the PHS research stock produces a marginal physical product of 0.01 approved NCEs in each of the seven therapeutic classes. This amounts to a total increase in pharmaceutical innovation of 0.07 additional approved NCEs. Using the present discounted stream of revenue earned by the average NCE (estimated by Grabowski and Vernon (1996)), the additional 0.07 approved NCEs will produce a discounted present value of $10.3 million in additional revenue at the time of introduciton.

The results suggest that industry firms are investing in response to research opportunities created through federal extramural funding of research. The emergence of our national research enterprise following World War II has created productive and profitable research opportunities for industry. Public basic research, which is conducted largely in academic institutions, creates a foundation of public knowledge that contributes to industry efforts to conceive

new therapeutic outcomes. This is not to say that the interaction between publicly funded research and industry research is unidirectional. Case study evidence has been used to shed light on the complexity of the relationship (Henderson and Cockburn (1997)); however, the purpose here is to generalize beyond a handful of specific case analyses and test whether there exists a broader relationship. Moreover, until now, we have not had any broader evidence on the timing, magnitude and significance of this relationship.

5.43 Public Regulation and Industry Demand

Table 5.1 shows that the estimates of the impact of FDA review time are not statistically significance either individually of jointly. This finding differs from the findings of Wiggins as well as with some of the findings of Ward and Dranove. In his linear model, Wiggins found that each of the second through the fifth lags had a significantly negative impact on industry R&D (a comparison with Wiggins' results appear in section 5.5). His interpretation describes regulation as reducing the number of new compounds entering the industry's innovative process. Ward and Dranove (1995), using the log of expected approval times calculated from a first stage regression, find that review times are either insignificant or have a positive and significant effect on industry R&D investment. Their preferred interpretation characterizes their estimate as a measure of the cost of FDA compliance plus the increase in rents associated with intellectual property protection. The interesting contrast between the

findings here and those of Ward and Dranove is that their regulatory measure became positive and significant in their regression that included the distributed lag of NIH obligations. In Table 5.1, the signs of all regulatory variables are negative. Although no statistical significance is found, this may suggest that Wiggins' interpretation is most relevant here. It is also the case, however, that excessive noise and collinearity in the average review time measures are leading to imprecise estimates.

These results provide an interesting contrast to Wiggins (1983) results obtained using the period of 1971-1976. In his regressions the second through the fifth lags of regulatory stringency were significant. This implies that there has been some type of change in the behavior of pharmaceutical firms toward FDA regulation. It may be that interacting with the FDA early in the discovery stage and investing in "governmental affairs" departments have transformed FDA regulation into a fixed cost rather than a variable cost of innovation. Further investigation into the impact of FDA regulation seems warranted.

Column (8) of Table 5.1 shows the elasticity of industry investment with respect to industry sales. With a point estimate of 0.24, a 1% increase in sales leads to a 0.24% increase in industry R&D investment. In 1985, for example, a 1% increase in sales implies a $7.1 million increase in industry R&D investment in that same year. Moreover, the sales variable is statistically significant with a t-statistic of 1.98 (p-value < 0.05).

The regression results in Table 5.1 include U.S. disease incidence for the 45-64 age group and U.S. disease severity for the 15-44 age group. The other

age groupings were insignificant and were dropped from the equation. The elasticity estimates indicate that a 1% increase in disease incidence results in a 0.40% increase in pharmaceutical investment. For disease severity, on the other hand, a 1% increase in the number of hospital days results in a 0.90% decrease in pharmaceutical investment. The impact of disease incidence on investment is in the expected direction. The impact of severity, however, was not expected to lower pharmaceutical investment. It is unclear why longer hospital stays would lower investment in drug research. Yet, the effect is strongly significant was a t-statistic of –3.99 (p-value < 0.0001).

5.5 Wiggins (1983) Revisited

Because of the similarity between this analysis and Wiggins (1983), it is interesting to re-examine the original Wiggins (1983) results it light of the new data available. In Table 5.2 his original model is estimated using the current data. For these regressions, the model is linear in the levels, all variables are in nominal dollars and the sample period is 1971-1976. Wiggins (1983) results appear in the right most column while the regressions with the current data are in columns (2) through (7). Although there may be slight differences in the measurement of PhRMA sales and R&D, the primary difference here is the introduction of a public basic research measure that was unavailable to Wiggins. Also, these regressions include an additional therapeutic class in the cross-sectional dimension, namely the gastrointestinal/genito-urinary class.

Table 5.2 - Re-Examination of the Wiggins Model

Dependent Variable = Level of Industry R&D Investment

	Equations						
	Wiggins	2	3	4	5	6	7
Intercept	n/a	84.417 [5.757]**	81.948 [5.563]**	83.712 [5.714]**	22.764 [0.931]	25.853 [0.993]	26.69 [1.200]
PHS Basic Research					0.234 [2.867]**	0.217 [2.572]**	0.216 [3.170]**
Sales	0.047 [2.47]	0.080** [4.861]**	0.0645 [3.019]**	0.0727 [3.219]**	0.046 [2.314]*	0.052 [2.409]*	0.043 [2.347]*
Regulation (current)		-0.067 [-1.041]	-0.049 [-0.744]	-0.056 [-0.840]	-0.064 [-1.084]	-0.068 [-1.148]	-0.058 [-1.028]
Regulation (lag 1)		-0.070 [-1.310]	-0.048 [-0.837]	-0.052 [-0.914]	-0.057 [-1.122]	-0.058 [-1.142]	-0.05 [-1.059]
Regulation (lag 2)	-0.486 [-2.38]	-0.131 [-2.589]**	-0.102 [-1.817]*	-0.103 [-1.807]*	-0.114 [-2.269]*	-0.111 [-2.170]*	-0.105 [-2.341]*
Regulation (lag 3)	-0.773 [-3.65]	-0.131 [-2.422]**	-0.109 [-1.924]*	-0.141 [-2.161]*	-0.129 [-2.529]**	-0.146 [-2.498]**	-0.121 [-2.580]**
Regulation (lag 4)	-0.885 [-3.44]	-0.056 [-0.938]	-0.05 [-0.825]	-0.066 [-0.927]	-0.076 [-1.395]	-0.075 [-1.170]	-0.072 [-1.364]
Regulation (lag 5)	-0.481 [-1.80]	0.008 [0.111]	0.007 [0.101]	-0.52 [-0.585]	-0.005 [-0..79]	-0.038 [-0.474]	-0.004 [-0.068]
CNS dummy	n/a	-29.179 [-1.650]	-20.333 [-1.062]	-23.341 [-1.211]	32.798 [1.303]	26.95 [1.033]	31.071 [1.271]
Cardio dummy	n/a	15.769 [1.531]	10.022 [0.881]	16.428 [1.229]	48.484 [2.886]**	48.802 [2.808]**	43.93 [3.482]**
Anti-inf dummy	n/a	15.934 [1.905]*	17.853 [2.106]*	18.052 [2.125]*	61.6111 [3.620]**	58.266 [3.351]**	58.733 [3.830]**
GI/GU dummy		-54.094 [-6.325]**	-57.85 [-6.358]**	-56.112 [-5.960]**	-8.841 [-0.467]	-11.74 [-0.611]	-13.672 [-0.926]
Derm dummy	n/a	-53.172 [-5.975]**	-61.01 [-5.477]**	-56.14 [-4.645]**	15.251 [0.537]	12.246 [0.427]	7.191 [0.350]
Resp dummy	n/a	-26.431 [-1.708]*	-37.951 [-2.071]*	-26.077 [-1.166]	44.383 [1.344]	44.237 [1.305]	34.849 [1.479]
Time			2.426 [1.158]		-0.921 [-0.419]		
YR 1972				5.946 [0.892]		2.163 [0.351]	
YR 1973				3.485 [0.462]		-4.182 [-0.566]	
YR 1974				12.457 [1.518]		0.92 [0.107]	
YR 1975				14.891 [1.596]		1.932 [0.198]	
YR 1976				5.423 [0.482]		-8.077 [-0.710]	
R-Squared	0.69	0.964	0.965	0.971	0.974	0.977	0.973
Rbar-Squared	n/a	0.96	0.947	0.948	0.958	0.958	0.96
Num Obs	42	42	42	42	42	42	42

Note: All variables are in logs.
Asymptotic t-statistics are in brackets [].
Years: 1971-1976
**Significance at the 5% level.
***Significance at the 1% level.

Columns (2) to (4) explore the relationship without incorporating research opportunities from publicly funded basic research. The estimates in column (2) show that concurrent sales and FDA regulation are significant and have the signs found by Wiggins. The impact of sales is twice that found by Wiggins and more statistically significant. Also, only the second and third lags of regulation are significant whereas the second through the fifth lags were significant in Wiggins' regression. When a linear time trend and year dummies are introduced, Columns (3) and (4), the coefficients generally show lower significance and are slightly smaller. Although these differences are probably due to differences in the data sets, it is broadly confirmed that average review times did lower industry R&D expenditure in this period.

Columns (5) through (7) introduce publicly supplied research opportunities into the relationship using the seventh lag of PHS funded research. The change in the estimates is quite interesting. First, the intercept and the therapeutic class dummies change dramatically. This is to be expected since these variables were postulated to capture the effects of research opportunities by Wiggins. Second, the estimate of industry sales falls and is now in line with the his original estimate. Third, the second and third lags of regulation are now more significant than previously although they are quite a bit smaller in magnitude than Wiggins' original estimates.

The most preferred specification appears in column (7). Here, the insignificant time variables are excluded. Public basic research has a strong

and large impact on the level of industry R&D investment. With an estimate of 0.22, each additional dollar of public basic research leads to a 22 cent increase in industry R&D investment seven years hence. This contrasts with the 4 cent increase resulting from an addition dollar of concurrent sales. Average review times have a significant impact in this sub-period although the fourth and fifth lags do not show any significance using the current data.

Overall, Wiggins' results are broadly confirmed. His exclusion of public research does not appear to have biased his sales and regulatory estimates. Revisiting his model has highlighted the importance of incorporating a measure of public research as well as shown that the effects of FDA review times on industry expenditure have changed over time.

5.6 Endogeneity Test for Scientific Opportunity

It has been suggested that estimates of the relationship between public and private funding of research are biased by the endogenous response of funding agents to the same set of scientific opportunities. To explore this issue, a reduced form equation for the stock of PHS funded basic research is specified using disease incidence and severity instruments for public research. The reduced form equation is:

(5.3) $B_{it} = h(Inc_{it}, Sev_{it})$

where i represents the medical therapeutic class, t represents time. B_{it} is the stock of PHS funded basic research; Inc_{it} and Sev_{it} are the measures of disease incidence and severity not already included in the estimation of equation (5.2).

Ward and Dranove (1995) maintain that government funding is a function of disease prevalence and severity.[3] While this is the basis for choosing the instruments for equation (5.3), there are two complications with Ward and Dranove's view. The first involves their measures of publicly funded research while the second involves causation. Apart from timing issues related to their use of financial obligations versus awards, Ward and Dranove use a very broad measure of public health research that includes many special and large programs designed to address immediate health problems. One would reasonably expect that the funding of these programs has been driven more by measured prevalence and severity, however, one would also expect that these programs have been somewhat successful in lowering targeted disease prevalence and severity. Clearly, the causation problem comes from categorizing prevalence and severity as determining funding while they are also an outcome of this funding.

Public research measured in this analysis is quite different from Ward and Dranove's measure. Here, publicly funded basic research is analyzed. While it

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[3] Ward and Dranove (1995) measure disease incidence by the number of physicians in a particular specialty. While this measure is problematic for the obvious reason that physician specialties have only an indirect correspondence to disease prevalence. Here, disease incidence is used because systematic prevalence measures are not available.

is still conceivable that basic research funding responds to perceived incidence and severity, it is difficult to know exactly how scientific review groups choose projects to fund. Presumably, these decisions are based on some notion of scientific merit and not on short-term goals to lowering disease incidence and severity. In the long-run, funded basic research may well lead to lower incidence and severity indirectly through therapeutic compounds or other embodiments of this knowledge. Thus, the issues of how public projects are picked for funding and the direction of causation cloud the relations specified in equation (5.3). The most simplistic a priori expectations imply that funding of basic research responds positively to increases in incidence and severity, $h_1 > 0$ and $h_2 > 0$.

Using the heteroscedasticity robust version of the Hausman specification test, column (1) of Table 5.1 shows the calculated test statistic has a value of 2.351. Comparing this with the chi-squared (one degree of freedom) critical value reveals that the null hypothesis of exogeneity cannot be rejected at a 10% level or higher. Consequently, no evidence is found for endogeneity of publicly funded research and industry research.

Table 5.3 shows the regression results of equation (5.3). As with industry sales, the regression includes the omitted measures of disease incidence and severity along with the other variables from equation (5.2). It is clear from this table that all the incidence and severity variables are insignificant. This contrasts with the maintained view of Ward and Dranove (1995). Their position holds that NIH funding of research responds positively to these variables in a

Table 5.3 - PHS Basic Research

Dependent Variable: PHS Basic Research (15% Dep.)	
	Equation
Variable or Statistic	1
Constant	1.8992
t-statistic	[0.8674]
Industry Sales	-0.0670
t-statistic	[-0.7004]
Incidence (age 0-14yrs)	0.5866
t-statistic	[0.3221]
Incidence (age 15-44yrs)	0.1280
t-statistic	[0.56447]
Incidence (age 45-64yrs)	0.3543
t-statistic	[1.0703]
Incidence (age 65+ yrs)	0.1202
t-statistic	[0.3876]
Severity (age 0-14yrs)	0.0047
t-statistic	[0.0340]
Severity (age 15-44yrs)	0.1081
t-statistic	[0.5421]
Severity (age 45-64yrs)	-0.0124
t-statistic	[-0.0425]
Severity (age 65+ yrs)	0.1450
t-statistic	[0.5025]
Current Regulation	-0.0413
t-statistic	[-2.1778]**
Lag 1 Regulation	-0.0288
t-statistic	[-1.6333]*
Lag 2 Regulation	-0.0255
t-statistic	[-1.3660]
Lag 3 Regulation	-0.0221
t-statistic	[-1.1935]
Lag 4 Regulation	-0.0223
t-statistic	[-1.1628]
Lag 5 Regulation	-0.0118
t-statistic	[-0.6127]
Class Dummies	Sig.
Time Dummies	Sig.
SSR	0.5370
R-Squared	0.9970
Number of Observations	105

Note: All variables are in logs.
Asymptotic t-statistics are in brackets [].
Years: 1971-1985
*Significance at the 10% level.
**Significance at the 5% level.

given year. The notion that funding responds to incidence and severity makes sense if one can properly account for the problems of timing and causation, which have not been adequately addressed in this specification. The timing problem comes from relating incidence and severity in a given year to funding in a given year. In our context that implies researchers are receiving awards for grant proposals prepared at roughly the same time as incidence and severity are being observed. Clearly, researchers must prepare proposals in advance and this relationship should not be expected to hold. The problem of causation was mentioned earlier. Consequently, the simple a priori expectations that $h_1>0$ and $h_2>0$ are not realized.

Since the chosen instruments for public basic research are weak, this violates one of the properties that instruments must have in order to test for endogeneity. Consequently, the econometric test is uninformative. Nevertheless, scientific opportunity is unlikely to affect lagged public funding. The analysis finds that the relevant public and private funding decisions are separated by a seven year period. In order for scientific opportunity to be causing a simultaneity bias, the relevant scientific opportunities would need to remain constant over the seven year period. This seems unlikely.

5.7 Conclusion

This chapter has explored the indirect impact of publicly funded research on pharmaceutical productivity. This effect works through industry R&D

investment to stimulate new product innovation. The analysis finds statistical support for an inducement effect of public basic research on industry R&D investment. Federally funded research begins to impact pharmaceutical investment as early as three years following financial award with its statistically strongest impact coming seven years after financial award. The effect is statistically significant with a heteroscedasticity/serial correlation robust t-statistic of 2.23 (p-value < 0.05). The magnitude of the impact is in the range of 0.42 to 0.46.

The results imply a 10% increase in the stock of public basic research leads to a 4.2% to 4.6 % increase in industry R&D investment after seven years. When combined the marginal impact of pharmaceutical investment on approved NCEs, a marginal ($1 million) increase in the PHS research stock produces a marginal physical product of 0.01 approved NCEs in each of the seven therapeutic classes. This amounts to a total increase in pharmaceutical productivity of 0.07 additional approved NCEs. If this increase in innovative output earns the average discounted revenue, then a discounted present value of $10.3 million in additional revenue will be produced.

The empirical results indicate that FDA review delays no longer affect industry R&D investment. This is not to say that FDA regulation imposes no costs on the industry. Review delays still have a direct impact on innovation (see chapter four) but do not seem to be increasing R&D expenditure for those compounds in the pipeline. The bulk of compliance costs appear to be borne early in the innovative process and are probably best measured using

proprietary data. Overall, Wiggins' idea that FDA regulation keeps potential compounds from ever entering the innovative pipeline seems most accurate

The elasticity of pharmaceutical R&D investment with respect to industry sales is 0.24. A increase of 1% in sales leads to a 0.24% increase in R&D expenditure. This would have increased industry investment by $7.1 million in 1985 and produced nearly $14.8 million in new revenues.

It is also found that industry sales increase with disease incidence and fall with disease "severity." A 1% increased incidence in the forty-five to sixty-four year old age group leads to an 0.40% increase in investment. The finding that disease "severity" in the fifteen to forty-four year old age group lowers industry investment is in the opposite direction of the expected effect.

Finally, there was no evidence found that supports an endogeneity bias due to scientific opportunity between public basic research and private industry R&D investment. Although the econometric test is not informative, the fact that public research is lagged seven years makes a simultaneity bias due to scientific opportunity unlikely in our context.

Chapter 6

The Total Impact of Public Basic Research on Pharmaceutical Innovation

6.1 Overview

This chapter calculates the total impact of publicly funded basic research and FDA regulatory stringency on pharmaceutical innovation. Recall that the production framework identifies two related channels through which federally funded basic research can influence industry output. First, basic research can contribute directly to private industry's product innovation. In this case, basic knowledge is used as a direct input to create the new product introduced by private industry. Second, this research can contribute indirectly to private industry's product innovation. This indirect contribution recognizes the role that basic knowledge plays in stimulating additional private R&D investment. The channels of influence for FDA regulatory stringency are analogous to those of public research, however, having a negative impact instead of a positive impact. The total impacts are the sum of the direct effects (chapter four) and the indirect effects (chapter five).

6.2 The Total Impacts

Recall from chapter three that the total impact is calculated as the sum of the direct and indirect marginal impacts. This relationship for PHS basic research is given by the following relation:

(6.1) $(dY_{it} / dB_{it}) = (dY_{it} / dB_{it}) + (dY_{it} / dI_{it}) * (dI_{it} / dB_{it})$

where i is medical therapeutic class and t represents time; Y_{it} is a count of approved new chemical entities; B_{it} is the stock of PHS funded basic research; I_{it} is the annual flow of industry R&D investment. The symbol, d, stands for the mathematical derivative.

Estimates of the marginal impacts are obtained from the elasticity estimates. For example, the direct marginal impact of public research is calculated as follows:

(6.2) $(MP)_B = (\text{Elasticity})_{YB} * [(\text{Sample Average})_Y / (\text{Sample Average})_B]$

$(MP)_B = (2.2) * [(19) / (633.9879)]$

$(MP)_B = 0.0659$

Using the other estimated elasticities and sample period averages, the total impact of public basic research is:

(6.3) $(\text{Total MP})_B = (0.0659) + (0.0458) * (0.1659)$

$(\text{Total MP})_B = 0.0735$

Further, using Grabowski and Vernon (1996), if the total marginal impact earns an average return, then the value of the total marginal product in each therapeutic class is:

(6.4) $(\text{Value Total MP})_B = (\text{Total MP})_B * (\text{Avg. Discounted Value (1986\$)})$

$(\text{Value Total MP})_B = (0.0735) * (\$193.1896)$

$(\text{Value Total MP})_B = \$14.20 \text{ Million}$

So, across all seven therapeutic classes:

(6.5) $(\text{Value Total MP})_{\text{all classes}} = (7) * (\$14.20) = \$99.4 \text{ million}$

It is evident that the total marginal impact of PHS basic research is determined mainly by the direct effect. The direct marginal impact (roughly 0.07) is seven times greater than the indirect marginal impact (roughly 0.01) on the number of approved NCEs. The indirect impact of PHS basic research must work through the marginal effect of private R&D before having an effect on the

number of approved new chemical entities. An increase in the marginal impact of private R&D will also increase the indirect effect of PHS basic research.

Analogous to publicly funded basic research, the total marginal impact of FDA regulatory stringency is given by:

$$(6.6) \quad (dY_{it} / dR_{it}) = (dY_{it} / dR_{it}) + (dY_{it} / dI_{it}) * (dI_{it} / dR_{it})$$

where all terms are defined as before and R_{it} represents the annual regulatory delay (measured in months).

Because none of the indirect elasticities were found to be statistically significant, the second term on the right-hand side of equation (6.6) is zero. This implies that the total marginal impact of FDA regulatory stringency is equal to the direct marginal impact. Because FDA regulatory stringency enters the empirical specification in chapter four as a nine period distributed lag, the total marginal impact of FDA regulatory stringency is calculated as the sum of the marginal impact of each lag. Using estimated and sample values, this total marginal impact is:

$$(6.6) \quad (\text{Total MP})_R = \Sigma\, (\text{Elasticity})_{YR} * [\, (\text{Sample Avg.})_Y / (\text{Sample Avg.})_R \,]$$

$$(\text{Total MP})_R = -0.284$$

Wiggins (1983) found the total impact of regulation came primarily from its direct effect. His estimate of the total effect is -0.156, which is quite a bit smaller than the direct effect found here. There are two reasons for the different findings. First, whereas Wiggins eliminated insignificant lags of stringency in his formulation, all lags were included in this analysis regardless of their statistical significance. There are no good a priori reasons to claim only certain lags matter. For instance, how sensible is it to say that lags two and five matter but that lags three and four are irrelevant? Second, a longer distributed lag was included in this analysis based on the interviews with industry regulatory personnel. Overall, the estimate of regulatory stringency is probably too large.

6.4 Recap of Dissertation Findings

This dissertation has described the role of publicly funded basic research in the discovery and development of new therapeutic compounds. It is found that public basic research is a very important factor in pharmaceutical innovation and that knowledge externalities from this research lead to industry-wide increasing returns to scale. It was noted in the introduction that federal funding of basic scientific research is one of the traditional priorities of our national research policy. The objective has been to build a productive foundation of knowledge that will stimulate national and industry innovation and growth. This dissertation has provided some evidence that, at least in part, this objective has been achieved.

Overall, this analysis has found evidence that the basic research component of our national research policy has been successful in stimulating industrial innovation. The analysis suggests that the decline in the growth rate of federal basic research spending will have a negative impact on pharmaceutical innovation. Although this result is found within the context of biomedical research and the pharmaceutical industry, it could be that federal R&D is quite important to industrial innovation and economic growth.

The main results from the estimation of the direct impact of PHS basic research and FDA regulatory stringency on the production of new chemical entities in the pharmaceutical industry are:

1. Publicly funded basic research has an economically and statistically significant direct effect on pharmaceutical innovation. The elasticity of the number of new chemical entities with respect to the stock of public basic research is found to lie in the range of 2.2 to 2.5.

2. Public basic research has a distinct role in the pharmaceutical innovative process. PHS basic research contributes to the creative conception of new avenues to therapeutic outcomes and helps guide the parameters used in chemical screening. Because public basic research affects the drug concept period of pharmaceutical innovation, its impact comes early in the pharmaceutical innovative process. The data indicate that an average of

seventeen years elapse between the stock of federal awards and the introduction of new therapeutic compounds.

3. While still substitutes, public basic research and private industry R&D have limited substitution possibilities in the pharmaceutical innovative process. The estimated elasticity of substitution of 0.29 indicates that the pharmaceutical innovative process is closer to a fixed proportions technology rather than a more flexible substitution technology like the Cobb-Douglas. This reflects the different nature of the public basic research and private R&D and lends support to the hypothesis that a division of labor has emerged in the biomedical research sector.

4. Using the Grabowski and Vernon (1996) estimate of the average return to an approved NCE, the public basic research has a net present value of $5582 in real 1986 dollars at the time of introduction.

5. Pharmaceutical innovation is characterized by increasing returns to scale at the industry level. This result is a direct consequence of the availability of publicly funded basic biomedical research.

6. Product quality regulation by the Food and Drug Administration continues to have a negative direct effect on new chemical entity innovation. This is a pure

production effect, however, and does not include any of the possible benefits stemming from increased safety and efficacy.

The main results from the estimation of the indirect impact of public basic research and FDA regulatory stringency are:

1. Public basic research has an economically and statistically signification indirect effect on pharmaceutical innovation by acting to induce private industry R&D investment. The magnitude of this impact is in the range of 0.42 to 0.46. This implies a 1% increase in the stock of public basic research leads to a .43% to .46% increase in industry R&D investment after seven years.

2. The empirical results find no significant impact of regulatory delay times (in months) on pharmaceutical investment. This result contrasts with the findings of Wiggins (1983). It may be that, in the sample period, compliance costs are more accurately thought of as fixed costs rather than variable costs of innovation.

3. The elasticity of pharmaceutical R&D with respect to industry sales is estimated to be 0.24. A 1% increase in industry sales in 1985 ($202 million) would have increased industry investment by $7.1 million in that year. Using the estimated impact of industry R&D on the number of approved NCEs, this increase produces 0.01 additional therapeutic compounds in each therapeutic class after twelve years.

4. It is also found that industry investment increases with disease incidence and fall with disease "severity." A 1% increased incidence in the forty-five to sixty-four year old age group leads to an 0.40% increase in investment. With regard to disease "severity," the analysis indicates that pharmaceutical investment falls as the number of inpatient days increase. This underlying reason for this is unclear.

5. There was no evidence found that supports an endogeneity bias due to scientific opportunity between public basic research and private industry R&D. Unfortunately, because of the weakness of the instruments, the econometric test is uninformative. Nevertheless, any bias due to scientific opportunity is unlikely since the funding decisions are separated by a seven year period.

6.5 Future Research

As one might image, there are numerous unanswered questions that deserve research. Here are a few that come to mind:

1. What characteristics help or hinder a firm's ability to exploit the pool of public research?
2. How do these factors affect their competitive position in the industry and their productivity?

3.. How do NCEs affect health output measures and, in turn, affect GDP and national economic growth? Further, how can these insights improve our estimate of the social return to public basic research?

4. How does federally funded basic research, or any other type of federal sponsorship, affect other industries in our economy?

APPENDICES

APPENDIX A

APPENDIX A

Keywords Used to Construct PHS Basic Research Variables

This appendix lists the keywords and character stings used in the data filters. Copies of worksheets were not able to be formatted for this appendix.

Table A.1 - Listing of Class Filter Keywords or Character Strings

Note: After running each of these filters, the results must be inspected. Character strings typically capture more than is desired.

Anti-Infective Class:

/AMEBICIDE/, /TRICHOMONICIDE/, /ANTHELMINTIC/, /ANTIBIOTIC/, /CYCLINES/, /CEPHAL/, /CILLIN/, /THROMYCIN/, /STREPTO/, /ISONIAZID/, /MALARIA/, /VIRAL/, /VIRUS/, /FUNG/, /BACTERIA/, /PARASIT/

Endocrine/Neoplasm Class:

/HORMONE/, /CORTIC/, /ANDRO/, /ESTRO/, /PROGESTO/, /DIABET/, /THYROID/, /INSULIN/, /ANABOLIC/, /ENDOCRIN/, /NEOPLASM/, /CANCER/, /TUMOR/, /CARCIN/, /CHEMO/

Cardiovascular Class:

/HEART/, /CARDIO/, /COAGU/, DIGITALIS/, /HEMOSTAT/, /HYPOTENSIVE/, /VASO/, /HEPARIN/, /ARRYTHMIC/, /CALCIUM/

Central Nervous System Class:

/PARASYMPATH/, /MUSCLE/, /NARCOTIC/, /OPI/, /SALICY/, /ASPIRIN/, /ACETAMIN/, /CONVUL/, /DEPRESS/, /BRAIN/, /NERV/, /TRANQUIL/, /AMPHETA/, /ANOREX/, /SEDAT/, /ANESTHE/, /ARTHRI/, /HYPNO/, / EYE /, /OPHTHA/, /MYDRIA/, /MIOTIC/, / EAR /, /AURI/, /RHEUMA/, /NEURO/

Gastro-intestinal/Genito-Urinary Class:

/ RENAL/, /URINE/, /KIDNEY/, /NEPH/, /UREM/, /BILE/, /GASTR/, /INTESTINE/, /COLIN/, /CHOLERETIC/, /CHOLESTEROL/, /EMETIC/, /HISTAMINE/, /CHOLINERGIC/, /LIPID/, /GENITO/, /CHOLAGOGUE/, /THIAZIDE/, /DIURETIC/

Dermatologic Class:

/SKIN/, /DERM/, /QUTAN/, /SEBACE/, /DANDRUFF/, /SEBOR/

Respiratory Class:

/LUNG/, /PULMONARY/, /BRONCH/, /RESPIR/

Table A.2 - Listing of Exclusion Filter Keywords or Character Strings

Note: After running each of this filter, the results must be inspected. Character strings typically capture more than is desired.

/OGRAPH/, /OGRAM/, /SURGICAL/, /DETECTION/, /INTOXICATION/, / BCG/, /POPULATION/, /EXERCISE/, /TOXICOLOGY/, /PATIENT/, /RHEUMATIC/, /CONTRAST/, /CLINICAL/, /DIAGNOS/, /HUMAN/, /INVESTIGAT/, / DRUG/, /RADI/, / MAN /, /INDICATOR/, / AGE /, /DEATH/, /TEACH/, /AGEING/, /FITNESS/, /THERAPY/, /PEOPLE/, /PERFORMANCE/, /ADOLESCENT/, /NATIONAL/, /SUPPORT/, /REHAB/, /ENVIRON/, /DENTAL/, /EMOTION/, /CENTER/, /LITERATURE/, /MORTALITY/, /CONSUM/, /FOLLOW-UP/, /PREGNAN/, /INFORMATION/, /PROCEDURE/, /COMMUNITY/, / AGENT/, /TECHNIQUE/, / DIET/, /SCREEN/, /X-RAY/, /COOPERAT/, /PREVAL/, /LEARN/, /URBAN/, /AREA/, /NURS/, /LIFE/, /CHILD/, / EEG /, / EKG /, / VCG /, /FETAL/, /INFANT/, /DATA/, /OMETER/, /PANEL/, /VACCINE/, /NEONATAL/, /RESEARCH/, /INSTRUMENT/, /EQUIPMENT/, /ULTRASOUND/, /PUBLIC/, /FELLOWSHIP/, /PROGRAM/, /DIRECTORY/, /TREATMENT/, /NUTRITION/, /THERAPEUTIC/, /EVALUATION/, /MEASUREMENT/, / YEAR /, /COLLABORAT/, / TRAIN/, /PREVENT/, /INDUSTR/, /COMMITTEE/, /INSTITUTE/, /CONGRESS/

Table A.3 - Activity Code Breakdown

1ST Round Elimination: Activity Code Breakdown
Year:_____

Activity Code	Number of Grants	Total Value of Grants
Total Value - All Grants		
A?? - Applied Training		
C?? - Construction Grants		
D?? - Environmental Demo		
E?? - Gen Support Education		
F04 - Nursing Fellowship F09 - Scientific Evaluation F10 - Fellowship Traineeship F11 - Direct Traineeship F13 - Hlth Science Scholars F15- Fogarty Scholarships F17 - Clinical Fellowship F35 - Visiting Scientist Fello		
G?? - National Lib of Med		
H?? - Staffing Grants		
J?? - Joint Facilities Grants		
K08 - Clinical Investigator K09 - Scientific Evaluation K10 - Special Proj. (NLM)		
M01 - Gen. Clinical Res. Ctr		
N43 - Sm. Bus. Innovation		
U?? - Cooperative Agreemnts		

Table A.3 (con't)

P02 - Categ. Clinical Res Ctr P06 - Animal Resources P07 - Biotech. Resources P09 - Scientific Evaluation P10 - Envir. Hlth Centers P11 - Pharma - Toxic Centers P13 - Dental Res Inst. Prog P15 - Outpatient Clin. Res. P16 - Hlth Services Res. Ctr. P17 - Spec. Centers of Res. P18 - Sickle Cell Centers P20 - Exploratory Grants P30 - Center Core Grants P40 - Animal Resources P41 - Biotech. Resource P50 - Specialized Center P60 - Comprehensive Ctr		
R02 - Nursing R04 - Anthropology R06 - Translation R07 - Int'l Ctr for Res. & Tr. R09 - Scientific Evaluation R10 - Coop. Clinical Res. R11 - MH Project Grants R12 - MH Special Grants R13 - Conferences R14 - Psycopharm Conferen R15 - MH Project Conferen R16 - MH Special Conferen R18 - Hosp. & Med. Facility R20 - MH Hosp. Improvemt R21 - Comm. Hlth Explore R24 - Biotech. Resources R25 - Drug Abuse Education R26 - Oregan Project NCI R27 - Computer Technology R43 - Sm Bus. Innovation R44 - Sm Bus. Innovation		

Table A.3 (con't)

S?? - Gen. Research Support		
T?? - Training Grants		
W?? - Foreign Currency Prog		
Activity Code - Rnd 1 Total		

After Eliminating inappropriate Institutes		
File Name	# of Grants	Value of Grants

After Direct Edit of Some Study Sections		
File Name	# of Grants	Value of Grants

After Eliminating inappropriate and Individual review Study Sections		
File Name	# of Grants	Value of Grants

After Exclusion Grants are eliminated		
File Name	# of Grants	Value of Grants

After Eliminating Class Filtered Grants		
File Name	# of Grants	Value of Grants

APPENDIX B

APPENDIX B

Regresion Tables

Table B.1 - Industry Lag 12, PHS Lag 15

Num of Obs	119
Log Likelihood	90.86149
Sum of Sqr Resid	129.20239
R-Squared	0.77086
Sigma Squared	0.83227

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-8.98260	7.06954	-1.27061	3.25441	-2.76013
curird	1.15545	0.96392	1.19870	0.58171	1.98631
lg1ird	-2.31443	1.32721	-1.74383	1.12964	-2.04883
lg2ird	1.66644	1.29748	1.28436	0.74268	2.24380
lg3ird	0.08986	1.29516	0.06938	0.56412	0.15929
lg4ird	1.10461	1.26004	0.87664	0.45215	2.44302
lg5ird	-1.79230	1.29478	-1.38425	0.77049	-2.32617
lg6ird	0.27066	1.31800	0.20536	1.22508	0.22094
lg7ird	1.06016	1.28813	0.82302	1.08883	0.97367
lg8ird	-1.09250	1.25935	-0.86752	0.42856	-2.54922
lg9ird	0.68209	1.13381	0.60159	0.21689	3.14481
lg10ird	-0.76660	1.11640	-0.68667	0.50827	-1.50827
lg11ird	-1.14263	1.11093	-1.02853	0.94301	-1.21168
lg12ird	1.77680	1.12995	1.57246	0.66456	2.67364
curreg	-0.17164	0.18201	-0.94301	0.12168	-1.41058
lagreg1	-0.09319	0.18278	-0.50985	0.17570	-0.53041
lagreg2	0.05877	0.17982	0.32680	0.04344	1.35271
lagreg3	0.15317	0.19190	0.79817	0.09994	1.53259
lagreg4	-0.20658	0.18594	-1.11100	0.15345	-1.34618
lagreg5	-0.06301	0.17415	-0.36180	0.12882	-0.48914
lagreg6	-0.13434	0.15078	-0.89094	0.12253	-1.09640
lagreg7	0.16862	0.14365	1.17383	0.08318	2.02724
lagreg8	-0.31087	0.13945	-2.22926	0.04149	-7.49322
lagreg9	-0.12298	0.13713	-0.89681	0.03842	-3.20071
PHS15	1.26856	0.94632	1.34052	0.34751	3.65043
y79	-0.36017	0.48625	-0.74071	0.22935	-1.57040
y80	-0.68464	0.57499	-1.19070	0.45437	-1.50679
y81	-0.62598	0.59124	-1.05876	0.38100	-1.64301
y82	-0.72731	0.65159	-1.11620	0.31692	-2.29496
y83	-1.44171	0.76318	-1.88908	0.47235	-3.05223
y84	-1.19476	0.81301	-1.46955	0.28887	-4.13602
y85	-0.61765	0.80812	-0.76431	0.53128	-1.16257
y86	-1.72244	0.84971	-2.02708	0.41210	-4.17962
y87	-1.65003	0.87750	-1.88037	0.45101	-3.65851
y88	-1.44204	0.87572	-1.64669	0.54030	-2.66896
y89	-1.50835	0.90324	-1.66992	0.50426	-2.99120
y90	-1.75169	0.94994	-1.84400	0.40723	-4.30145
y91	-1.42518	1.00941	-1.41189	0.44102	-3.23156
y92	-1.56855	1.06471	-1.47322	0.54464	-2.87996
y93	-1.81371	1.11889	-1.62100	0.67344	-2.69320
y94	-2.24712	1.20468	-1.86533	0.62058	-3.62100
cns	1.49582	0.62346	2.39922	0.22433	6.66789
car	1.22880	0.73085	1.68132	0.28452	4.31893
ant	1.18100	0.69961	1.68808	0.17412	6.78271
giu	1.65315	1.04772	1.57786	0.46475	3.55706
der	3.61557	3.38669	1.06758	1.47266	2.45513
res	3.13959	2.37257	1.32329	1.08611	2.89068

Table B.2 - Industry Lag 12, PHS Lag 16

Num of Obs	119
Log Likelihood	91.17339
Sum of Sqr Resid	128.15357
R-Squared	0.77272
Sigma Squared	0.82233

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-10.74545	7.35637	-1.46070	3.84133	-2.79733
curird	1.10170	0.96847	1.13756	0.59789	1.84265
lg1ird	-2.34392	1.32962	-1.76285	1.10986	-2.11190
lg2ird	1.77701	1.30730	1.35930	0.75980	2.33878
lg3ird	0.08301	1.29939	0.06389	0.56013	0.14820
lg4ird	1.07848	1.26202	0.85456	0.43524	2.47791
lg5ird	-1.79714	1.29521	-1.38752	0.75457	-2.38166
lg6ird	0.29062	1.31893	0.22035	1.21700	0.23880
lg7ird	1.09895	1.28128	0.85769	1.07382	1.02340
lg8ird	-1.15806	1.25546	-0.92242	0.40658	-2.84827
lg9ird	0.69966	1.12952	0.61943	0.22364	3.12847
lg10ird	-0.77551	1.11262	-0.69701	0.52962	-1.46428
lg11ird	-1.15530	1.10405	-1.04642	0.93413	-1.23677
lg12ird	1.77984	1.12311	1.58475	0.66734	2.66707
curreg	-0.16304	0.18212	-0.89521	0.12105	-1.34687
lagreg1	-0.08536	0.18284	-0.46687	0.17461	-0.48888
lagreg2	0.06286	0.17980	0.34963	0.04080	1.54073
lagreg3	0.16140	0.19239	0.83890	0.09765	1.65282
lagreg4	-0.19819	0.18609	-1.06504	0.15463	-1.28172
lagreg5	-0.06001	0.17476	-0.34339	0.13123	-0.45730
lagreg6	-0.13222	0.15075	-0.87706	0.11838	-1.11686
lagreg7	0.16182	0.14378	1.12546	0.08381	1.93064
lagreg8	-0.31305	0.13943	-2.24516	0.04196	-7.46028
lagreg9	-0.12147	0.13694	-0.88702	0.03960	-3.06723
PHS16	1.57734	1.00720	1.56606	0.43897	3.59331
y79	-0.44796	0.49728	-0.90082	0.23666	-1.89283
y80	-0.88680	0.62393	-1.42131	0.49789	-1.78112
y81	-0.86420	0.65756	-1.31425	0.43536	-1.98501
y82	-1.00715	0.73431	-1.37156	0.39571	-2.54514
y83	-1.79105	0.87077	-2.05686	0.52323	-3.42307
y84	-1.62113	0.95747	-1.69314	0.41416	-3.91424
y85	-1.09807	0.98151	-1.11876	0.65359	-1.68007
y86	-2.20950	1.02092	-2.16423	0.55356	-3.99141
y87	-2.12652	1.03901	-2.04669	0.56337	-3.77467
y88	-1.94485	1.04986	-1.85248	0.65170	-2.98427
y89	-1.98685	1.06272	-1.86960	0.63232	-3.14216
y90	-2.25026	1.11290	-2.02198	0.51058	-4.40728
y91	-1.87157	1.14285	-1.63763	0.55630	-3.36435
y92	-2.10300	1.23565	-1.70194	0.69441	-3.02848
y93	-2.34943	1.28616	-1.82670	0.82054	-2.86326
y94	-2.77261	1.36080	-2.03748	0.76994	-3.60106
cns	1.67014	0.65256	2.55935	0.25996	6.42456
car	1.39096	0.73990	1.87993	0.31543	4.40971
ant	1.37417	0.72820	1.88707	0.22826	6.02016
giu	1.89649	1.08711	1.74453	0.52699	3.59869
der	4.65524	3.58166	1.29974	1.80658	2.57683
res	3.95849	2.56357	1.54413	1.33418	2.96697

Table B.3 - Industry Lag 12, PHS Lag 17

Num of Obs	119
Log Likelihood	91.95852
Sum of Sqr Resid	123.9466
R-Squared	0.78018
Sigma Squared	0.80209

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-14.94784	8.03942	-1.85932	5.05233	-2.95860
curird	0.99723	0.97669	1.02103	0.62046	1.60724
lg1ird	-2.31566	1.33139	-1.73927	1.05362	-2.19782
lg2ird	1.88129	1.31563	1.42995	0.78339	2.40147
lg3ird	0.09163	1.30071	0.07045	0.52276	0.17529
lg4ird	1.08264	1.26561	0.85543	0.42929	2.52194
lg5ird	-1.83958	1.29377	-1.42188	0.76288	-2.41137
lg6ird	0.32968	1.32360	0.24907	1.19204	0.27656
lg7ird	1.05712	1.27798	0.82718	1.04266	1.01387
lg8ird	-1.18441	1.24679	-0.94996	0.40098	-2.95376
lg9ird	0.72595	1.11794	0.64936	0.21318	3.40534
lg10ird	-0.75210	1.10622	-0.67988	0.53674	-1.40124
lg11ird	-1.16089	1.09329	-1.06183	0.91383	-1.27036
lg12ird	1.78054	1.11184	1.60143	0.67709	2.62970
curreg	-0.13099	0.18373	-0.71295	0.11670	-1.12246
lagreg1	-0.06742	0.18312	-0.36814	0.17089	-0.39451
lagreg2	0.06974	0.17928	0.38900	0.03666	1.90229
lagreg3	0.16879	0.19272	0.87584	0.09681	1.74363
lagreg4	-0.17713	0.18749	-0.94476	0.15500	-1.14275
lagreg5	-0.04882	0.17568	-0.27790	0.13300	-0.36707
lagreg6	-0.11712	0.15160	-0.77253	0.11778	-0.99437
lagreg7	0.15523	0.14378	1.07967	0.08135	1.90833
lagreg8	-0.32239	0.14006	-2.30181	0.04350	-7.41188
lagreg9	-0.12015	0.13674	-0.87868	0.03799	-3.16276
PHS17	2.24577	1.11445	2.01514	0.63143	3.55667
y79	-0.66396	0.52246	-1.27084	0.26043	-2.54946
y80	-1.29293	0.69995	-1.84716	0.55439	-2.33217
y81	-1.42364	0.78793	-1.80682	0.55694	-2.55617
y82	-1.62679	0.87784	-1.85317	0.54240	-2.99926
y83	-2.52620	1.04281	-2.42249	0.65850	-3.83631
y84	-2.50901	1.18256	-2.12168	0.64261	-3.90442
y85	-2.08686	1.24720	-1.67324	0.89240	-2.33848
y86	-3.27177	1.31121	-2.49523	0.84657	-3.86474
y87	-3.19974	1.32920	-2.40726	0.81316	-3.93495
y88	-3.02900	1.34432	-2.25319	0.89355	-3.38985
y89	-3.11266	1.37219	-2.26839	0.89592	-3.47424
y90	-3.35031	1.40223	-2.38927	0.78376	-4.27469
y91	-3.00123	1.43927	-2.08524	0.85112	-3.52620
y92	-3.19322	1.50167	-2.12644	0.97763	-3.26627
y93	-3.57331	1.60249	-2.22985	1.13946	-3.13597
y94	-3.99364	1.66661	-2.39627	1.11520	-3.58111
cns	2.03827	0.70079	2.90854	0.35530	5.73674
car	1.74313	0.76437	2.28047	0.40091	4.34795
ant	1.80280	0.78715	2.29030	0.35561	5.06957
giu	2.48982	1.18288	2.10489	0.67470	3.69024
der	7.00553	3.96835	1.76535	2.45558	2.85290
res	5.76062	2.89935	1.98687	1.82553	3.15558

Table B.4 - Industry Lag 12, PHS Lag 18

Num of Obs	119
Log Likelihood	91.86173
Sum of Sqr Resid	124.23301
R-Squared	0.77967
Sigma Squared	0.7988

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-16.85523	9.04179	-1.86415	7.00221	-2.40713
curird	1.18978	0.96202	1.23676	0.54366	2.18848
lg1ird	-2.53168	1.33779	-1.89244	1.00311	-2.52383
lg2ird	1.89409	1.31407	1.44139	0.80259	2.35996
lg3ird	0.20049	1.30197	0.15399	0.47088	0.42578
lg4ird	1.09517	1.26242	0.86752	0.44884	2.43999
lg5ird	-1.76252	1.28799	-1.36842	0.74645	-2.36119
lg6ird	0.13493	1.31816	0.10236	1.13471	0.11891
lg7ird	1.19615	1.28012	0.93440	1.00713	1.18768
lg8ird	-1.17591	1.24536	-0.94423	0.39642	-2.96633
lg9ird	0.77789	1.11559	0.69729	0.25455	3.05592
lg10ird	-0.74531	1.09532	-0.68045	0.55102	-1.35260
lg11ird	-1.09928	1.08902	-1.00942	0.92808	-1.18447
lg12ird	1.65105	1.09733	1.50461	0.64404	2.56358
curreg	-0.11481	0.18465	-0.62179	0.11402	-1.00699
lagreg1	-0.03943	0.18529	-0.21280	0.17627	-0.22369
lagreg2	0.09108	0.18032	0.50510	0.03927	2.31938
lagreg3	0.16957	0.19256	0.88060	0.09498	1.78523
lagreg4	-0.16014	0.18793	-0.85210	0.15268	-1.04883
lagreg5	-0.02758	0.17646	-0.15631	0.13543	-0.20365
lagreg6	-0.10975	0.15243	-0.72004	0.11962	-0.91751
lagreg7	0.16056	0.14422	1.11329	0.08696	1.84633
lagreg8	-0.31564	0.14015	-2.25222	0.04473	-7.05667
lagreg9	-0.12226	0.13703	-0.89218	0.03085	-3.96297
PHS18	2.45921	1.25845	1.95415	0.86351	2.84790
y79	-0.75420	0.55051	-1.36998	0.31133	-2.42251
y80	-1.49645	0.78531	-1.90555	0.66652	-2.24516
y81	-1.74101	0.94415	-1.84400	0.68365	-2.54665
y82	-2.09261	1.10748	-1.88953	0.81186	-2.57754
y83	-3.00767	1.28055	-2.34873	0.88875	-3.38416
y84	-3.04816	1.45812	-2.09047	0.99182	-3.07330
y85	-2.76017	1.59449	-1.73107	1.25378	-2.20148
y86	-4.02915	1.69614	-2.37548	1.24355	-3.24004
y87	-4.04022	1.75212	-2.30591	1.25579	-3.21727
y88	-3.88971	1.77806	-2.18761	1.31417	-2.95982
y89	-3.98873	1.81351	-2.19945	1.37869	-2.89314
y90	-4.27490	1.85980	-2.29858	1.28076	-3.33778
y91	-3.87720	1.87243	-2.07068	1.33789	-2.89799
y92	-4.10684	1.94921	-2.10693	1.50169	-2.73481
y93	-4.40007	2.00878	-2.19042	1.59649	-2.75609
y94	-4.92882	2.11542	-2.32994	1.60156	-3.07751
cns	2.12611	0.75704	2.80846	0.42078	5.05284
car	1.77451	0.79651	2.22784	0.47012	3.77457
ant	1.95389	0.88193	2.21547	0.53657	3.64143
giu	2.82042	1.32733	2.12489	0.93097	3.02956
der	7.94473	4.51613	1.75919	3.34622	2.37424
res	6.53707	3.35521	1.94834	2.44434	2.67437

Table B.5 - Industry Lag 12, PHS Lag 19

Num of Obs	119
Log Likelihood	91.53659
Sum of Sqr Resid	127.28431
R-Squared	0.77426
Sigma Squared	0.80302

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-17.01104	9.90278	-1.71780	8.99025	-1.89217
curird	1.36312	0.95082	1.43363	0.46346	2.94120
lg1ird	-2.50595	1.33868	-1.87196	0.99654	-2.51466
lg2ird	1.63343	1.29347	1.26283	0.74303	2.19834
lg3ird	0.33780	1.30286	0.25928	0.41995	0.80438
lg4ird	1.13510	1.26394	0.89807	0.42791	2.65268
lg5ird	-1.64920	1.28275	-1.28568	0.67260	-2.45199
lg6ird	-0.01038	1.32103	-0.00786	1.10127	-0.00943
lg7ird	1.21742	1.28293	0.94894	0.99495	1.22360
lg8ird	-1.06137	1.24554	-0.85214	0.37775	-2.80974
lg9ird	0.74666	1.11634	0.66885	0.24815	3.00884
lg10ird	-0.67758	1.09615	-0.61815	0.49535	-1.36788
lg11ird	-1.08803	1.08610	-1.00178	0.88948	-1.22322
lg12ird	1.59672	1.09397	1.45957	0.60602	2.63476
curreg	-0.12167	0.18412	-0.66080	0.11728	-1.03741
lagreg1	-0.03537	0.18626	-0.18990	0.18127	-0.19512
lagreg2	0.11999	0.18394	0.65235	0.05348	2.24376
lagreg3	0.17161	0.19331	0.88777	0.09255	1.85428
lagreg4	-0.15797	0.18742	-0.84289	0.15646	-1.00966
lagreg5	-0.01744	0.17675	-0.09869	0.13891	-0.12557
lagreg6	-0.09120	0.15527	-0.58734	0.12564	-0.72584
lagreg7	0.16485	0.14465	1.13961	0.09248	1.78265
lagreg8	-0.29141	0.14063	-2.07224	0.05139	-5.67071
lagreg9	-0.10866	0.13684	-0.79406	0.03413	-3.18384
PHS19	2.32217	1.32597	1.75130	1.09466	2.12137
y79	-0.74175	0.56714	-1.30788	0.37673	-1.96891
y80	-1.48300	0.83386	-1.77847	0.79073	-1.87547
y81	-1.78965	1.05446	-1.69721	0.85757	-2.08687
y82	-2.22354	1.28440	-1.73119	1.10249	-2.01684
y83	-3.22140	1.51646	-2.12429	1.27914	-2.51841
y84	-3.20792	1.68699	-1.90157	1.39818	-2.29436
y85	-2.97106	1.87307	-1.58620	1.70891	-1.73857
y86	-4.32853	2.03202	-2.13017	1.71372	-2.52581
y87	-4.42292	2.13794	-2.06878	1.84680	-2.39491
y88	-4.34573	2.20778	-1.96837	1.94086	-2.23908
y89	-4.46267	2.25517	-1.97886	2.02662	-2.20203
y90	-4.75709	2.30701	-2.06202	1.95646	-2.43147
y91	-4.39654	2.33759	-1.88080	2.00283	-2.19516
y92	-4.57769	2.39065	-1.91483	2.15861	-2.12066
y93	-4.90143	2.46881	-1.98534	2.26342	-2.16550
y94	-5.32041	2.51723	-2.11359	2.21860	-2.39810
cns	2.00642	0.76816	2.61197	0.51980	3.85997
car	1.59971	0.78214	2.04530	0.55163	2.89997
ant	1.88666	0.93698	2.01356	0.71113	2.65304
giu	2.93351	1.47742	1.98556	1.26145	2.32549
der	7.79649	4.91207	1.58721	4.34977	1.79239
res	6.46526	3.68214	1.75584	3.18631	2.02907

Table B.6 - Industry Lag 12, PHS Lag 20

Num of Obs	119
Log Likelihood	90.83429
Sum of Sqr Resid	131.57881
R-Squared	0.76664
Sigma Squared	0.81429

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-13.25281	10.03849	-1.32020	9.60317	-1.38004
currd	1.53099	0.94410	1.62163	0.42105	3.63610
lg1ird	-2.52755	1.33895	-1.88770	1.03896	-2.43277
lg2ird	1.54559	1.28736	1.20059	0.74496	2.07473
lg3ird	0.29911	1.30127	0.22986	0.43503	0.68756
lg4ird	1.19621	1.26402	0.94635	0.46578	2.56819
lg5ird	-1.59851	1.28582	-1.24318	0.66673	-2.39753
lg6ird	-0.07934	1.32678	-0.05980	1.12551	-0.07049
lg7ird	1.27504	1.28927	0.98896	0.96059	1.32735
lg8ird	-0.99498	1.24845	-0.79698	0.37470	-2.65540
lg9ird	0.75558	1.12858	0.66950	0.26688	2.83117
lg10ird	-0.71985	1.10261	-0.65286	0.48519	-1.48366
lg11ird	-1.04268	1.09804	-0.94958	0.94429	-1.10420
lg12ird	1.55646	1.09478	1.42171	0.59145	2.63162
curreg	-0.16055	0.18127	-0.88570	0.12646	-1.26953
lagreg1	-0.06735	0.18440	-0.36526	0.18161	-0.37086
lagreg2	0.10799	0.18604	0.58046	0.05746	1.87931
lagreg3	0.16713	0.19368	0.86293	0.08989	1.85918
lagreg4	-0.17005	0.18666	-0.91099	0.15254	-1.11477
lagreg5	-0.02772	0.17585	-0.15762	0.13796	-0.20092
lagreg6	-0.11083	0.15455	-0.71711	0.12405	-0.89345
lagreg7	0.17732	0.14534	1.22002	0.09526	1.86150
lagreg8	-0.28141	0.14138	-1.99044	0.05250	-5.36050
lagreg9	-0.09461	0.13770	-0.68708	0.04260	-2.22075
PHS 20	1.63038	1.26380	1.29006	1.15563	1.41081
y79	-0.53695	0.54990	-0.97644	0.38395	-1.39848
y80	-1.11344	0.80466	-1.38375	0.82843	-1.34403
y81	-1.31782	1.04192	-1.26480	0.90749	-1.45216
y82	-1.71974	1.32695	-1.29601	1.27345	-1.35045
y83	-2.65581	1.58786	-1.67257	1.48028	-1.79413
y84	-2.59026	1.78136	-1.45409	1.65556	-1.56458
y85	-2.26236	1.96933	-1.14879	1.95984	-1.15436
y86	-3.58942	2.15845	-1.66296	1.99851	-1.79605
y87	-3.69891	2.31025	-1.60109	2.21879	-1.66709
y88	-3.63858	2.41646	-1.50575	2.32786	-1.56306
y89	-3.79473	2.50667	-1.51385	2.48762	-1.52545
y90	-4.09076	2.57070	-1.59130	2.42938	-1.68387
y91	-3.72420	2.60451	-1.42991	2.45295	-1.51825
y92	-3.92292	2.67893	-1.46436	2.61353	-1.50100
y93	-4.18404	2.72711	-1.53424	2.65734	-1.57452
y94	-4.62526	2.79686	-1.65373	2.64491	-1.74874
cns	1.62135	0.72937	2.22294	0.56739	2.85759
car	1.17360	0.71539	1.64050	0.56131	2.09083
ant	1.44113	0.91119	1.58159	0.76637	1.88047
giu	2.49809	1.55845	1.60293	1.45539	1.71644
der	5.64062	4.95643	1.13804	4.78334	1.17922
res	4.86635	3.72179	1.30753	3.53034	1.37843

Table B.7 - Industry Lag 14, PHS Lag 15

Num of Obs	119
Log Likelihood	90.90157
Sum of Sqr Resid	129.37992
R-Squared	0.77054
Sigma Squared	0.85197

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-8.14760	7.74675	-1.05174	2.87593	-2.83303
curird	1.18817	0.97789	1.21504	0.70803	1.67814
lg1ird	-2.28047	1.35333	-1.68508	1.29656	-1.75885
lg2ird	1.63929	1.31338	1.24814	0.75374	2.17487
lg3ird	0.02083	1.32602	0.01571	0.63257	0.03294
lg4ird	1.14889	1.29618	0.88637	0.53177	2.16050
lg5ird	-1.78536	1.32314	-1.34934	0.55585	-3.21197
lg6ird	0.27812	1.31809	0.21100	1.18991	0.23373
lg7ird	1.04768	1.28783	0.81352	1.10522	0.94794
lg8ird	-1.03038	1.27786	-0.80633	0.40464	-2.54641
lg9ird	0.74237	1.17137	0.63377	0.33471	2.21799
lg10ird	-0.76909	1.11853	-0.68759	0.49002	-1.56951
lg11ird	-1.17704	1.12055	-1.05042	0.97076	-1.21249
lg12ird	1.92368	1.27742	1.50591	0.69324	2.77493
lg13ird	-0.23783	1.17846	-0.20182	1.22204	-0.19462
lg14ird	-0.04975	0.92015	-0.05407	1.02329	-0.04862
curreg	-0.17698	0.18561	-0.95346	0.08888	-1.99128
lagreg1	-0.09382	0.18410	-0.50965	0.15855	-0.59177
lagreg2	0.05876	0.17955	0.32727	0.04236	1.38728
lagreg3	0.15790	0.19264	0.81963	0.09801	1.61097
lagreg4	-0.20435	0.18646	-1.09599	0.14782	-1.38249
lagreg5	-0.05617	0.17598	-0.31917	0.13546	-0.41463
lagreg6	-0.13363	0.15245	-0.87660	0.14390	-0.92866
lagreg7	0.16615	0.14398	1.15394	0.07684	2.16241
lagreg8	-0.32172	0.14489	-2.22053	0.03142	-10.24022
lagreg9	-0.12534	0.13968	-0.89735	0.05331	-2.35105
PHS 15	1.17209	1.01325	1.15677	0.29357	3.99259
y79	-0.34948	0.48777	-0.71648	0.24348	-1.43538
y80	-0.65690	0.58310	-1.12657	0.44814	-1.46583
y81	-0.58522	0.61270	-0.95514	0.35249	-1.66025
y82	-0.68141	0.67683	-1.00675	0.27533	-2.47483
y83	-1.39859	0.78062	-1.79164	0.45676	-3.06201
y84	-1.13686	0.83772	-1.35709	0.27926	-4.07097
y85	-0.53664	0.86089	-0.62335	0.50390	-1.06497
y86	-1.66302	0.88566	-1.87771	0.33010	-5.03790
y87	-1.57337	0.91755	-1.71475	0.47532	-3.31010
y88	-1.34334	0.94408	-1.42290	0.56413	-2.38124
y89	-1.43101	0.96065	-1.48962	0.46764	-3.06005
y90	-1.68380	0.98424	-1.71076	0.39292	-4.28531
y91	-1.35843	1.03888	-1.30759	0.41547	-3.26961
y92	-1.49529	1.09698	-1.36309	0.52023	-2.87429
y93	-1.73125	1.15693	-1.49643	0.65664	-2.63655
y94	-2.17736	1.23115	-1.76855	0.56398	-3.86073
cns	1.45506	0.64035	2.27229	0.19888	7.31635
car	1.13054	0.82768	1.36590	0.22794	4.95987
ant	1.13643	0.71928	1.57997	0.16226	7.00379
giu	1.54721	1.12209	1.37887	0.42390	3.64993
der	3.20605	3.72663	0.86031	1.26424	2.53596
res	2.82824	2.65649	1.06465	0.91642	3.08620

Table B.8 - Industry Lag 14, PHS Lag 16

Num of Obs	119
Log Likelihood	91.19025
Sum of Sqr Resid	128.85904
R-Squared	0.77147
Sigma Squared	0.8436

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-10.43257	8.23952	-1.26616	3.15896	-3.30254
currird	1.13276	0.98286	1.15252	0.71092	1.59337
lg1ird	-2.35071	1.36032	-1.72806	1.28099	-1.83508
lg2ird	1.74460	1.32201	1.31966	0.76883	2.26918
lg3ird	0.06326	1.33129	0.04752	0.62928	0.10053
lg4ird	1.13036	1.29805	0.87081	0.52466	2.15448
lg5ird	-1.82372	1.32520	-1.37618	0.56067	-3.25276
lg6ird	0.29703	1.31986	0.22504	1.17478	0.25284
lg7ird	1.09435	1.28297	0.85298	1.08230	1.01114
lg8ird	-1.11911	1.27902	-0.87497	0.38493	-2.90729
lg9ird	0.70831	1.16940	0.60570	0.36008	1.96707
lg10ird	-0.78001	1.11597	-0.69895	0.49686	-1.56988
lg11ird	-1.17824	1.11249	-1.05910	0.95466	-1.23419
lg12ird	1.88801	1.27307	1.48304	0.69697	2.70888
lg13ird	-0.21392	1.17451	-0.18214	1.19129	-0.17957
lg14ird	0.07237	0.93561	0.07735	1.00941	0.07169
currreg	-0.16918	0.18576	-0.91076	0.08815	-1.91935
lagreg1	-0.08309	0.18446	-0.45044	0.15754	-0.52741
lagreg2	0.06281	0.17966	0.34960	0.04109	1.52851
lagreg3	0.16432	0.19328	0.85019	0.10042	1.63639
lagreg4	-0.19821	0.18661	-1.06215	0.14997	-1.32165
lagreg5	-0.05570	0.17640	-0.31580	0.13935	-0.39975
lagreg6	-0.13423	0.15229	-0.88144	0.14091	-0.95262
lagreg7	0.15991	0.14408	1.10990	0.07623	2.09780
lagreg8	-0.31800	0.14482	-2.19593	0.03318	-9.58485
lagreg9	-0.12003	0.13949	-0.86055	0.05319	-2.25680
PHS 16	1.54099	1.10687	1.39220	0.34473	4.47013
y79	-0.44100	0.50046	-0.88120	0.24661	-1.78826
y80	-0.86963	0.64103	-1.35663	0.47987	-1.81224
y81	-0.84877	0.69863	-1.21492	0.40708	-2.08503
y82	-0.99019	0.78320	-1.26429	0.33372	-2.96709
y83	-1.77162	0.91164	-1.94332	0.46698	-3.79374
y84	-1.58874	1.01015	-1.57278	0.37210	-4.26970
y85	-1.05943	1.07603	-0.98457	0.59812	-1.77127
y86	-2.18728	1.09712	-1.99366	0.44791	-4.88325
y87	-2.08350	1.11443	-1.86956	0.53625	-3.88529
y88	-1.89390	1.16128	-1.63086	0.62904	-3.01078
y89	-1.95991	1.16398	-1.68380	0.56827	-3.44890
y90	-2.21981	1.18642	-1.87101	0.44091	-5.03467
y91	-1.84057	1.20461	-1.52794	0.48067	-3.82914
y92	-2.06559	1.30579	-1.58187	0.61979	-3.33273
y93	-2.30827	1.36432	-1.69189	0.76181	-3.03000
y94	-2.74053	1.42389	-1.92467	0.65833	-4.16288
cns	1.65465	0.68434	2.41788	0.21945	7.54013
car	1.36014	0.86449	1.57335	0.23651	5.75087
ant	1.35713	0.76233	1.78024	0.19095	7.10721
giu	1.85727	1.18900	1.56205	0.44070	4.21436
der	4.50596	4.05068	1.11240	1.44089	3.12721
res	3.84418	2.94711	1.30439	1.04398	3.68224

Table B.9 - Industry Lag 14, PHS Lag 17

Num of Obs	119
Log Likelihood	91.9928
Sum of Sqr Resid	125.01129
R-Squared	0.77829
Sigma Squared	0.82484

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-15.63597	9.04459	-1.72877	3.72652	-4.19586
curird	1.02072	0.99206	1.02888	0.71802	1.42156
lg1ird	-2.38800	1.36630	-1.74779	1.23067	-1.94041
lg2ird	1.85418	1.32980	1.39433	0.79024	2.34634
lg3ird	0.15004	1.33608	0.11230	0.60590	0.24763
lg4ird	1.14100	1.30233	0.87612	0.51480	2.21638
lg5ird	-1.91591	1.32488	-1.44610	0.58545	-3.27255
lg6ird	0.33602	1.32624	0.25337	1.14063	0.29459
lg7ird	1.07129	1.28178	0.83578	1.04135	1.02875
lg8ird	-1.18778	1.27232	-0.93355	0.38966	-3.04827
lg9ird	0.66209	1.16124	0.57016	0.37129	1.78319
lg10ird	-0.76293	1.11092	-0.68676	0.48527	-1.57219
lg11ird	-1.16380	1.09937	-1.05861	0.91760	-1.26832
lg12ird	1.82159	1.26272	1.44259	0.69658	2.61503
lg13ird	-0.16762	1.16713	-0.14362	1.14625	-0.14623
lg14ird	0.24676	0.94359	0.26152	0.98671	0.25009
curreg	-0.13642	0.18732	-0.72826	0.08475	-1.60959
lagreg1	-0.06019	0.18492	-0.32552	0.15262	-0.39441
lagreg2	0.06991	0.17930	0.38992	0.03729	1.87478
lagreg3	0.16989	0.19407	0.87541	0.10490	1.61945
lagreg4	-0.17908	0.18797	-0.95273	0.15250	-1.17431
lagreg5	-0.04777	0.17688	-0.27005	0.14179	-0.33688
lagreg6	-0.12243	0.15288	-0.80080	0.14052	-0.87128
lagreg7	0.15334	0.14420	1.06342	0.07095	2.16121
lagreg8	-0.31928	0.14478	-2.20532	0.03589	-8.89640
lagreg9	-0.11332	0.13910	-0.81468	0.05061	-2.23908
PHS 17	2.33693	1.23232	1.89637	0.46741	4.99976
y79	-0.67546	0.52829	-1.27858	0.25539	-2.64486
y80	-1.32054	0.72645	-1.81779	0.51613	-2.55854
y81	-1.48316	0.85184	-1.74113	0.50219	-2.95339
y82	-1.69586	0.95240	-1.78061	0.42588	-3.98203
y83	-2.59466	1.10930	-2.33901	0.52502	-4.94205
y84	-2.57953	1.26585	-2.03779	0.52899	-4.87635
y85	-2.18529	1.38281	-1.58032	0.75508	-2.89409
y86	-3.38240	1.43332	-2.35984	0.66963	-5.05113
y87	-3.28448	1.44720	-2.26954	0.67713	-4.85062
y88	-3.12928	1.49931	-2.08714	0.75394	-4.15058
y89	-3.23862	1.52346	-2.12583	0.71737	-4.51455
y90	-3.45537	1.52174	-2.27066	0.58778	-5.87868
y91	-3.09786	1.54484	-2.00530	0.66682	-4.64574
y92	-3.28999	1.61144	-2.04165	0.80177	-4.10338
y93	-3.67990	1.72931	-2.12796	0.97402	-3.77807
y94	-4.10218	1.77749	-2.30785	0.90226	-4.54656
cns	2.08198	0.74291	2.80249	0.29442	7.07137
car	1.82986	0.90222	2.02817	0.27772	6.58888
ant	1.85001	0.82971	2.22969	0.26815	6.89923
giu	2.58407	1.30831	1.97512	0.49973	5.17098
der	7.37585	4.51505	1.63362	1.79660	4.10544
res	6.04764	3.34453	1.80822	1.32206	4.57442

Table B.10 - Industry Lag 14, PHS Lag 18

Num of Obs	119
Log Likelihood	91.90163
Sum of Sqr Resid	125.45525
R-Squared	0.7775
Sigma Squared	0.81965

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-17.03649	9.93585	-1.71465	5.87205	-2.90128
currd	1.23589	0.97579	1.26655	0.65697	1.88119
lg1ird	-2.58444	1.38251	-1.86939	1.20752	-2.14028
lg2ird	1.84460	1.32953	1.38740	0.81178	2.27228
lg3ird	0.21838	1.34025	0.16294	0.55522	0.39332
lg4ird	1.17980	1.29877	0.90840	0.51365	2.29688
lg5ird	-1.83132	1.31492	-1.39273	0.56520	-3.24014
lg6ird	0.14208	1.32113	0.10754	1.09044	0.13030
lg7ird	1.19965	1.28491	0.93365	1.00480	1.19392
lg8ird	-1.14207	1.26731	-0.90118	0.37404	-3.05334
lg9ird	0.75421	1.15299	0.65414	0.38442	1.96195
lg10ird	-0.76149	1.10151	-0.69132	0.49393	-1.54171
lg11ird	-1.12113	1.09716	-1.02185	0.93403	-1.20031
lg12ird	1.77773	1.25417	1.41746	0.69550	2.55604
lg13ird	-0.30370	1.15088	-0.26389	1.07347	-0.28292
lg14ird	0.21574	0.93619	0.23045	1.00572	0.21451
currreg	-0.12369	0.18813	-0.65748	0.08484	-1.45799
lagreg1	-0.03246	0.18753	-0.17310	0.15655	-0.20736
lagreg2	0.09186	0.18026	0.50962	0.03968	2.31505
lagreg3	0.17391	0.19409	0.89599	0.10161	1.71151
lagreg4	-0.16133	0.18844	-0.85612	0.15113	-1.06749
lagreg5	-0.02269	0.17739	-0.12789	0.14231	-0.15942
lagreg6	-0.11442	0.15338	-0.74598	0.13875	-0.82462
lagreg7	0.15753	0.14459	1.08949	0.07737	2.03618
lagreg8	-0.31823	0.14501	-2.19463	0.04022	-7.91183
lagreg9	-0.11683	0.13927	-0.83888	0.04850	-2.40896
PHS 18	2.49003	1.35528	1.83728	0.68489	3.63567
y79	-0.75664	0.55622	-1.36032	0.29662	-2.55091
y80	-1.50139	0.81117	-1.85088	0.60707	-2.47315
y81	-1.76582	1.00459	-1.75775	0.56935	-3.10146
y82	-2.12567	1.18402	-1.79530	0.68085	-3.12210
y83	-3.03923	1.34932	-2.25241	0.68794	-4.41789
y84	-3.06824	1.53911	-1.99351	0.85362	-3.59440
y85	-2.79147	1.72500	-1.61824	1.04401	-2.67379
y86	-4.08416	1.82153	-2.24216	1.01510	-4.02339
y87	-4.06116	1.87347	-2.16772	1.04381	-3.89071
y88	-3.91344	1.93250	-2.02507	1.05373	-3.71389
y89	-4.04926	1.96856	-2.05696	1.16527	-3.47495
y90	-4.32187	1.98943	-2.17241	1.01971	-4.23835
y91	-3.91777	1.98682	-1.97188	1.09330	-3.58344
y92	-4.14306	2.06821	-2.00321	1.27388	-3.25233
y93	-4.43628	2.13771	-2.07524	1.34802	-3.29095
y94	-4.97599	2.23525	-2.22615	1.30223	-3.82113
cns	2.14339	0.79042	2.71170	0.31380	6.83052
car	1.80309	0.91018	1.98103	0.31836	5.66363
ant	1.97437	0.91817	2.15033	0.44945	4.39283
giu	2.84743	1.44502	1.97052	0.75507	3.77106
der	8.06059	4.98715	1.61627	2.66321	3.02664
res	6.62497	3.74228	1.77030	1.86931	3.54408

Table B.11 - Industry Lag 14, PHS Lag 19

Num of Obs	119
Log Likelihood	91.62458
Sum of Sqr Resid	127.25382
R-Squared	0.77431
Sigma Squared	0.82386

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-16.11767	10.34160	-1.55853	8.31822	-1.93764
curird	1.39385	0.96560	1.44350	0.61732	2.25791
lg1ird	-2.46500	1.37263	-1.79582	1.21165	-2.03441
lg2ird	1.59014	1.31422	1.20995	0.76209	2.08655
lg3ird	0.24547	1.34035	0.18314	0.50706	0.48410
lg4ird	1.21546	1.29829	0.93620	0.50898	2.38802
lg5ird	-1.67098	1.30557	-1.27988	0.48501	-3.44528
lg6ird	0.01540	1.32229	0.01165	1.06869	0.01441
lg7ird	1.18550	1.28314	0.92391	1.00276	1.18223
lg8ird	-0.98330	1.25869	-0.78121	0.35987	-2.73240
lg9ird	0.82051	1.15129	0.71269	0.36401	2.25411
lg10ird	-0.69222	1.10140	-0.62850	0.46983	-1.47337
lg11ird	-1.14519	1.09726	-1.04369	0.90664	-1.26311
lg12ird	1.84273	1.25399	1.46950	0.65992	2.79238
lg13ird	-0.39390	1.14535	-0.34392	1.04598	-0.37659
lg14ird	0.00249	0.90628	0.00275	1.03815	0.00240
curreg	-0.13162	0.18750	-0.70196	0.08880	-1.48224
lagreg1	-0.03491	0.18789	-0.18580	0.16265	-0.21463
lagreg2	0.11930	0.18375	0.64922	0.05520	2.16134
lagreg3	0.18001	0.19463	0.92490	0.09367	1.92166
lagreg4	-0.15725	0.18816	-0.83576	0.15399	-1.02119
lagreg5	-0.00979	0.17789	-0.05502	0.14517	-0.06743
lagreg6	-0.09220	0.15624	-0.59014	0.14413	-0.63971
lagreg7	0.16114	0.14486	1.11236	0.08323	1.93610
lagreg8	-0.30668	0.14609	-2.09932	0.04542	-6.75224
lagreg9	-0.11058	0.13948	-0.79281	0.05181	-2.13455
PHS 19	2.24172	1.35796	1.65080	1.00417	2.23241
y79	-0.73020	0.56909	-1.28309	0.37513	-1.94650
y80	-1.44586	0.84286	-1.71542	0.75204	-1.92258
y81	-1.73393	1.07755	-1.60914	0.78067	-2.22109
y82	-2.15597	1.31522	-1.63924	1.02733	-2.09861
y83	-3.15413	1.54379	-2.04310	1.17594	-2.68222
y84	-3.11338	1.71676	-1.81353	1.32590	-2.34812
y85	-2.83712	1.92782	-1.47168	1.58149	-1.79396
y86	-4.22023	2.08425	-2.02482	1.57326	-2.68247
y87	-4.27725	2.18816	-1.95472	1.73074	-2.47134
y88	-4.16941	2.27918	-1.82935	1.77853	-2.34431
y89	-4.32351	2.32740	-1.85765	1.88462	-2.29409
y90	-4.62446	2.36300	-1.95703	1.81421	-2.54901
y91	-4.26988	2.38664	-1.78907	1.86341	-2.29144
y92	-4.44010	2.44092	-1.81902	2.02749	-2.18995
y93	-4.75124	2.52443	-1.88211	2.11519	-2.24625
y94	-5.19256	2.56489	-2.02448	2.05729	-2.52399
cns	1.96243	0.77503	2.55789	0.47756	4.15116
car	1.51830	0.83617	1.81579	0.46311	3.27846
ant	1.86018	0.94627	1.96580	0.67293	2.76428
giu	2.80734	1.53762	1.82577	1.15895	2.42230
der	7.38611	5.11447	1.44416	3.95890	1.86570
res	6.13349	3.85676	1.59032	2.85928	2.14512

Table B.12 - Industry Lag 14, PHS Lag 20

Num of Obs	119
Log Likelihood	90.83429
Sum of Sqr Resid	131.57881
R-Squared	0.76664
Sigma Squared	0.81429

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-13.25281	10.03849	-1.32020	9.60317	-1.38004
currd	1.53099	0.94410	1.62163	0.42105	3.63610
lg1ird	-2.52755	1.33895	-1.88770	1.03896	-2.43277
lg2ird	1.54559	1.28736	1.20059	0.74496	2.07473
lg3ird	0.29911	1.30127	0.22986	0.43503	0.68756
lg4ird	1.19621	1.26402	0.94635	0.46578	2.56819
lg5ird	-1.59851	1.28582	-1.24318	0.66673	-2.39753
lg6ird	-0.07934	1.32678	-0.05980	1.12551	-0.07049
lg7ird	1.27504	1.28927	0.98896	0.96059	1.32735
lg8ird	-0.99498	1.24845	-0.79698	0.37470	-2.65540
lg9ird	0.75558	1.12858	0.66950	0.26688	2.83117
lg10ird	-0.71985	1.10261	-0.65286	0.48519	-1.48366
lg11ird	-1.04268	1.09804	-0.94958	0.94429	-1.10420
lg12ird	1.55646	1.09478	1.42171	0.59145	2.63162
lg13ird	-0.16055	0.18127	-0.88570	0.12646	-1.26953
lg14ird	-0.06735	0.18440	-0.36526	0.18161	-0.37086
currreg	0.10799	0.18604	0.58046	0.05746	1.87931
lagreg1	0.16713	0.19368	0.86293	0.08989	1.85918
lagreg2	-0.17005	0.18666	-0.91099	0.15254	-1.11477
lagreg3	-0.02772	0.17585	-0.15762	0.13796	-0.20092
lagreg4	-0.11083	0.15455	-0.71711	0.12405	-0.89345
lagreg5	0.17732	0.14534	1.22002	0.09526	1.86150
lagreg6	-0.28141	0.14138	-1.99044	0.05250	-5.36050
lagreg7	-0.09461	0.13770	-0.68708	0.04260	-2.22075
lagreg8	1.63038	1.26380	1.29006	1.15563	1.41081
lagreg9	-0.53695	0.54990	-0.97644	0.38395	-1.39848
PHS 20	-1.11344	0.80466	-1.38375	0.82843	-1.34403
y79	-1.31782	1.04192	-1.26480	0.90749	-1.45216
y80	-1.71974	1.32695	-1.29601	1.27345	-1.35045
y81	-2.65581	1.58786	-1.67257	1.48028	-1.79413
y82	-2.59026	1.78136	-1.45409	1.65556	-1.56458
y83	-2.26236	1.96933	-1.14879	1.95984	-1.15436
y84	-3.58942	2.15845	-1.66296	1.99851	-1.79605
y85	-3.69891	2.31025	-1.60109	2.21879	-1.66709
y86	-3.63858	2.41646	-1.50575	2.32786	-1.56306
y87	-3.79473	2.50667	-1.51385	2.48762	-1.52545
y88	-4.09076	2.57070	-1.59130	2.42938	-1.68387
y89	-3.72420	2.60451	-1.42991	2.45295	-1.51825
y90	-3.92292	2.67893	-1.46436	2.61353	-1.50100
y91	-4.18404	2.72711	-1.53424	2.65734	-1.57452
y92	-4.62526	2.79686	-1.65373	2.64491	-1.74874
y93	1.62135	0.72937	2.22294	0.56739	2.85759
y94	1.17360	0.71539	1.64050	0.56131	2.09083
cns	1.44113	0.91119	1.58159	0.76637	1.88047
car	2.49809	1.55845	1.60293	1.45539	1.71644
ant	5.64062	4.95643	1.13804	4.78334	1.17922
giu	4.86635	3.72179	1.30753	3.53034	1.37843
der	7.38611	5.11447	1.44416	3.95890	1.86570
res	6.13349	3.85676	1.59032	2.85928	2.14512

Table B.13 - Industry Lag 12, PHS Nested 12,17,22

Num of Obs	119
Log Likelihood	92.15151
Sum of Sqr Resid	124.23083
R-Squared	0.77967
Sigma Squared	0.81582

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-16.57264	9.50335	-1.74387	7.02428	-2.35934
curird	1.13937	1.00743	1.13097	0.57614	1.97760
lg1ird	-2.40982	1.34115	-1.79682	1.00937	-2.38744
lg2ird	1.85343	1.32996	1.39360	0.77802	2.38223
lg3ird	0.22204	1.32249	0.16790	0.43465	0.51086
lg4ird	1.11641	1.27144	0.87806	0.43303	2.57812
lg5ird	-1.77030	1.29680	-1.36513	0.71762	-2.46691
lg6ird	0.21469	1.34506	0.15961	1.16080	0.18495
lg7ird	1.13635	1.28500	0.88432	0.98346	1.15546
lg8ird	-1.16502	1.24347	-0.93691	0.37638	-3.09529
lg9ird	0.70150	1.11534	0.62896	0.22512	3.11612
lg10ird	-0.72865	1.10284	-0.66070	0.52097	-1.39863
lg11ird	-1.16079	1.09275	-1.06226	0.89825	-1.29228
lg12ird	1.76550	1.10705	1.59477	0.64703	2.72860
curreg	-0.12725	0.18380	-0.69230	0.11689	-1.08858
lagreg1	-0.06401	0.18304	-0.34973	0.16822	-0.38053
lagreg2	0.08524	0.18160	0.46941	0.04404	1.93536
lagreg3	0.17551	0.19375	0.90589	0.09853	1.78120
lagreg4	-0.15880	0.18991	-0.83617	0.15389	-1.03193
lagreg5	-0.03691	0.17765	-0.20774	0.14424	-0.25587
lagreg6	-0.10397	0.15356	-0.67708	0.12463	-0.83424
lagreg7	0.16160	0.14445	1.11873	0.08011	2.01706
lagreg8	-0.30104	0.14515	-2.07406	0.05981	-5.03323
lagreg9	-0.10120	0.14009	-0.72237	0.05390	-1.87753
PHS 12	-0.46237	1.31245	-0.35229	0.67702	-0.68295
PHS 17	2.40835	1.48615	1.62053	0.92605	2.60067
PHS 22	0.44051	0.81856	0.53815	0.47659	0.92429
y79	-0.74499	0.53886	-1.38253	0.31689	-2.35098
y80	-1.46200	0.75066	-1.94762	0.69041	-2.11757
y81	-1.71579	0.92097	-1.86302	0.74425	-2.30540
y82	-2.07712	1.14588	-1.81268	0.98591	-2.10680
y83	-3.10084	1.40468	-2.20750	1.14328	-2.71223
y84	-3.18227	1.61743	-1.96749	1.32209	-2.40700
y85	-2.88116	1.80370	-1.59736	1.61646	-1.78239
y86	-4.15232	1.95261	-2.12655	1.65633	-2.50694
y87	-4.14191	2.04427	-2.02611	1.72116	-2.40647
y88	-4.00751	2.11345	-1.89619	1.77050	-2.26349
y89	-4.14820	2.21075	-1.87638	1.91374	-2.16759
y90	-4.43738	2.30293	-1.92684	1.83930	-2.41254
y91	-4.09781	2.34751	-1.74560	1.90844	-2.14720
y92	-4.31263	2.42145	-1.78101	2.07542	-2.07795
y93	-4.71883	2.51435	-1.87676	2.19103	-2.15371
y94	-5.15364	2.57437	-2.00190	2.17501	-2.36947
cns	2.06859	0.77300	2.67605	0.38270	5.40530
car	1.69323	0.86830	1.95005	0.38627	4.38357
ant	1.90766	0.92714	2.05758	0.49541	3.85064
giu	2.83321	1.43718	1.97136	1.02323	2.76889
der	7.77298	4.68430	1.65937	3.27776	2.37143
res	6.51756	3.43154	1.89931	2.52827	2.57788

Table B.14 - Industry Lag 12, PHS Nested 9,17,25

Num of Obs	119
Log Likelihood	92.12054
Sum of Sqr Resid	125.45063
R-Squared	0.77751
Sigma Squared	0.81991

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-16.02741	10.17516	-1.57515	4.69136	-3.41637
curird	1.07396	0.99299	1.08154	0.63280	1.69717
lg1ird	-2.36723	1.33659	-1.77109	1.04800	-2.25880
lg2ird	1.80779	1.32527	1.36410	0.82163	2.20026
lg3ird	0.14869	1.30439	0.11399	0.48928	0.30389
lg4ird	1.11822	1.27006	0.88044	0.44925	2.48908
lg5ird	-1.78944	1.30336	-1.37295	0.77816	-2.29957
lg6ird	0.30525	1.32584	0.23023	1.18097	0.25848
lg7ird	1.07322	1.28019	0.83833	1.00608	1.06674
lg8ird	-1.18800	1.24768	-0.95217	0.39466	-3.01020
lg9ird	0.71228	1.11994	0.63600	0.23001	3.09673
lg10ird	-0.74095	1.10389	-0.67122	0.50838	-1.45746
lg11ird	-1.16099	1.09057	-1.06457	0.89080	-1.30332
lg12ird	1.75856	1.11336	1.57951	0.70709	2.48703
curreg	-0.13137	0.18405	-0.71378	0.12180	-1.07860
lagreg1	-0.06604	0.18293	-0.36100	0.16744	-0.39440
lagreg2	0.08279	0.18106	0.45727	0.05255	1.57544
lagreg3	0.17849	0.19373	0.92136	0.10695	1.66899
lagreg4	-0.16472	0.18894	-0.87177	0.15500	-1.06271
lagreg5	-0.04074	0.17609	-0.23134	0.14767	-0.27586
lagreg6	-0.11156	0.15327	-0.72783	0.12597	-0.88559
lagreg7	0.16105	0.14377	1.12019	0.07599	2.11942
lagreg8	-0.30506	0.14319	-2.13053	0.05521	-5.52586
lagreg9	-0.10979	0.13796	-0.79581	0.04581	-2.39688
PHS 9	0.07222	1.33287	0.05418	0.66274	0.10897
PHS 17	2.07199	1.19470	1.73432	0.73637	2.81378
PHS 25	0.21326	0.40442	0.52732	0.19431	1.09749
y79	-0.63680	0.52583	-1.21103	0.26652	-2.38926
y80	-1.24188	0.70951	-1.75032	0.58928	-2.10746
y81	-1.37886	0.80271	-1.71775	0.59267	-2.32652
y82	-1.63409	0.90537	-1.80489	0.59969	-2.72488
y83	-2.56302	1.07664	-2.38058	0.69953	-3.66394
y84	-2.57929	1.22854	-2.09948	0.70532	-3.65689
y85	-2.21574	1.30918	-1.69246	0.93731	-2.36393
y86	-3.45283	1.40503	-2.45748	0.90468	-3.81662
y87	-3.44877	1.45725	-2.36663	0.88522	-3.89593
y88	-3.32858	1.49764	-2.22255	0.92965	-3.58047
y89	-3.44767	1.55009	-2.22417	0.97414	-3.53919
y90	-3.72268	1.61065	-2.31129	0.84891	-4.38523
y91	-3.39616	1.66339	-2.04171	0.91860	-3.69712
y92	-3.62138	1.75142	-2.06769	1.06593	-3.39739
y93	-4.01339	1.85350	-2.16530	1.18670	-3.38198
y94	-4.42852	1.91478	-2.31281	1.14341	-3.87309
cns	2.08511	0.95089	2.19279	0.45870	4.54570
car	1.76651	1.08858	1.62277	0.49478	3.57029
ant	1.94580	1.10296	1.76416	0.39674	4.90450
giu	2.67696	1.41714	1.88899	0.62679	4.27090
der	7.51364	5.23746	1.43459	2.43892	3.08073
res	6.15821	3.48463	1.76725	1.71976	3.58085

Table B.15 - Industry Lag 14, PHS Nested 12,17,22

Num of Obs	119
Log Likelihood	92.37649
Sum of Sqr Resid	124.95949
R-Squared	0.77838
Sigma Squared	0.82629

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-17.95168	9.74869	-1.84145	6.92910	-2.59077
curird	1.15163	1.02342	1.12527	0.64230	1.79296
lg1ird	-2.47335	1.37212	-1.80258	1.18044	-2.09528
lg2ird	1.85827	1.34629	1.38029	0.78644	2.36288
lg3ird	0.26457	1.34586	0.19658	0.48905	0.54100
lg4ird	1.19932	1.30794	0.91695	0.48857	2.45474
lg5ird	-1.86090	1.33045	-1.39870	0.53133	-3.50234
lg6ird	0.24814	1.35371	0.18330	1.12336	0.22089
lg7ird	1.19762	1.29209	0.92688	0.95179	1.25828
lg8ird	-1.13653	1.26950	-0.89526	0.36677	-3.09875
lg9ird	0.65821	1.15877	0.56802	0.39691	1.65831
lg10ird	-0.74107	1.10587	-0.67012	0.48125	-1.53987
lg11ird	-1.17209	1.09368	-1.07169	0.89938	-1.30322
lg12ird	1.76555	1.26378	1.39704	0.64959	2.71796
lg13ird	-0.24360	1.16387	-0.20930	1.07948	-0.22567
lg14ird	0.25846	0.97233	0.26582	1.02633	0.25183
curreg	-0.11868	0.18823	-0.63051	0.08641	-1.37352
lagreg1	-0.04694	0.18468	-0.25417	0.15535	-0.30216
lagreg2	0.08339	0.18152	0.45938	0.03965	2.10313
lagreg3	0.17266	0.19566	0.88243	0.10142	1.70236
lagreg4	-0.14569	0.19225	-0.75779	0.15294	-0.95259
lagreg5	-0.02464	0.18016	-0.13675	0.15894	-0.15501
lagreg6	-0.11566	0.15592	-0.74180	0.14181	-0.81559
lagreg7	0.14626	0.14618	1.00053	0.08059	1.81492
lagreg8	-0.30533	0.14828	-2.05914	0.04513	-6.76526
lagreg9	-0.09225	0.14178	-0.65067	0.06236	-1.47934
PHS 14	-1.28591	1.75187	-0.73402	0.97279	-1.32188
PHS 17	3.48370	2.30255	1.51297	1.15875	3.00643
HPS 22	0.39480	0.84338	0.46812	0.53669	0.73562
y79	-0.85907	0.56681	-1.51562	0.35647	-2.40993
y80	-1.65125	0.81391	-2.02879	0.73282	-2.25328
y81	-1.96712	1.00911	-1.94937	0.75448	-2.60724
y82	-2.35278	1.21746	-1.93253	1.00266	-2.34654
y83	-3.42796	1.47700	-2.32089	1.15083	-2.97868
y84	-3.61752	1.74462	-2.07353	1.44641	-2.50103
y85	-3.39579	1.96870	-1.72489	1.70055	-1.99688
y86	-4.70549	2.11167	-2.22832	1.76856	-2.66064
y87	-4.66845	2.19467	-2.12717	1.87512	-2.48969
y88	-4.56161	2.28291	-1.99815	1.90585	-2.39348
y89	-4.73950	2.37393	-1.99647	2.08294	-2.27538
y90	-4.94225	2.40963	-2.05104	1.97356	-2.50422
y91	-4.61647	2.46242	-1.87476	2.09445	-2.20415
y92	-4.83989	2.53890	-1.90630	2.27391	-2.12845
y93	-5.28134	2.64513	-1.99663	2.36822	-2.23009
y94	-5.70191	2.68776	-2.12144	2.33530	-2.44162
cns	2.17936	0.75408	2.89007	0.36916	5.90351
car	1.79238	0.89314	2.00683	0.25323	7.07795
ant	2.01445	0.89430	2.25256	0.53307	3.77896
giu	3.05981	1.47717	2.07141	1.03591	2.95373
der	8.57090	4.81120	1.78145	3.20187	2.67684
res	7.20723	3.65840	1.97005	2.42966	2.96636

Table B.16 - Industry Lag 14, PHS Nested 9,17,25

Num of Obs	119
Log Likelihood	92.13606
Sum of Sqr Resid	126.2564
R-Squared	0.77608
Sigma Squared	0.84255

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-15.98923	10.63423	-1.50356	4.11581	-3.88483
curird	1.10184	1.00852	1.09253	0.72101	1.52819
lg1ird	-2.39060	1.36801	-1.74750	1.23494	-1.93581
lg2ird	1.77544	1.34458	1.32044	0.83412	2.12852
lg3ird	0.14984	1.33688	0.11208	0.58033	0.25820
lg4ird	1.16995	1.30381	0.89733	0.53218	2.19839
lg5ird	-1.82862	1.33742	-1.36727	0.60780	-3.00858
lg6ird	0.31211	1.32736	0.23514	1.13546	0.27488
lg7ird	1.07156	1.28307	0.83515	1.01361	1.05716
lg8ird	-1.16074	1.27539	-0.91011	0.40307	-2.87978
lg9ird	0.70315	1.16921	0.60139	0.36955	1.90272
lg10ird	-0.74939	1.10812	-0.67627	0.45704	-1.63965
lg11ird	-1.17814	1.09929	-1.07173	0.89193	-1.32089
lg12ird	1.84772	1.26438	1.46136	0.69172	2.67119
lg13ird	-0.19959	1.17183	-0.17033	1.17330	-0.17011
lg14ird	0.12063	0.97229	0.12406	1.01527	0.11881
curreg	-0.13730	0.18747	-0.73240	0.09035	-1.51972
lagreg1	-0.06244	0.18472	-0.33801	0.15030	-0.41542
lagreg2	0.08284	0.18108	0.45748	0.05455	1.51851
lagreg3	0.18100	0.19529	0.92684	0.11279	1.60473
lagreg4	-0.16564	0.18969	-0.87325	0.15113	-1.09600
lagreg5	-0.03763	0.17773	-0.21172	0.15772	-0.23858
lagreg6	-0.11471	0.15475	-0.74126	0.14884	-0.77065
lagreg7	0.15899	0.14420	1.10257	0.06435	2.47064
lagreg8	-0.30772	0.14609	-2.10634	0.04400	-6.99341
lagreg9	-0.10689	0.13982	-0.76446	0.05496	-1.94468
PHS 9	0.07550	1.35160	0.05586	0.59764	0.12634
PHS 17	2.07086	1.39086	1.48891	0.54243	3.81772
PHS 25	0.21061	0.41851	0.50323	0.22338	0.94280
y79	-0.63479	0.53697	-1.18218	0.26211	-2.42185
y80	-1.23611	0.75403	-1.63934	0.54637	-2.26241
y81	-1.38103	0.89330	-1.54598	0.53749	-2.56941
y82	-1.63709	0.99790	-1.64054	0.46779	-3.49963
y83	-2.56339	1.15509	-2.21921	0.55846	-4.59008
y84	-2.56919	1.32073	-1.94528	0.56841	-4.51993
y85	-2.20694	1.44124	-1.53127	0.78282	-2.81920
y86	-3.45776	1.51079	-2.28871	0.71854	-4.81223
y87	-3.43095	1.54492	-2.22080	0.75850	-4.52334
y88	-3.30929	1.60567	-2.06101	0.79617	-4.15651
y89	-3.45147	1.64371	-2.09981	0.79648	-4.33339
y90	-3.71842	1.67290	-2.22274	0.67439	-5.51375
y91	-3.38864	1.71274	-1.97849	0.77353	-4.38074
y92	-3.60981	1.80054	-2.00484	0.92927	-3.88459
y93	-3.99999	1.91470	-2.08910	1.05239	-3.80087
y94	-4.42214	1.96581	-2.24952	0.98106	-4.50749
cns	2.08676	0.96310	2.16671	0.46304	4.50663
car	1.77052	1.15833	1.52851	0.52882	3.34806
ant	1.94693	1.10794	1.75726	0.38961	4.99716
giu	2.67246	1.47513	1.81167	0.54867	4.87083
der	7.50740	5.47754	1.37058	2.27796	3.29567
res	6.15053	3.73420	1.64708	1.52262	4.03944

Table B.17 - Industry Lag 12, PHS Lag 15 (10% Depreciation)

Num of Obs	119
Log Likelihood	90.95091
Sum of Sqr Resid	128.9766
R-Squared	0.77126
Sigma Squared	0.83023

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-10.91476	7.94731	-1.37339	3.66732	-2.97622
currd	1.15814	0.96259	1.20314	0.57500	2.01415
lg1ird	-2.32845	1.32797	-1.75339	1.12025	-2.07851
lg2ird	1.67713	1.29882	1.29127	0.74274	2.25803
lg3ird	0.09544	1.29564	0.07367	0.55878	0.17081
lg4ird	1.10505	1.26067	0.87655	0.45044	2.45324
lg5ird	-1.78012	1.29367	-1.37603	0.76228	-2.33526
lg6ird	0.26553	1.31745	0.20155	1.21405	0.21872
lg7ird	1.06561	1.28613	0.82854	1.08098	0.98578
lg8ird	-1.10441	1.25807	-0.87786	0.42079	-2.62462
lg9ird	0.68592	1.13208	0.60589	0.21813	3.14454
lg10ird	-0.76637	1.11497	-0.68734	0.50874	-1.50640
lg11ird	-1.14414	1.10908	-1.03162	0.93813	-1.21960
lg12ird	1.78099	1.12820	1.57861	0.66474	2.67924
curreg	-0.16976	0.18204	-0.93251	0.12195	-1.39201
lagreg1	-0.09002	0.18279	-0.49246	0.17520	-0.51378
lagreg2	0.06449	0.18006	0.35815	0.04317	1.49388
lagreg3	0.15772	0.19226	0.82035	0.09996	1.57790
lagreg4	-0.20236	0.18605	-1.08766	0.15326	-1.32032
lagreg5	-0.06025	0.17424	-0.34580	0.13038	-0.46212
lagreg6	-0.13094	0.15097	-0.86733	0.12291	-1.06528
lagreg7	0.16903	0.14360	1.17709	0.08149	2.07416
lagreg8	-0.30930	0.13941	-2.21859	0.04212	-7.34401
lagreg9	-0.12142	0.13700	-0.88626	0.03838	-3.16357
PHS 15	1.50200	1.06714	1.40751	0.39970	3.75780
y79	-0.40782	0.49536	-0.82328	0.23495	-1.73579
y80	-0.77840	0.60383	-1.28912	0.47007	-1.65593
y81	-0.76025	0.64508	-1.17854	0.40540	-1.87533
y82	-0.90072	0.72684	-1.23922	0.35122	-2.56451
y83	-1.65155	0.85416	-1.93355	0.50959	-3.24093
y84	-1.44064	0.92523	-1.55706	0.33684	-4.27688
y85	-0.89868	0.94193	-0.95408	0.59504	-1.51028
y86	-2.03542	0.99763	-2.04027	0.48478	-4.19864
y87	-1.98985	1.03770	-1.91756	0.52424	-3.79570
y88	-1.80748	1.04904	-1.72298	0.61960	-2.91717
y89	-1.89399	1.08616	-1.74375	0.58077	-3.26114
y90	-2.15773	1.13803	-1.89603	0.48888	-4.41361
y91	-1.84184	1.20387	-1.52994	0.53230	-3.46014
y92	-2.00666	1.26566	-1.58547	0.64062	-3.13236
y93	-2.26822	1.32396	-1.71321	0.78134	-2.90298
y94	-2.71248	1.41052	-1.92303	0.74126	-3.65927
cns	1.62238	0.68044	2.38429	0.24671	6.57602
car	1.34781	0.77935	1.72940	0.30372	4.43768
ant	1.33773	0.77427	1.72773	0.20742	6.44932
giu	1.86643	1.12456	1.65970	0.50547	3.69250
der	4.44264	3.78859	1.17263	1.66626	2.66624
res	3.79072	2.69852	1.40474	1.23895	3.05963

Table B.18 - Industry Lag 12, PHS Lag 16 (10% Depreciation)

Num of Obs	119
Log Likelihood	91.27322
Sum of Sqr Resid	127.83786
R-Squared	0.77328
Sigma Squared	0.82032

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-13.13581	8.35885	-1.57149	4.49612	-2.92159
currd	1.11907	0.96557	1.15897	0.58642	1.90829
lg1ird	-2.36109	1.33056	-1.77450	1.09730	-2.15173
lg2ird	1.77761	1.30729	1.35977	0.75981	2.33956
lg3ird	0.09465	1.29974	0.07282	0.55053	0.17192
lg4ird	1.08091	1.26254	0.85614	0.43400	2.49056
lg5ird	-1.77711	1.29381	-1.37355	0.74531	-2.38439
lg6ird	0.27264	1.31818	0.20683	1.20209	0.22680
lg7ird	1.11118	1.27986	0.86821	1.06256	1.04576
lg8ird	-1.16437	1.25321	-0.92912	0.39961	-2.91377
lg9ird	0.70596	1.12726	0.62626	0.22533	3.13302
lg10ird	-0.77219	1.11060	-0.69529	0.52706	-1.46510
lg11ird	-1.15649	1.10171	-1.04973	0.92793	-1.24632
lg12ird	1.78001	1.12077	1.58820	0.66663	2.67016
curreg	-0.16109	0.18212	-0.88449	0.12142	-1.32674
lagreg1	-0.08236	0.18276	-0.45063	0.17373	-0.47405
lagreg2	0.06975	0.18003	0.38742	0.04049	1.72274
lagreg3	0.16652	0.19281	0.86364	0.09771	1.70417
lagreg4	-0.19178	0.18631	-1.02935	0.15453	-1.24105
lagreg5	-0.05527	0.17486	-0.31610	0.13286	-0.41601
lagreg6	-0.12773	0.15100	-0.84590	0.11932	-1.07044
lagreg7	0.16285	0.14373	1.13307	0.08212	1.98313
lagreg8	-0.31000	0.13941	-2.22370	0.04275	-7.25115
lagreg9	-0.11905	0.13683	-0.87007	0.03955	-3.01024
PHS 16	1.86008	1.14088	1.63038	0.51878	3.58550
y79	-0.50887	0.50929	-0.99919	0.24487	-2.07817
y80	-1.00585	0.66071	-1.52238	0.52008	-1.93402
y81	-1.03783	0.72465	-1.43217	0.47048	-2.20590
y82	-1.23492	0.82880	-1.49001	0.45151	-2.73508
y83	-2.06714	0.98588	-2.09674	0.57869	-3.57211
y84	-1.94308	1.09739	-1.77063	0.49576	-3.91936
y85	-1.46641	1.14785	-1.27753	0.74824	-1.95981
y86	-2.62191	1.20717	-2.17195	0.66248	-3.95775
y87	-2.57925	1.24374	-2.07378	0.67519	-3.82005
y88	-2.43209	1.27253	-1.91123	0.77077	-3.15541
y89	-2.50734	1.30038	-1.92816	0.76094	-3.29507
y90	-2.79801	1.35956	-2.05803	0.64931	-4.30917
y91	-2.44181	1.39845	-1.74608	0.70529	-3.46215
y92	-2.69251	1.49846	-1.79686	0.85161	-3.16167
y93	-2.96370	1.55677	-1.90375	0.98609	-3.00550
y94	-3.40410	1.63369	-2.08369	0.94740	-3.59310
cns	1.82190	0.71588	2.54498	0.29438	6.18884
car	1.52922	0.79324	1.92781	0.34663	4.41162
ant	1.56725	0.81353	1.92647	0.28488	5.50135
giu	2.17316	1.18360	1.83606	0.59749	3.63713
der	5.68148	4.04225	1.40552	2.09785	2.70824
res	4.77353	2.93894	1.62423	1.55770	3.06447

Table B.19 - Industry Lag 12, PHS Lag 17 (10% Depreciation)

Num of Obs	119
Log Likelihood	92.02087
Sum of Sqr Resid	123.94608
R-Squared	0.78018
Sigma Squared	0.80159

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-17.92620	9.19330	-1.94992	6.22171	-2.88123
currd	1.05714	0.97031	1.08948	0.59540	1.77552
lg1ird	-2.34999	1.33203	-1.76422	1.03860	-2.26265
lg2ird	1.86026	1.31372	1.41603	0.78162	2.38000
lg3ird	0.11775	1.30104	0.09050	0.50765	0.23194
lg4ird	1.08890	1.26601	0.86011	0.42978	2.53360
lg5ird	-1.80206	1.29154	-1.39528	0.75055	-2.40099
lg6ird	0.28072	1.32239	0.21228	1.17084	0.23976
lg7ird	1.08680	1.27718	0.85094	1.02858	1.05660
lg8ird	-1.17647	1.24438	-0.94543	0.39135	-3.00615
lg9ird	0.73812	1.11571	0.66157	0.21789	3.38761
lg10ird	-0.74629	1.10341	-0.67635	0.52927	-1.41004
lg11ird	-1.15571	1.09086	-1.05945	0.90620	-1.27533
lg12ird	1.76650	1.10893	1.59297	0.67135	2.63127
curreg	-0.13171	0.18349	-0.71783	0.11808	-1.11549
lagreg1	-0.06521	0.18299	-0.35634	0.17009	-0.38336
lagreg2	0.07908	0.17954	0.44047	0.03730	2.11994
lagreg3	0.17432	0.19320	0.90230	0.09756	1.78673
lagreg4	-0.16816	0.18787	-0.89508	0.15538	-1.08227
lagreg5	-0.04064	0.17582	-0.23116	0.13520	-0.30061
lagreg6	-0.11054	0.15203	-0.72710	0.12024	-0.91933
lagreg7	0.15749	0.14375	1.09563	0.08028	1.96172
lagreg8	-0.31529	0.13997	-2.25253	0.04389	-7.18286
lagreg9	-0.11536	0.13665	-0.84418	0.03791	-3.04272
PHS 17	2.57085	1.25760	2.04426	0.76250	3.37160
y79	-0.73340	0.53764	-1.36412	0.27794	-2.63867
y80	-1.43028	0.74282	-1.92547	0.59404	-2.40771
y81	-1.63346	0.86661	-1.88490	0.61760	-2.64485
y82	-1.91719	0.99205	-1.93255	0.64471	-2.97374
y83	-2.88038	1.18263	-2.43557	0.76539	-3.76330
y84	-2.91798	1.34872	-2.16351	0.79143	-3.68698
y85	-2.56219	1.44527	-1.77281	1.05849	-2.42060
y86	-3.80895	1.53507	-2.48129	1.03062	-3.69580
y87	-3.80041	1.57974	-2.40573	1.01468	-3.74542
y88	-3.68455	1.61929	-2.27541	1.10939	-3.32125
y89	-3.81694	1.66785	-2.28854	1.13549	-3.36148
y90	-4.10515	1.71600	-2.39229	1.04374	-3.93312
y91	-3.78834	1.76573	-2.14548	1.12123	-3.37873
y92	-4.01869	1.84129	-2.18254	1.26514	-3.17648
y93	-4.41857	1.94920	-2.26686	1.43076	-3.08826
y94	-4.86673	2.01969	-2.40964	1.41573	-3.43760
cns	2.20918	0.76896	2.87295	0.40979	5.39106
car	1.88761	0.82001	2.30193	0.45198	4.17635
ant	2.03364	0.88307	2.30292	0.45491	4.47038
giu	2.84938	1.30609	2.18161	0.81117	3.51266
der	8.23793	4.48470	1.83689	2.94873	2.79372
res	6.75882	3.32466	2.03293	2.19678	3.07669

Table B.20 - Industry Lag 12, PHS Lag 18 (10% Depreciation)

Num of Obs	119
Log Likelihood	91.86941
Sum of Sqr Resid	124.87125
R-Squared	0.77854
Sigma Squared	0.79892

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-19.52824	10.26496	-1.90242	8.48044	-2.30274
currd	1.27215	0.95653	1.32996	0.50885	2.50004
lg1ird	-2.55308	1.33879	-1.90700	0.99253	-2.57229
lg2ird	1.84067	1.30885	1.40633	0.79105	2.32688
lg3ird	0.23537	1.30215	0.18075	0.45338	0.51914
lg4ird	1.10546	1.26308	0.87521	0.45065	2.45304
lg5ird	-1.72034	1.28617	-1.33757	0.73083	-2.35397
lg6ird	0.07425	1.31914	0.05629	1.11417	0.06664
lg7ird	1.22581	1.28113	0.95682	0.99074	1.23726
lg8ird	-1.14997	1.24311	-0.92508	0.38482	-2.98831
lg9ird	0.78619	1.11444	0.70546	0.25863	3.03987
lg10ird	-0.73152	1.09316	-0.66918	0.53225	-1.37440
lg11ird	-1.09419	1.08759	-1.00607	0.92102	-1.18802
lg12ird	1.63519	1.09549	1.49265	0.63825	2.56201
currreg	-0.11973	0.18400	-0.65074	0.11706	-1.02283
lagreg1	-0.04169	0.18483	-0.22559	0.17585	-0.23711
lagreg2	0.09924	0.18083	0.54880	0.04288	2.31462
lagreg3	0.17302	0.19296	0.89662	0.09693	1.78499
lagreg4	-0.15230	0.18839	-0.80841	0.15408	-0.98846
lagreg5	-0.01950	0.17675	-0.11033	0.14016	-0.13913
lagreg6	-0.10249	0.15302	-0.66979	0.12319	-0.83203
lagreg7	0.16390	0.14422	1.13652	0.08595	1.90697
lagreg8	-0.30528	0.14016	-2.17818	0.04652	-6.56252
lagreg9	-0.11456	0.13690	-0.83685	0.03199	-3.58124
PHS 18	2.71591	1.39315	1.94948	1.03097	2.63432
y79	-0.80041	0.56416	-1.41877	0.33469	-2.39150
y80	-1.59192	0.82398	-1.93198	0.72313	-2.20142
y81	-1.90134	1.01880	-1.86624	0.76432	-2.48760
y82	-2.33254	1.22240	-1.90817	0.95173	-2.45085
y83	-3.31322	1.42655	-2.32253	1.04155	-3.18103
y84	-3.39997	1.62934	-2.08671	1.19487	-2.84547
y85	-3.17506	1.79958	-1.76434	1.47834	-2.14772
y86	-4.50647	1.93171	-2.33289	1.49619	-3.01196
y87	-4.58421	2.01957	-2.26989	1.53991	-2.97694
y88	-4.49658	2.07627	-2.16570	1.61719	-2.78049
y89	-4.65301	2.13918	-2.17514	1.71720	-2.70965
y90	-4.99556	2.21090	-2.25951	1.64028	-3.04555
y91	-4.64545	2.24524	-2.06902	1.71440	-2.70966
y92	-4.91479	2.33918	-2.10107	1.89915	-2.58788
y93	-5.24417	2.41406	-2.17234	1.99825	-2.62438
y94	-5.78203	2.52297	-2.29175	2.00806	-2.87941
cns	2.25807	0.82200	2.74704	0.49591	4.55336
car	1.87502	0.84618	2.21588	0.53816	3.48415
ant	2.14925	0.97812	2.19733	0.66632	3.22556
giu	3.15569	1.47045	2.14607	1.10965	2.84387
der	8.98716	5.03945	1.78336	3.96852	2.26461
res	7.40153	3.79242	1.95166	2.92295	2.53221

Table B.21 - Industry Lag 12, PHS Lag 19 (10% Depreciation)

Num of Obs	119
Log Likelihood	91.49206
Sum of Sqr Resid	128.31454
R-Squared	0.77243
Sigma Squared	0.80293

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-18.48680	10.84420	-1.70476	9.90491	-1.86643
currd	1.45076	0.94811	1.53017	0.42888	3.38266
lg1ird	-2.52730	1.33912	-1.88728	0.99643	-2.53635
lg2ird	1.58924	1.29063	1.23137	0.73368	2.16613
lg3ird	0.35322	1.30255	0.27117	0.41514	0.85084
lg4ird	1.15253	1.26425	0.91163	0.43644	2.64077
lg5ird	-1.61858	1.28280	-1.26175	0.66675	-2.42759
lg6ird	-0.06387	1.32366	-0.04825	1.09165	-0.05851
lg7ird	1.24704	1.28452	0.97082	0.97572	1.27808
lg8ird	-1.03344	1.24463	-0.83032	0.37187	-2.77901
lg9ird	0.75256	1.11714	0.67365	0.25373	2.96596
lg10ird	-0.67003	1.09604	-0.61132	0.47688	-1.40503
lg11ird	-1.07854	1.08724	-0.99200	0.89161	-1.20966
lg12ird	1.58153	1.09360	1.44617	0.60349	2.62066
curreg	-0.13069	0.18316	-0.71353	0.12190	-1.07206
lagreg1	-0.04305	0.18531	-0.23230	0.17974	-0.23951
lagreg2	0.12032	0.18411	0.65353	0.05515	2.18167
lagreg3	0.17069	0.19330	0.88302	0.09446	1.80698
lagreg4	-0.15378	0.18774	-0.81910	0.15628	-0.98401
lagreg5	-0.01285	0.17691	-0.07265	0.14373	-0.08942
lagreg6	-0.08942	0.15548	-0.57514	0.12700	-0.70411
lagreg7	0.16854	0.14461	1.16547	0.09142	1.84369
lagreg8	-0.28138	0.14101	-1.99541	0.05417	-5.19477
lagreg9	-0.10040	0.13697	-0.73300	0.03737	-2.68696
PHS 19	2.40882	1.40569	1.71363	1.17855	2.04388
y79	-0.73779	0.57028	-1.29374	0.37871	-1.94819
y80	-1.48210	0.84504	-1.75388	0.81110	-1.82727
y81	-1.81409	1.08676	-1.66927	0.88043	-2.06044
y82	-2.29579	1.34864	-1.70230	1.17262	-1.95782
y83	-3.32898	1.60526	-2.07380	1.34703	-2.47135
y84	-3.34442	1.79679	-1.86133	1.51402	-2.20897
y85	-3.14609	2.01010	-1.56514	1.83188	-1.71741
y86	-4.54115	2.19396	-2.06984	1.86686	-2.43251
y87	-4.68400	2.32883	-2.01131	2.02614	-2.31179
y88	-4.65444	2.42715	-1.91766	2.13228	-2.18285
y89	-4.82310	2.50425	-1.92597	2.26403	-2.13032
y90	-5.17207	2.58633	-1.99978	2.20720	-2.34327
y91	-4.85263	2.64042	-1.83782	2.27510	-2.13293
y92	-5.08082	2.71870	-1.86884	2.45248	-2.07171
y93	-5.43146	2.81162	-1.93179	2.55165	-2.12861
y94	-5.87297	2.87167	-2.04514	2.51288	-2.33715
cns	2.05001	0.80798	2.53720	0.55505	3.69334
car	1.61527	0.80632	2.00326	0.57592	2.80468
ant	1.97411	1.00255	1.96910	0.78995	2.49902
giu	3.12039	1.59596	1.95518	1.37031	2.27715
der	8.24732	5.27601	1.56317	4.67835	1.76287
res	6.87557	3.99614	1.72055	3.45119	1.99223

Table B.22 - Industry Lag 12, PHS Lag 20 (10% Depreciation)

Num of Obs	119
Log Likelihood	90.83492
Sum of Sqr Resid	132.15497
R-Squared	0.76562
Sigma Squared	0.81439

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-13.76404	10.45397	-1.31663	9.59022	-1.43522
currd	1.57795	0.94665	1.66688	0.41637	3.78975
lg1ird	-2.53202	1.33878	-1.89129	1.04546	-2.42193
lg2ird	1.50987	1.28563	1.17442	0.73787	2.04624
lg3ird	0.31569	1.30123	0.24261	0.43556	0.72478
lg4ird	1.19953	1.26407	0.94894	0.46871	2.55923
lg5ird	-1.58277	1.28677	-1.23003	0.66929	-2.36483
lg6ird	-0.09813	1.32936	-0.07382	1.13043	-0.08681
lg7ird	1.28424	1.29043	0.99520	0.95171	1.34940
lg8ird	-0.97389	1.24789	-0.78043	0.37582	-2.59138
lg9ird	0.74747	1.12923	0.66193	0.26630	2.80684
lg10ird	-0.71074	1.10366	-0.64399	0.47087	-1.50942
lg11ird	-1.04324	1.09982	-0.94855	0.93974	-1.11014
lg12ird	1.55021	1.09583	1.41464	0.59516	2.60470
curreg	-0.16474	0.18095	-0.91043	0.12884	-1.27869
lagreg1	-0.07352	0.18351	-0.40063	0.17903	-0.41065
lagreg2	0.10489	0.18545	0.56559	0.05555	1.88805
lagreg3	0.16355	0.19317	0.84663	0.09181	1.78137
lagreg4	-0.16750	0.18694	-0.89601	0.15196	-1.10226
lagreg5	-0.02514	0.17597	-0.14285	0.14106	-0.17820
lagreg6	-0.11095	0.15429	-0.71909	0.12345	-0.89876
lagreg7	0.17781	0.14520	1.22456	0.09513	1.86903
lagreg8	-0.27403	0.14199	-1.92993	0.05462	-5.01660
lagreg9	-0.08939	0.13812	-0.64718	0.04589	-1.94787
PHS 20	1.62427	1.26758	1.28139	1.10867	1.46506
y79	-0.51507	0.54195	-0.95041	0.35705	-1.44258
y80	-1.07116	0.78245	-1.36898	0.78359	-1.36698
y81	-1.27103	1.01509	-1.25214	0.83450	-1.52310
y82	-1.68294	1.30848	-1.28618	1.20372	-1.39811
y83	-2.62751	1.57752	-1.66560	1.38543	-1.89654
y84	-2.56966	1.77853	-1.44483	1.58557	-1.62065
y85	-2.26287	1.98411	-1.14050	1.88067	-1.20323
y86	-3.60325	2.18467	-1.64933	1.92882	-1.86811
y87	-3.73376	2.35278	-1.58696	2.15520	-1.73244
y88	-3.69773	2.47836	-1.49201	2.26595	-1.63187
y89	-3.87933	2.58864	-1.49860	2.45982	-1.57708
y90	-4.21215	2.68026	-1.57154	2.40985	-1.74788
y91	-3.87520	2.73665	-1.41604	2.45417	-1.57903
y92	-4.10268	2.83268	-1.44834	2.63021	-1.55983
y93	-4.39225	2.90156	-1.51376	2.67413	-1.64250
y94	-4.84088	2.97728	-1.62594	2.65328	-1.82449
cns	1.61674	0.73175	2.20940	0.53313	3.03256
car	1.15476	0.70749	1.63219	0.52061	2.21807
ant	1.46372	0.93173	1.57098	0.76209	1.92068
giu	2.55263	1.60732	1.58813	1.42799	1.78756
der	5.68986	5.03860	1.12925	4.61781	1.23215
res	4.95038	3.81527	1.29752	3.41802	1.44832

Table B.23 - Industry Lag 12, PHS Lag 15 (20% Depreciation)

Num of Obs	119
Log Likelihood	90.77965
Sum of Sqr Resid	129.45617
R-Squared	0.77041
Sigma Squared	0.83427

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-7.66510	6.51472	-1.17658	2.99916	-2.55575
curird	1.16316	0.96364	1.20704	0.58308	1.99485
lg1ird	-2.30456	1.32653	-1.73729	1.13612	-2.02844
lg2ird	1.65123	1.29571	1.27438	0.74172	2.22624
lg3ird	0.08750	1.29468	0.06759	0.56708	0.15431
lg4ird	1.10484	1.25946	0.87724	0.45417	2.43265
lg5ird	-1.79763	1.29561	-1.38748	0.77618	-2.31601
lg6ird	0.26959	1.31831	0.20450	1.23290	0.21866
lg7ird	1.05945	1.28988	0.82136	1.09344	0.96891
lg8ird	-1.07895	1.26014	-0.85622	0.43470	-2.48208
lg9ird	0.67974	1.13528	0.59874	0.21666	3.13739
lg10ird	-0.76571	1.11751	-0.68520	0.50602	-1.51321
lg11ird	-1.14118	1.11253	-1.02575	0.94680	-1.20530
lg12ird	1.77062	1.13134	1.56507	0.66458	2.66428
curreg	-0.17405	0.18194	-0.95664	0.12176	-1.42941
lagreg1	-0.09670	0.18270	-0.52929	0.17593	-0.54965
lagreg2	0.05416	0.17965	0.30146	0.04370	1.23940
lagreg3	0.14933	0.19160	0.77939	0.10010	1.49191
lagreg4	-0.20952	0.18587	-1.12723	0.15361	-1.36392
lagreg5	-0.06475	0.17406	-0.37199	0.12758	-0.50754
lagreg6	-0.13691	0.15066	-0.90879	0.12244	-1.11824
lagreg7	0.16851	0.14369	1.17272	0.08463	1.99116
lagreg8	-0.31134	0.13947	-2.23225	0.04088	-7.61647
lagreg9	-0.12370	0.13722	-0.90142	0.03853	-3.21074
PHS 15	1.10139	0.86322	1.27591	0.31034	3.54897
y79	-0.32533	0.48045	-0.67713	0.22526	-1.44425
y80	-0.61573	0.55579	-1.10785	0.44269	-1.39087
y81	-0.52963	0.55562	-0.95322	0.36247	-1.46115
y82	-0.60626	0.60311	-1.00522	0.29431	-2.05993
y83	-1.29640	0.70539	-1.83786	0.44626	-2.90505
y84	-1.02413	0.74096	-1.38216	0.25928	-3.94993
y85	-0.42380	0.72283	-0.58630	0.48711	-0.87002
y86	-1.50866	0.75776	-1.99094	0.36217	-4.16563
y87	-1.42197	0.78097	-1.82078	0.40314	-3.52725
y88	-1.19998	0.77411	-1.55013	0.48879	-2.45498
y89	-1.25721	0.79856	-1.57434	0.46031	-2.73125
y90	-1.49125	0.84576	-1.76321	0.36261	-4.11256
y91	-1.16282	0.90244	-1.28853	0.38904	-2.98892
y92	-1.29402	0.95587	-1.35377	0.49040	-2.63872
y93	-1.53096	1.00952	-1.51653	0.60785	-2.51866
y94	-1.95970	1.09580	-1.78837	0.54417	-3.60127
cns	1.40570	0.58600	2.39879	0.20817	6.75256
car	1.14077	0.69871	1.63268	0.27045	4.21799
ant	1.07145	0.65101	1.64583	0.15308	6.99921
giu	1.51181	1.00301	1.50727	0.44198	3.42053
der	3.03698	3.12230	0.97268	1.33928	2.26763
res	2.69447	2.16229	1.24612	0.98101	2.74662

Table B.24 - Industry Lag 12, PHS Lag 16 (20% Depreciation)

Num of Obs	119
Log Likelihood	91.08372
Sum of Sqr Resid	128.52412
R-Squared	0.77206
Sigma Squared	0.82435

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-9.08930	6.70342	-1.35592	3.43112	-2.64908
currd	1.09929	0.96950	1.13387	0.60204	1.82593
lg1ird	-2.33204	1.32881	-1.75499	1.11916	-2.08375
lg2ird	1.76961	1.30657	1.35440	0.75876	2.33224
lg3ird	0.07605	1.29903	0.05854	0.56662	0.13421
lg4ird	1.07752	1.26154	0.85413	0.43718	2.46468
lg5ird	-1.80922	1.29631	-1.39567	0.76110	-2.37712
lg6ird	0.29854	1.31945	0.22626	1.22760	0.24319
lg7ird	1.09344	1.28257	0.85254	1.08139	1.01114
lg8ird	-1.14877	1.25705	-0.91386	0.41174	-2.79004
lg9ird	0.69514	1.13141	0.61441	0.22272	3.12114
lg10ird	-0.77660	1.11417	-0.69702	0.52927	-1.46731
lg11ird	-1.15351	1.10605	-1.04292	0.93888	-1.22861
lg12ird	1.77702	1.12502	1.57955	0.66813	2.65969
curreg	-0.16578	0.18205	-0.91059	0.12116	-1.36823
lagreg1	-0.08889	0.18283	-0.48619	0.17521	-0.50731
lagreg2	0.05722	0.17965	0.31849	0.04133	1.38424
lagreg3	0.15692	0.19205	0.81710	0.09795	1.60200
lagreg4	-0.20293	0.18596	-1.09130	0.15479	-1.31105
lagreg5	-0.06323	0.17468	-0.36195	0.13018	-0.48566
lagreg6	-0.13553	0.15057	-0.90013	0.11790	-1.14953
lagreg7	0.16125	0.14381	1.12126	0.08516	1.89338
lagreg8	-0.31435	0.13944	-2.25432	0.04124	-7.62265
lagreg9	-0.12270	0.13702	-0.89548	0.03979	-3.08363
PHS 16	1.37294	0.91211	1.50524	0.38340	3.58095
y79	-0.40218	0.48922	-0.82209	0.23086	-1.74211
y80	-0.79744	0.59821	-1.33305	0.48240	-1.65306
y81	-0.73626	0.61071	-1.20558	0.40991	-1.79615
y82	-0.84352	0.66990	-1.25917	0.35909	-2.34903
y83	-1.59451	0.79324	-2.01013	0.48509	-3.28705
y84	-1.39203	0.86234	-1.61426	0.36141	-3.85170
y85	-0.83787	0.86868	-0.96453	0.58895	-1.42264
y86	-1.91980	0.89641	-2.14164	0.48009	-3.99882
y87	-1.81219	0.90513	-2.00213	0.49033	-3.69585
y88	-1.61076	0.90668	-1.77654	0.57435	-2.80447
y89	-1.63367	0.91303	-1.78928	0.55359	-2.95104
y90	-1.88489	0.96201	-1.95932	0.42673	-4.41703
y91	-1.49600	0.98955	-1.51179	0.46592	-3.21084
y92	-1.72055	1.07996	-1.59315	0.59990	-2.86805
y93	-1.95287	1.12795	-1.73135	0.71750	-2.72177
y94	-2.36722	1.20347	-1.96699	0.65680	-3.60418
cns	1.56137	0.60955	2.56150	0.23603	6.61527
car	1.28880	0.70314	1.83292	0.29315	4.39645
ant	1.23895	0.67080	1.84696	0.19186	6.45740
giu	1.70916	1.02849	1.66181	0.48443	3.52818
der	3.92801	3.26695	1.20235	1.60876	2.44165
res	3.39270	2.31218	1.46732	1.18285	2.86824

Table B.25 - Industry Lag 12, PHS Lag 17 (20% Depreciation)

Num of Obs	119
Log Likelihood	91.90392
Sum of Sqr Resid	124.13129
R-Squared	0.77985
Sigma Squared	0.80258

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-12.78483	7.24538	-1.76455	4.24606	-3.01099
currd	0.96013	0.98105	0.97867	0.63322	1.51626
lg1ird	-2.28754	1.33096	-1.71871	1.06388	-2.15018
lg2ird	1.89096	1.31650	1.43636	0.78242	2.41682
lg3ird	0.07156	1.30038	0.05503	0.53374	0.13407
lg4ird	1.08089	1.26525	0.85429	0.43029	2.51198
lg5ird	-1.86766	1.29568	-1.44145	0.77130	-2.42146
lg6ird	0.36269	1.32467	0.27380	1.20668	0.30057
lg7ird	1.03579	1.27897	0.80987	1.05234	0.98427
lg8ird	-1.18560	1.24864	-0.94951	0.40862	-2.90149
lg9ird	0.71562	1.11989	0.63902	0.20951	3.41576
lg10ird	-0.75435	1.10850	-0.68051	0.53923	-1.39893
lg11ird	-1.16381	1.09549	-1.06237	0.92000	-1.26501
lg12ird	1.79026	1.11445	1.60641	0.68271	2.62228
curreg	-0.13176	0.18382	-0.71677	0.11615	-1.13436
lagreg1	-0.07075	0.18315	-0.38629	0.17139	-0.41279
lagreg2	0.06153	0.17915	0.34346	0.03714	1.65694
lagreg3	0.16330	0.19232	0.84910	0.09702	1.68311
lagreg4	-0.18432	0.18726	-0.98429	0.15487	-1.19011
lagreg5	-0.05493	0.17558	-0.31282	0.13207	-0.41588
lagreg6	-0.12214	0.15128	-0.80741	0.11612	-1.05182
lagreg7	0.15371	0.14379	1.06903	0.08195	1.87582
lagreg8	-0.32673	0.14015	-2.33134	0.04331	-7.54406
lagreg9	-0.12300	0.13680	-0.89914	0.03841	-3.20276
PHS 17	2.00149	1.00721	1.98716	0.53468	3.74336
y79	-0.60876	0.51138	-1.19044	0.24757	-2.45897
y80	-1.18364	0.66744	-1.77341	0.52601	-2.25020
y81	-1.25991	0.72861	-1.72920	0.51196	-2.46097
y82	-1.40440	0.79347	-1.76994	0.47061	-2.98421
y83	-2.25796	0.94087	-2.39986	0.58173	-3.88145
y84	-2.20115	1.06118	-2.07425	0.53809	-4.09071
y85	-1.73153	1.10290	-1.56998	0.77318	-2.23947
y86	-2.87240	1.14982	-2.49814	0.71892	-3.99542
y87	-2.75623	1.15076	-2.39513	0.67530	-4.08148
y88	-2.54898	1.15049	-2.21555	0.74521	-3.42046
y89	-2.60238	1.16677	-2.23043	0.73585	-3.53657
y90	-2.80988	1.18906	-2.36311	0.60674	-4.63108
y91	-2.44597	1.22156	-2.00234	0.67203	-3.63967
y92	-2.61800	1.27922	-2.04657	0.78871	-3.31935
y93	-2.99301	1.37836	-2.17144	0.94657	-3.16195
y94	-3.39641	1.44107	-2.35686	0.91526	-3.71087
cns	1.91179	0.65194	2.93244	0.31669	6.03681
car	1.63372	0.72370	2.25747	0.36283	4.50270
ant	1.63656	0.71923	2.27544	0.28464	5.74951
giu	2.23407	1.10257	2.02624	0.58123	3.84371
der	6.09558	3.59599	1.69510	2.09562	2.90872
res	5.03791	2.59854	1.93875	1.56035	3.22871

Table B.26 - Industry Lag 12, PHS Lag 18 (20% Depreciation)

Num of Obs	119
Log Likelihood	91.83871
Sum of Sqr Resid	124.00166
R-Squared	0.78008
Sigma Squared	0.79865

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-14.62530	8.10106	-1.80535	5.79942	-2.52186
curird	1.13502	0.96638	1.17450	0.56330	2.01493
lg1ird	-2.51553	1.33699	-1.88149	1.01323	-2.48270
lg2ird	1.93091	1.31799	1.46505	0.80842	2.38851
lg3ird	0.17005	1.30169	0.13064	0.48612	0.34982
lg4ird	1.09162	1.26174	0.86517	0.44889	2.43179
lg5ird	-1.79441	1.28978	-1.39125	0.75738	-2.36924
lg6ird	0.18083	1.31780	0.13722	1.15162	0.15702
lg7ird	1.17339	1.27969	0.91694	1.01940	1.15107
lg8ird	-1.19120	1.24737	-0.95497	0.40668	-2.92912
lg9ird	0.76811	1.11705	0.68762	0.25104	3.05965
lg10ird	-0.75517	1.09752	-0.68806	0.56342	-1.34034
lg11ird	-1.10178	1.09088	-1.00999	0.93444	-1.17908
lg12ird	1.66074	1.09925	1.51080	0.64976	2.55592
curreg	-0.11238	0.18507	-0.60725	0.11228	-1.00088
lagreg1	-0.03954	0.18554	-0.21309	0.17641	-0.22411
lagreg2	0.08283	0.17992	0.46035	0.03679	2.25119
lagreg3	0.16480	0.19210	0.85785	0.09422	1.74910
lagreg4	-0.16725	0.18758	-0.89163	0.15134	-1.10511
lagreg5	-0.03440	0.17622	-0.19520	0.13245	-0.25971
lagreg6	-0.11651	0.15190	-0.76704	0.11651	-1.00005
lagreg7	0.15791	0.14421	1.09495	0.08773	1.79994
lagreg8	-0.32277	0.14021	-2.30208	0.04387	-7.35771
lagreg9	-0.12757	0.13718	-0.92994	0.03076	-4.14735
PHS 18	2.22707	1.14431	1.94621	0.71642	3.10862
y79	-0.70661	0.53832	-1.31261	0.28920	-2.44331
y80	-1.39918	0.75000	-1.86558	0.61730	-2.26662
y81	-1.58584	0.87796	-1.80629	0.60937	-2.60241
y82	-1.87098	1.00911	-1.85409	0.69140	-2.70606
y83	-2.73041	1.15768	-2.35853	0.75513	-3.61584
y84	-2.73209	1.31488	-2.07783	0.82002	-3.33174
y85	-2.39363	1.42476	-1.68003	1.06172	-2.25449
y86	-3.61297	1.50355	-2.40295	1.03457	-3.49224
y87	-3.57332	1.53642	-2.32575	1.02471	-3.48716
y88	-3.37570	1.54018	-2.19176	1.06784	-3.16124
y89	-3.43330	1.55694	-2.20516	1.11111	-3.08997
y90	-3.68232	1.58845	-2.31819	0.99422	-3.70374
y91	-3.25393	1.58877	-2.04808	1.04544	-3.11250
y92	-3.46216	1.65799	-2.08816	1.19605	-2.89467
y93	-3.73489	1.71048	-2.18354	1.28682	-2.90242
y94	-4.26318	1.81928	-2.34333	1.28698	-3.31254
cns	2.00817	0.70413	2.85198	0.35502	5.65648
car	1.67831	0.75413	2.22549	0.40711	4.12245
ant	1.78954	0.80604	2.22017	0.42833	4.17791
giu	2.54355	1.22134	2.08258	0.78458	3.24193
der	7.03314	4.09172	1.71887	2.80765	2.50499
res	5.80281	3.00824	1.92897	2.03939	2.84536

Table B.27 - Industry Lag 12, PHS Lag 19 (20% Depreciation)

Num of Obs	119
Log Likelihood	91.54301
Sum of Sqr Resid	126.70392
R-Squared	0.77529
Sigma Squared	0.8033

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-15.32770	9.01573	-1.70011	7.87571	-1.94620
currd	1.29249	0.95450	1.35411	0.49233	2.62526
lg1ird	-2.48482	1.33821	-1.85682	1.00124	-2.48174
lg2ird	1.66535	1.29580	1.28519	0.74968	2.22140
lg3ird	0.31886	1.30260	0.24479	0.43051	0.74068
lg4ird	1.12336	1.26350	0.88909	0.42246	2.65907
lg5ird	-1.67524	1.28327	-1.30544	0.67945	-2.46558
lg6ird	0.04258	1.31934	0.03227	1.11622	0.03815
lg7ird	1.19066	1.28196	0.92878	1.01186	1.17671
lg8ird	-1.08068	1.24669	-0.86684	0.38435	-2.81174
lg9ird	0.73515	1.11650	0.65844	0.24228	3.03430
lg10ird	-0.68537	1.09722	-0.62464	0.51135	-1.34031
lg11ird	-1.09708	1.08628	-1.00995	0.88839	-1.23491
lg12ird	1.60645	1.09505	1.46701	0.61107	2.62890
curreg	-0.11564	0.18490	-0.62544	0.11339	-1.01989
lagreg1	-0.03112	0.18695	-0.16644	0.18220	-0.17077
lagreg2	0.11702	0.18360	0.63735	0.05047	2.31862
lagreg3	0.16980	0.19305	0.87956	0.09106	1.86466
lagreg4	-0.16329	0.18706	-0.87297	0.15595	-1.04707
lagreg5	-0.02262	0.17652	-0.12813	0.13454	-0.16811
lagreg6	-0.09516	0.15478	-0.61480	0.12299	-0.77373
lagreg7	0.16101	0.14466	1.11301	0.09375	1.71747
lagreg8	-0.29975	0.14039	-2.13516	0.04910	-6.10520
lagreg9	-0.11542	0.13683	-0.84354	0.03253	-3.54841
PHS 19	2.17987	1.23593	1.76376	0.97196	2.24276
y79	-0.72509	0.56046	-1.29374	0.36251	-2.00021
y80	-1.44291	0.81283	-1.77517	0.75053	-1.92253
y81	-1.71068	1.00843	-1.69638	0.79864	-2.14198
y82	-2.08911	1.20625	-1.73191	0.99253	-2.10483
y83	-3.04384	1.41373	-2.15306	1.16110	-2.62152
y84	-2.99686	1.56382	-1.91638	1.23434	-2.42791
y85	-2.71884	1.72459	-1.57651	1.53096	-1.77591
y86	-4.03762	1.86124	-2.16931	1.50641	-2.68029
y87	-4.08695	1.94249	-2.10397	1.61697	-2.52754
y88	-3.96782	1.98891	-1.99497	1.69710	-2.33800
y89	-4.03989	2.01229	-2.00761	1.74760	-2.31168
y90	-4.28990	2.04154	-2.10130	1.66271	-2.58007
y91	-3.89840	2.05585	-1.89625	1.69430	-2.30089
y92	-4.04472	2.09231	-1.93314	1.83363	-2.20586
y93	-4.35183	2.16267	-2.01225	1.94164	-2.24131
y94	-4.75623	2.20560	-2.15644	1.89042	-2.51596
cns	1.93510	0.72543	2.66754	0.46442	4.16674
car	1.55081	0.75153	2.06355	0.50453	3.07379
ant	1.77606	0.87266	2.03522	0.61548	2.88564
giu	2.71681	1.36791	1.98610	1.12220	2.42095
der	7.17141	4.53728	1.58055	3.88467	1.84608
res	5.94521	3.37069	1.76380	2.82734	2.10276

Table B.28 - Industry Lag 12, PHS Lag 20 (20% Depreciation)

Num of Obs	119
Log Likelihood	90.80243
Sum of Sqr Resid	131.17883
R-Squared	0.76735
Sigma Squared	0.81526

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-12.30732	9.48287	-1.29785	9.21307	-1.33585
currd	1.48427	0.94267	1.57454	0.43518	3.41067
lg1ird	-2.51883	1.33877	-1.88145	1.03669	-2.42968
lg2ird	1.57639	1.28928	1.22270	0.75135	2.09807
lg3ird	0.27568	1.30078	0.21193	0.44111	0.62497
lg4ird	1.19411	1.26379	0.94486	0.46437	2.57146
lg5ird	-1.61488	1.28550	-1.25623	0.66763	-2.41881
lg6ird	-0.04915	1.32402	-0.03712	1.12763	-0.04358
lg7ird	1.26486	1.28837	0.98175	0.97071	1.30303
lg8ird	-1.01220	1.24956	-0.81005	0.37596	-2.69234
lg9ird	0.75695	1.12868	0.67065	0.26654	2.83992
lg10ird	-0.73141	1.10265	-0.66332	0.50087	-1.46027
lg11ird	-1.04548	1.09740	-0.95269	0.94735	-1.10359
lg12ird	1.55875	1.09468	1.42393	0.59135	2.63594
curreg	-0.15795	0.18156	-0.86996	0.12406	-1.27317
lagreg1	-0.06368	0.18519	-0.34387	0.18402	-0.34607
lagreg2	0.10829	0.18641	0.58095	0.05838	1.85499
lagreg3	0.16834	0.19394	0.86799	0.08820	1.90867
lagreg4	-0.17418	0.18630	-0.93497	0.15282	-1.13978
lagreg5	-0.03152	0.17564	-0.17944	0.13427	-0.23472
lagreg6	-0.11298	0.15448	-0.73132	0.12381	-0.91249
lagreg7	0.17580	0.14537	1.20930	0.09589	1.83340
lagreg8	-0.28904	0.14089	-2.05145	0.05016	-5.76214
lagreg9	-0.10000	0.13740	-0.72780	0.03994	-2.50344
PHS 20	1.56730	1.23102	1.27317	1.14751	1.36583
y79	-0.53959	0.55346	-0.97495	0.39935	-1.35117
y80	-1.11464	0.81256	-1.37176	0.84802	-1.31441
y81	-1.30447	1.04424	-1.24920	0.93747	-1.39148
y82	-1.67868	1.31254	-1.27895	1.28448	-1.30690
y83	-2.59117	1.55869	-1.66240	1.50247	-1.72461
y84	-2.50752	1.74040	-1.44078	1.64563	-1.52374
y85	-2.14928	1.90730	-1.12687	1.94772	-1.10348
y86	-3.45511	2.08253	-1.65909	1.97013	-1.75375
y87	-3.53853	2.21690	-1.59616	2.18073	-1.62264
y88	-3.45178	2.30403	-1.49815	2.28224	-1.51245
y89	-3.58104	2.37482	-1.50792	2.40847	-1.48685
y90	-3.84200	2.41374	-1.59172	2.33788	-1.64337
y91	-3.44891	2.42800	-1.42047	2.34123	-1.47311
y92	-3.62304	2.48543	-1.45771	2.48611	-1.45731
y93	-3.86059	2.51744	-1.53354	2.52810	-1.52707
y94	-4.29798	2.58530	-1.66247	2.52146	-1.70456
cns	1.59139	0.71469	2.22668	0.57342	2.77524
car	1.15699	0.71017	1.62919	0.57437	2.01436
ant	1.38120	0.87898	1.57136	0.74137	1.86305
giu	2.37813	1.48991	1.59615	1.42265	1.67162
der	5.33482	4.77761	1.11663	4.73159	1.12749
res	4.60217	3.56235	1.29189	3.48257	1.32149

Table B.29 - CES Estimation, Industry Stock, PHS Lag 17

Num of Obs	119
Log Likelihood	85.60683
Sum of Sqr Resid	157.39969
R-Squared	0.72085
Sigma Squared	0.86354

Parameter	Estimate	Poisson Std Err	Poisson t-stat	Robust Std Err	Robust t-stat
one	-12.57139	7.34271	-1.71209	3.43194	-3.66306
pmastk	0.37727	0.60367	0.62495	0.08840	4.26772
curreg	-0.00160	0.16680	-0.00959	0.11096	-0.01441
lagreg1	-0.07798	0.17226	-0.45271	0.19918	-0.39151
lagreg2	0.01255	0.17057	0.07356	0.06404	0.19591
lagreg3	0.10685	0.17085	0.62539	0.08246	1.29580
lagreg4	-0.10738	0.17491	-0.61392	0.11282	-0.95177
lagreg5	0.04804	0.16374	0.29341	0.08669	0.55420
lagreg6	-0.17629	0.13971	-1.26185	0.08480	-2.07888
lagreg7	0.00773	0.13460	0.05746	0.06765	0.11432
lagreg8	-0.21319	0.13068	-1.63131	0.07941	-2.68475
lagreg9	-0.09284	0.12469	-0.74457	0.06190	-1.49975
Sub. Term "ln IB"	-0.39956	0.38627	-1.03441	0.18243	-2.19025
PHS 17	2.17691	1.07206	2.03059	0.51710	4.20987
y79	-0.80972	0.47188	-1.71595	0.19330	-4.18897
y80	-1.29032	0.62151	-2.07609	0.41322	-3.12261
y81	-1.18566	0.72201	-1.64216	0.30088	-3.94057
y82	-1.44470	0.84000	-1.71987	0.33353	-4.33158
y83	-2.23738	0.97755	-2.28875	0.44679	-5.00762
y84	-2.28497	1.07709	-2.12143	0.37905	-6.02818
y85	-1.98746	1.14403	-1.73724	0.50197	-3.95934
y86	-2.67459	1.20855	-2.21305	0.50347	-5.31229
y87	-2.75211	1.25028	-2.20120	0.49959	-5.50873
y88	-2.88482	1.27791	-2.25745	0.54848	-5.25969
y89	-2.83874	1.31414	-2.16016	0.63553	-4.46674
y90	-3.07269	1.36072	-2.25814	0.55788	-5.50781
y91	-2.76602	1.40481	-1.96897	0.58017	-4.76759
y92	-3.01832	1.44518	-2.08854	0.67811	-4.45111
y93	-3.38523	1.54156	-2.19597	0.82557	-4.10047
y94	-3.68344	1.58429	-2.32499	0.68446	-5.38155
cns	1.63057	0.68381	2.38452	0.19438	8.38861
car	1.18282	0.71853	1.64617	0.19423	6.08970
ant	1.39464	0.78660	1.77300	0.27105	5.14535
giu	2.29671	1.07898	2.12859	0.49002	4.68699
der	5.94926	3.71685	1.60062	1.62456	3.66208
res	4.72136	2.65658	1.77724	1.11399	4.23824

Table B.30 - Indirect Effect, PHS Concurrent Lag

Total SS:	62.081
R-squared:	0.979
Residual SS:	1.324
F(29,75):	118.708
Durbin-Watson:	1.169
Degrees of Freedom:	75
Rbar-squared:	0.97
Std error of Est.:	0.133
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	7.9002	2.2464	3.5169	0.0010		
PHS BASIC Concurrent	0.1744	0.1760	0.9909	0.3250	0.2890	0.8707
LOGSALE	0.1488	0.1251	1.1896	0.2380	0.1256	0.8624
INCTHRE (age 45-64)	0.7132	0.2266	3.1475	0.0020	0.9299	0.6558
SEVTWO (age 15-44)	-1.0936	0.2361	-4.6326	0.0000	-1.3408	0.5758
CURREG	-0.0248	0.0292	-0.8492	0.3980	-0.0201	-0.1778
LAG1REG	-0.0167	0.0263	-0.6351	0.5270	-0.0145	-0.2097
LAG2REG	-0.0031	0.0270	-0.1159	0.9080	-0.0029	-0.2836
LAG3REG	-0.0223	0.0274	-0.8155	0.4170	-0.0205	-0.2937
LAG4REG	-0.0158	0.0288	-0.5483	0.5850	-0.0140	-0.3334
CNS	0.9411	0.2959	3.1807	0.0020	0.4283	0.2878
CAR	-0.3710	0.1902	-1.9501	0.0550	-0.1688	0.3282
ANT	0.5022	0.2464	2.0376	0.0450	0.2285	0.3460
GIU	-0.0935	0.2181	-0.4287	0.6690	-0.0426	-0.2333
DER	-1.3017	0.6507	-2.0005	0.0490	-0.5924	-0.6446
RES	-1.0855	0.3764	-2.8837	0.0050	-0.4940	-0.3747
YR72	0.0825	0.0757	1.0906	0.2790	0.0268	-0.1031
YR73	0.1165	0.0815	1.4292	0.1570	0.0378	-0.0815
YR74	0.1942	0.0848	2.2904	0.0250	0.0630	-0.0456
YR75	0.1853	0.0901	2.0564	0.0430	0.0601	-0.0396
YR76	0.0258	0.0943	0.2732	0.7850	0.0084	-0.0588
YR77	0.0847	0.0977	0.8662	0.3890	0.0275	-0.0363
YR78	0.0963	0.1010	0.9530	0.3440	0.0312	-0.0254
YR79	0.0693	0.1053	0.6587	0.5120	0.0225	-0.0110
YR80	0.1540	0.1087	1.4169	0.1610	0.0500	0.0211
YR81	0.1697	0.1113	1.5247	0.1320	0.0551	0.0363
YR82	0.2622	0.1166	2.2484	0.0270	0.0850	0.0772
YR83	0.3291	0.1215	2.7095	0.0080	0.1068	0.1135
YR84	0.2998	0.1345	2.2286	0.0290	0.0973	0.1318
YR85	0.3604	0.1465	2.4610	0.0160	0.1169	0.1550

Table B.31 - Indirect Effect, PHS Lag 1

Total SS:	62.081
R-squared:	0.979
Residual SS:	1.317
F(29,75):	119.297
Durbin-Watson:	1.174
Degrees of Freedom:	75
Rbar-squared:	0.971
Std error of Est.:	0.133
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	7.7872	2.2426	3.4723	0.0010		
PHS BASIC LAG 1	0.1853	0.1595	1.1623	0.2490	0.3070	0.8727
LOGSALE	0.1630	0.1267	1.2864	0.2020	0.1375	0.8624
INCTHRE (age 45-64)	0.6746	0.2349	2.8716	0.0050	0.8796	0.6558
SEVTWO (age 15-44)	-1.0734	0.2343	-4.5809	0.0000	-1.3160	0.5758
CURREG	-0.0237	0.0291	-0.8158	0.4170	-0.0192	-0.1778
LAG1REG	-0.0155	0.0263	-0.5915	0.5560	-0.0135	-0.2097
LAG2REG	-0.0021	0.0270	-0.0772	0.9390	-0.0019	-0.2836
LAG3REG	-0.0211	0.0274	-0.7695	0.4440	-0.0194	-0.2937
LAG4REG	-0.0143	0.0289	-0.4968	0.6210	-0.0127	-0.3334
CNS	0.9181	0.2832	3.2420	0.0020	0.4178	0.2878
CAR	-0.3492	0.1888	-1.8497	0.0680	-0.1589	0.3282
ANT	0.4650	0.2497	1.8626	0.0660	0.2116	0.3460
GIU	-0.1024	0.1951	-0.5249	0.6010	-0.0466	-0.2333
DER	-1.3085	0.6166	-2.1219	0.0370	-0.5955	-0.6446
RES	-1.0673	0.3562	-2.9962	0.0040	-0.4857	-0.3747
YR72	0.0893	0.0761	1.1729	0.2450	0.0290	-0.1031
YR73	0.1218	0.0818	1.4894	0.1410	0.0395	-0.0815
YR74	0.2071	0.0860	2.4075	0.0190	0.0672	-0.0456
YR75	0.1969	0.0911	2.1612	0.0340	0.0639	-0.0396
YR76	0.0478	0.0952	0.5019	0.6170	0.0155	-0.0588
YR77	0.0982	0.0968	1.0140	0.3140	0.0319	-0.0363
YR78	0.1099	0.0990	1.1109	0.2700	0.0357	-0.0254
YR79	0.0853	0.1001	0.8526	0.3970	0.0277	-0.0110
YR80	0.1662	0.1032	1.6104	0.1120	0.0539	0.0211
YR81	0.1794	0.1046	1.7155	0.0900	0.0582	0.0363
YR82	0.2693	0.1098	2.4532	0.0160	0.0874	0.0772
YR83	0.3367	0.1131	2.9775	0.0040	0.1092	0.1135
YR84	0.3061	0.1239	2.4709	0.0160	0.0993	0.1318
YR85	0.3617	0.1355	2.6699	0.0090	0.1173	0.1550

Table B.32 - Indirect Effect, PHS Lag 2

Total SS:	62.081
R-squared:	0.979
Residual SS:	1.299
F(29,75):	121.027
Durbin-Watson:	1.181
Degrees of Freedom:	75
Rbar-squared:	0.971
Std error of Est.:	0.132
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	7.5153	2.2318	3.3674	0.0010		
PHS BASIC LAG 2	0.2317	0.1485	1.5604	0.1230	0.3832	0.8742
LOGSALE	0.1862	0.1277	1.4575	0.1490	0.1571	0.8624
INCTHRE (age 45-64)	0.6050	0.2409	2.5114	0.0140	0.7889	0.6558
SEVTWO (age 15-44)	-1.0487	0.2331	-4.4995	0.0000	-1.2857	0.5758
CURREG	-0.0232	0.0285	-0.8119	0.4190	-0.0188	-0.1778
LAG1REG	-0.0146	0.0260	-0.5639	0.5740	-0.0127	-0.2097
LAG2REG	-0.0003	0.0268	-0.0113	0.9910	-0.0003	-0.2836
LAG3REG	-0.0189	0.0273	-0.6916	0.4910	-0.0173	-0.2937
LAG4REG	-0.0127	0.0286	-0.4431	0.6590	-0.0113	-0.3334
CNS	0.9074	0.2752	3.2970	0.0010	0.4130	0.2878
CAR	-0.2929	0.1890	-1.5500	0.1250	-0.1333	0.3282
ANT	0.4133	0.2528	1.6347	0.1060	0.1881	0.3460
GIU	-0.0851	0.1796	-0.4740	0.6370	-0.0387	-0.2333
DER	-1.2426	0.5952	-2.0878	0.0400	-0.5655	-0.6446
RES	-0.9818	0.3466	-2.8326	0.0060	-0.4468	-0.3747
YR72	0.0942	0.0756	1.2459	0.2170	0.0306	-0.1031
YR73	0.1324	0.0819	1.6178	0.1100	0.0430	-0.0815
YR74	0.2175	0.0859	2.5310	0.0130	0.0706	-0.0456
YR75	0.2151	0.0922	2.3342	0.0220	0.0698	-0.0396
YR76	0.0633	0.0957	0.6616	0.5100	0.0205	-0.0588
YR77	0.1227	0.0976	1.2562	0.2130	0.0398	-0.0363
YR78	0.1209	0.0982	1.2310	0.2220	0.0392	-0.0254
YR79	0.0945	0.0982	0.9621	0.3390	0.0306	-0.0110
YR80	0.1759	0.1002	1.7564	0.0830	0.0571	0.0211
YR81	0.1830	0.1006	1.8196	0.0730	0.0594	0.0363
YR82	0.2667	0.1057	2.5237	0.0140	0.0865	0.0772
YR83	0.3298	0.1090	3.0263	0.0030	0.1070	0.1135
YR84	0.2962	0.1179	2.5136	0.0140	0.0961	0.1318
YR85	0.3433	0.1287	2.6688	0.0090	0.1114	0.1550

Table B.33 - Indirect Effect, PHS Lag 3

Total SS:	62.081
R-squared:	0.98
Residual SS:	1.265
F(29,75):	124.306
Durbin-Watson:	1.188
Degrees of Freedom:	75
Rbar-squared:	0.972
Std error of Est.:	0.13
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	7.1554	2.2052	3.2448	0.0020		
PHS BASIC LAG 3	0.2976	0.1405	2.1187	0.0370	0.4913	0.8762
LOGSALE	0.2168	0.1276	1.6982	0.0940	0.1829	0.8624
INCTHRE (age 45-64)	0.5118	0.2434	2.1026	0.0390	0.6674	0.6558
SEVTWO (age 15-44)	-1.0150	0.2311	-4.3920	0.0000	-1.2444	0.5758
CURREG	-0.0233	0.0279	-0.8338	0.4070	-0.0189	-0.1778
LAG1REG	-0.0159	0.0254	-0.6263	0.5330	-0.0138	-0.2097
LAG2REG	0.0001	0.0263	0.0055	0.9960	0.0001	-0.2836
LAG3REG	-0.0162	0.0269	-0.6004	0.5500	-0.0149	-0.2937
LAG4REG	-0.0106	0.0282	-0.3747	0.7090	-0.0094	-0.3334
CNS	0.8976	0.2690	3.3368	0.0010	0.4085	0.2878
CAR	-0.2133	0.1887	-1.1308	0.2620	-0.0971	0.3282
ANT	0.3461	0.2539	1.3631	0.1770	0.1575	0.3460
GIU	-0.0586	0.1686	-0.3474	0.7290	-0.0267	-0.2333
DER	-1.1405	0.5782	-1.9724	0.0520	-0.5190	-0.6446
RES	-0.8507	0.3418	-2.4891	0.0150	-0.3872	-0.3747
YR72	0.0894	0.0739	1.2097	0.2300	0.0290	-0.1031
YR73	0.1283	0.0797	1.6094	0.1120	0.0416	-0.0815
YR74	0.2219	0.0842	2.6344	0.0100	0.0720	-0.0456
YR75	0.2180	0.0898	2.4266	0.0180	0.0707	-0.0396
YR76	0.0751	0.0945	0.7946	0.4290	0.0244	-0.0588
YR77	0.1290	0.0962	1.3412	0.1840	0.0418	-0.0363
YR78	0.1358	0.0973	1.3949	0.1670	0.0440	-0.0254
YR79	0.0912	0.0969	0.9415	0.3490	0.0296	-0.0110
YR80	0.1709	0.0988	1.7307	0.0880	0.0554	0.0211
YR81	0.1786	0.0984	1.8153	0.0730	0.0579	0.0363
YR82	0.2517	0.1039	2.4238	0.0180	0.0817	0.0772
YR83	0.3073	0.1076	2.8560	0.0060	0.0997	0.1135
YR84	0.2650	0.1167	2.2718	0.0260	0.0860	0.1318
YR85	0.3032	0.1269	2.3883	0.0190	0.0984	0.1550

Table B.34 - Indirect Effect, PHS Lag 4

Total SS:	62.081
R-squared:	0.98
Residual SS:	1.24
F(29,75):	126.942
Durbin-Watson:	1.22
Degrees of Freedom:	75
Rbar-squared:	0.972
Std error of Est.:	0.129
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	6.9067	2.1866	3.1587	0.0020		
PHS BASIC LAG 4	0.3331	0.1344	2.4779	0.0150	0.5485	0.8783
LOGSALE	0.2327	0.1266	1.8385	0.0700	0.1964	0.8624
INCTHRE (age 45-64)	0.4562	0.2427	1.8797	0.0640	0.5949	0.6558
SEVTWO (age 15-44)	-0.9797	0.2302	-4.2561	0.0000	-1.2012	0.5758
CURREG	-0.0236	0.0275	-0.8552	0.3950	-0.0191	-0.1778
LAG1REG	-0.0189	0.0250	-0.7558	0.4520	-0.0164	-0.2097
LAG2REG	-0.0031	0.0259	-0.1201	0.9050	-0.0029	-0.2836
LAG3REG	-0.0166	0.0265	-0.6258	0.5330	-0.0152	-0.2937
LAG4REG	-0.0093	0.0279	-0.3325	0.7400	-0.0082	-0.3334
CNS	0.8799	0.2651	3.3194	0.0010	0.4004	0.2878
CAR	-0.1623	0.1881	-0.8630	0.3910	-0.0739	0.3282
ANT	0.3087	0.2526	1.2220	0.2260	0.1405	0.3460
GIU	-0.0556	0.1609	-0.3456	0.7310	-0.0253	-0.2333
DER	-1.0700	0.5700	-1.8772	0.0640	-0.4870	-0.6446
RES	-0.7540	0.3426	-2.2007	0.0310	-0.3431	-0.3747
YR72	0.0799	0.0729	1.0959	0.2770	0.0259	-0.1031
YR73	0.1057	0.0782	1.3518	0.1810	0.0343	-0.0815
YR74	0.1993	0.0819	2.4338	0.0170	0.0647	-0.0456
YR75	0.2030	0.0875	2.3215	0.0230	0.0659	-0.0396
YR76	0.0575	0.0918	0.6262	0.5330	0.0187	-0.0588
YR77	0.1204	0.0944	1.2745	0.2060	0.0390	-0.0363
YR78	0.1204	0.0959	1.2554	0.2130	0.0391	-0.0254
YR79	0.0899	0.0959	0.9376	0.3510	0.0292	-0.0110
YR80	0.1520	0.0986	1.5406	0.1280	0.0493	0.0211
YR81	0.1601	0.0984	1.6268	0.1080	0.0519	0.0363
YR82	0.2356	0.1035	2.2766	0.0260	0.0764	0.0772
YR83	0.2828	0.1082	2.6129	0.0110	0.0917	0.1135
YR84	0.2342	0.1179	1.9869	0.0510	0.0760	0.1318
YR85	0.2640	0.1291	2.0452	0.0440	0.0857	0.1550

Table B.35 - Indirect Effect, PHS Lag 5

Total SS:	62.081
R-squared:	0.981
Residual SS:	1.202
F(29,75):	130.943
Durbin-Watson:	1.231
Degrees of Freedom:	75
Rbar-squared:	0.973
Std error of Est.:	0.127
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	6.5958	2.1575	3.0572	0.0030		
PHS BASIC LAG 5	0.3807	0.1295	2.9405	0.0040	0.6255	0.8805
LOGSALE	0.2442	0.1240	1.9699	0.0530	0.2061	0.8624
INCTHRE (age 45-64)	0.4094	0.2362	1.7335	0.0870	0.5338	0.6558
SEVTWO (age 15-44)	-0.9471	0.2277	-4.1588	0.0000	-1.1611	0.5758
CURREG	-0.0218	0.0271	-0.8036	0.4240	-0.0177	-0.1778
LAG1REG	-0.0211	0.0246	-0.8571	0.3940	-0.0183	-0.2097
LAG2REG	-0.0076	0.0254	-0.2975	0.7670	-0.0070	-0.2836
LAG3REG	-0.0199	0.0259	-0.7677	0.4450	-0.0183	-0.2937
LAG4REG	-0.0090	0.0274	-0.3294	0.7430	-0.0080	-0.3334
CNS	0.8759	0.2608	3.3587	0.0010	0.3986	0.2878
CAR	-0.1062	0.1846	-0.5752	0.5670	-0.0483	0.3282
ANT	0.2906	0.2469	1.1769	0.2430	0.1322	0.3460
GIU	-0.0395	0.1555	-0.2537	0.8000	-0.0180	-0.2333
DER	-0.9435	0.5651	-1.6698	0.0990	-0.4294	-0.6446
RES	-0.6174	0.3456	-1.7866	0.0780	-0.2810	-0.3747
YR72	0.0636	0.0718	0.8855	0.3790	0.0206	-0.1031
YR73	0.0746	0.0777	0.9598	0.3400	0.0242	-0.0815
YR74	0.1535	0.0813	1.8878	0.0630	0.0498	-0.0456
YR75	0.1571	0.0858	1.8305	0.0710	0.0510	-0.0396
YR76	0.0206	0.0899	0.2290	0.8190	0.0067	-0.0588
YR77	0.0774	0.0927	0.8344	0.4070	0.0251	-0.0363
YR78	0.0862	0.0950	0.9075	0.3670	0.0280	-0.0254
YR79	0.0484	0.0962	0.5026	0.6170	0.0157	-0.0110
YR80	0.1257	0.0985	1.2765	0.2060	0.0408	0.0211
YR81	0.1138	0.1007	1.1303	0.2620	0.0369	0.0363
YR82	0.1894	0.1060	1.7864	0.0780	0.0614	0.0772
YR83	0.2384	0.1105	2.1575	0.0340	0.0773	0.1135
YR84	0.1799	0.1215	1.4812	0.1430	0.0584	0.1318
YR85	0.2000	0.1338	1.4946	0.1390	0.0649	0.1550

Table B.36 - Indirect Effect, PHS Lag 6

Total SS:	62.081
R-squared:	0.981
Residual SS:	1.175
F(29,75):	134.056
Durbin-Watson:	1.238
Degrees of Freedom:	75
Rbar-squared:	0.974
Std error of Est.:	0.125
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	6.3384	2.1399	2.9620	0.0040		
PHS BASIC LAG 6	0.4204	0.1292	3.2552	0.0020	0.6896	0.8825
LOGSALE	0.2419	0.1213	1.9941	0.0500	0.2041	0.8624
INCTHRE (age 45-64)	0.3954	0.2291	1.7261	0.0880	0.5156	0.6558
SEVTWO (age 15-44)	-0.9248	0.2257	-4.0969	0.0000	-1.1339	0.5758
CURREG	-0.0219	0.0268	-0.8158	0.4170	-0.0177	-0.1778
LAG1REG	-0.0218	0.0244	-0.8952	0.3740	-0.0189	-0.2097
LAG2REG	-0.0115	0.0252	-0.4561	0.6500	-0.0106	-0.2836
LAG3REG	-0.0248	0.0255	-0.9726	0.3340	-0.0228	-0.2937
LAG4REG	-0.0120	0.0270	-0.4460	0.6570	-0.0107	-0.3334
CNS	0.8867	0.2579	3.4377	0.0010	0.4035	0.2878
CAR	-0.0677	0.1826	-0.3709	0.7120	-0.0308	0.3282
ANT	0.3059	0.2407	1.2710	0.2080	0.1392	0.3460
GIU	-0.0207	0.1535	-0.1349	0.8930	-0.0094	-0.2333
DER	-0.8009	0.5689	-1.4077	0.1630	-0.3645	-0.6446
RES	-0.4799	0.3570	-1.3441	0.1830	-0.2184	-0.3747
YR72	0.0548	0.0712	0.7700	0.4440	0.0178	-0.1031
YR73	0.0447	0.0783	0.5710	0.5700	0.0145	-0.0815
YR74	0.1069	0.0833	1.2835	0.2030	0.0347	-0.0456
YR75	0.0937	0.0884	1.0603	0.2920	0.0304	-0.0396
YR76	-0.0426	0.0916	-0.4652	0.6430	-0.0138	-0.0588
YR77	0.0218	0.0942	0.2318	0.8170	0.0071	-0.0363
YR78	0.0236	0.0976	0.2418	0.8100	0.0077	-0.0254
YR79	-0.0024	0.0988	-0.0245	0.9810	-0.0008	-0.0110
YR80	0.0674	0.1024	0.6588	0.5120	0.0219	0.0211
YR81	0.0741	0.1032	0.7182	0.4750	0.0240	0.0363
YR82	0.1282	0.1119	1.1454	0.2560	0.0416	0.0772
YR83	0.1781	0.1166	1.5276	0.1310	0.0578	0.1135
YR84	0.1244	0.1268	0.9809	0.3300	0.0403	0.1318
YR85	0.1351	0.1408	0.9591	0.3410	0.0438	0.1550

Table B.37 - Indirect Effect, PHS Lag 7

Total SS:	62.081
R-squared:	0.981
Residual SS:	1.169
F(29,75):	134.714
Durbin-Watson:	1.245
Degrees of Freedom:	75
Rbar-squared:	0.974
Std error of Est.:	0.125
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	6.0088	2.1641	2.7766	0.0070		
PHS BASIC LAG 7	0.4562	0.1375	3.3179	0.0010	0.7478	0.8839
LOGSALE	0.2383	0.1205	1.9767	0.0520	0.2010	0.8624
INCTHRE (age 45-64)	0.4001	0.2265	1.7664	0.0810	0.5218	0.6558
SEVTWO (age 15-44)	-0.9046	0.2263	-3.9968	0.0000	-1.1090	0.5758
CURREG	-0.0212	0.0267	-0.7934	0.4300	-0.0172	-0.1778
LAG1REG	-0.0233	0.0243	-0.9604	0.3400	-0.0203	-0.2097
LAG2REG	-0.0133	0.0251	-0.5295	0.5980	-0.0122	-0.2836
LAG3REG	-0.0286	0.0254	-1.1238	0.2650	-0.0263	-0.2937
LAG4REG	-0.0159	0.0268	-0.5919	0.5560	-0.0141	-0.3334
CNS	0.8946	0.2575	3.4749	0.0010	0.4071	0.2878
CAR	-0.0409	0.1866	-0.2191	0.8270	-0.0186	0.3282
ANT	0.3403	0.2373	1.4343	0.1560	0.1549	0.3460
GIU	-0.0024	0.1552	-0.0153	0.9880	-0.0011	-0.2333
DER	-0.6324	0.5908	-1.0705	0.2880	-0.2878	-0.6446
RES	-0.3363	0.3867	-0.8698	0.3870	-0.1531	-0.3747
YR72	0.0483	0.0712	0.6791	0.4990	0.0157	-0.1031
YR73	0.0275	0.0795	0.3455	0.7310	0.0089	-0.0815
YR74	0.0657	0.0874	0.7520	0.4540	0.0213	-0.0456
YR75	0.0360	0.0945	0.3815	0.7040	0.0117	-0.0396
YR76	-0.1163	0.0990	-1.1748	0.2440	-0.0377	-0.0588
YR77	-0.0527	0.1017	-0.5189	0.6050	-0.0171	-0.0363
YR78	-0.0417	0.1045	-0.3993	0.6910	-0.0135	-0.0254
YR79	-0.0747	0.1076	-0.6945	0.4900	-0.0242	-0.0110
YR80	0.0083	0.1099	0.0756	0.9400	0.0027	0.0211
YR81	0.0077	0.1127	0.0687	0.9450	0.0025	0.0363
YR82	0.0829	0.1188	0.6978	0.4870	0.0269	0.0772
YR83	0.1099	0.1284	0.8559	0.3950	0.0357	0.1135
YR84	0.0583	0.1389	0.4201	0.6760	0.0189	0.1318
YR85	0.0757	0.1525	0.4968	0.6210	0.0246	0.1550

Table B.38 - Indirect Effect, PHS Lag 8

Total SS:	62.081
R-squared:	0.981
Residual SS:	1.195
F(29,75):	131.757
Durbin-Watson:	1.246
Degrees of Freedom:	75
Rbar-squared:	0.973
Std error of Est.:	0.126
Probability of F:	0

Dependent Variable: Log of Industry R&D Investment

Variable	Estimate	Standard Error	t-value	Prob > |t|	Standardized Estimate	Cor with Dep Var
CONSTANT	5.9795	2.2150	2.6996	0.0090	—	—
PHS BASIC LAG 8	0.4620	0.1527	3.0259	0.0030	0.7581	0.8850
LOGSALE	0.2191	0.1209	1.8116	0.0740	0.1849	0.8624
INCTHRE (age 45-64)	0.4484	0.2262	1.9823	0.0510	0.5846	0.6558
SEVTWO (age 15-44)	-0.9154	0.2290	-3.9982	0.0000	-1.1223	0.5758
CURREG	-0.0228	0.0270	-0.8439	0.4010	-0.0185	-0.1778
LAG1REG	-0.0234	0.0246	-0.9533	0.3430	-0.0204	-0.2097
LAG2REG	-0.0149	0.0255	-0.5867	0.5590	-0.0137	-0.2836
LAG3REG	-0.0300	0.0257	-1.1658	0.2470	-0.0276	-0.2937
LAG4REG	-0.0185	0.0271	-0.6846	0.4960	-0.0165	-0.3334
CNS	0.9186	0.2612	3.5168	0.0010	0.4180	0.2878
CAR	-0.0591	0.1932	-0.3058	0.7610	-0.0269	0.3282
ANT	0.3972	0.2371	1.6755	0.0980	0.1808	0.3460
GIU	0.0099	0.1624	0.0611	0.9510	0.0045	-0.2333
DER	-0.5486	0.6278	-0.8738	0.3850	-0.2497	-0.6446
RES	-0.2741	0.4298	-0.6377	0.5260	-0.1247	-0.3747
YR72	0.0270	0.0732	0.3690	0.7130	0.0088	-0.1031
YR73	0.0028	0.0839	0.0328	0.9740	0.0009	-0.0815
YR74	0.0320	0.0952	0.3361	0.7380	0.0104	-0.0456
YR75	-0.0190	0.1071	-0.1775	0.8600	-0.0062	-0.0396
YR76	-0.1856	0.1145	-1.6210	0.1090	-0.0602	-0.0588
YR77	-0.1385	0.1205	-1.1499	0.2540	-0.0449	-0.0363
YR78	-0.1272	0.1237	-1.0277	0.3070	-0.0413	-0.0254
YR79	-0.1488	0.1260	-1.1813	0.2410	-0.0483	-0.0110
YR80	-0.0722	0.1301	-0.5551	0.5800	-0.0234	0.0211
YR81	-0.0569	0.1311	-0.4338	0.6660	-0.0185	0.0363
YR82	0.0121	0.1398	0.0868	0.9310	0.0039	0.0772
YR83	0.0641	0.1459	0.4393	0.6620	0.0208	0.1135
YR84	-0.0073	0.1630	-0.0448	0.9640	-0.0024	0.1318
YR85	0.0176	0.1774	0.0992	0.9210	0.0057	0.1550

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