

**THE INFLUENCE OF SCIENTIFIC CLAIMS  
ON AN EMERGING ENVIRONMENTAL ISSUE**

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at the

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December, 2007

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## **DEDICATION**

This dissertation is dedicated to the memory of my brother Dr. Jonathan Stuart Langholt, a physician and engineer. I didn't realize it at the time, but I learned quite a bit from all those late night chats when we should have been sleeping. I owe my interest in science to him.

## **ACKNOWLEDGMENTS**

This dissertation could not have been completed without the help of others. I specifically like to thank my advisor Dr. William Bowen, who has been a support and mentor throughout this process, as well as an intellectual sounding board. I am not sure how he did it, but he always seemed to know just how much to push without discouraging me. For that, I thank him. I would also like to thank Drs. Alemagno and Schwartz for taking time out of their very busy schedules to serve on my committee. Their comments have been remarkably insightful and their help much appreciated. Thanks also to my colleague Dr. Steve Signs for all his help with the toxicology.

This path has not been entirely without obstacles, and so I would also like to thank my doctors at the Ireland Cancer Center. I am the poster child for all that can go right. Finally, I would like to thank my family, especially my kids, my grandkids, my mom, and my husband. This has been a long haul and you have been with me every step of the way. Thank you for your unconditional love, support, and patience.

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**ABSTRACT**

The environmental movement relies on scientific claims to justify its calls for protectionist policies. These claims can be followed in the scientific literature using bibliometric methods such as citation analysis. Citation analysis was used to deconstruct the literature of endocrine disrupting chemical (EDC) sciences as it emerged and developed time from 1980 through 2004. This study explored how the attributes of scientific papers such as topic, journal, experimental model, document type, and support or negation of hypotheses impacted their influence (quantified as times cited) within the field over time. To accomplish this, unique bibliographic data were acquired for each attribute of the more than 3,400 studies identified by keyword searches. Content-specific data (non-bibliographic) were generated for the nearly 500 articles cited  $\geq 45$  times. The influence of individual articles on the field of EDC science, and their citation relationships was also visually represented using the bibliometric mapping.

Results demonstrated that a confluence of scientific claims propelled the EDC issue into a prominent position within overall environmental literature. The EDC term appeared nowhere before 1993, but its use rapidly gained traction thereafter until by 2004 it was found in over 3,400 published papers. The results of this study suggest that the influence of individual scientific claims within the literature of EDC science were not random, but were impacted by both bibliographic and non-bibliographic attributes. Temporal variations in the influence of each attribute were also demonstrated.

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## **CHAPTER I**

### **INTRODUCTION**

#### **1.1 Objectives**

The modern world relies on scientific information for understanding and managing threats to human health and the environment yet many important questions remain unanswered about how this information emerges and evolves. Of primary concern to this dissertation is whether the characteristics of scientific information influence whether and how it is communicated. Are there characteristics of scientific studies that make them more likely to make their way from the laboratory, to the scientist's notebook, into the scientific literature, and finally to an activist, an elected official, or to other scientists? The significance of such an understanding becomes especially relevant when the concerns include weighing the severity of potential environmental threats on human health, and responding to those threats. The dependence of society on science is rife with complexity and despite considerable effort there are many critical factors that are not understood.

The objectives of this dissertation are to resolve some of this complexity and in the process reveal the intellectual history of an emergent controversy using its scientific literature and determine how certain attributes of this literature have influenced its path.

These objectives will be met using the bibliographic information available for relevant research published in peer-reviewed scientific journals. The scientific controversy involves areas of science that are among those most critical for managing concerns pertaining to human and environmental health.

## **1.2 The Case: Endocrine Disrupting Chemicals in the Environment**

Among the many possible issues that might be suitable as a case for deciphering the factors that influence the trajectory of a body of knowledge, the issue of endocrine disrupting chemicals is particularly compelling. The emergence and evolution of the scientific information that comprises the existing body of knowledge about endocrine disrupting chemicals are technically noteworthy, politically salient, and potentially of great significance to human and environmental health.

Scientists became alarmed when news began to spread that some of the most commonly used synthetic organic chemicals might be interfering with the normal function of endocrine systems. The endocrine system is a finely balanced network of glands, hormones, and target cells, which are all critical for regulating metabolism, growth, reproduction, as well as respond to the myriad external stimuli to which living organisms must react. The implications that exposure to environmental chemicals could disrupt this balance were considerable, and frightening. First, the endocrine system is essential for maintaining biochemical functioning throughout the life-cycle of organisms and as such, even minute disruptions in this system can cause profound impacts ranging from metabolic disorders, developmental anomalies, reproductive dysfunction, neurobehavioral abnormalities, even cancer.

Second, the discovery that chemicals were capable of inducing adverse impacts in exceedingly low doses coupled with the fact that the impacts of endocrine disrupting chemicals appeared to depend more upon the timing of the dose than on the dose itself was completely contrary to commonly accepted principles. Third, another frightening scenario was emerging from studies; it was beginning to appear that the impacts from exposure to endocrine disrupting chemicals might not be manifest in the exposed organism, but in their offspring. What was being discovered about endocrine disrupting chemicals challenged classical principles of toxicology—the principles upon which chemical control laws are based. To make matters worse, the suspect chemicals included those which had been considered rather benign and thus were found in a wide range of products including baby bottles, water bottles, and other commonly used plastics.

The issue of endocrine disrupting chemicals is fascinating on other fronts as well. At first glance, the issue appears to have sprung from obscurity—with no mention in the scientific literature or in chemical control laws—to almost overnight becoming the focus of government programs, regulations, and scientific study. Also unique is that because this case concerns an array of industrial chemicals hypothesized to interfere with or mimic normal hormonal function, and thus to have the potential to alter biological processes including reproduction, neurological and developmental processes, and to cause cancer, its science traverses a range of disciplines as seemingly diverse as reptilian reproduction, analytical chemistry, avian behavior, and breast cancer. This is a story of how a scientific issue morphs as it traverses between the realms of the scientist, the politician, the policy maker, the industrial world, and the public. Finally, it is the story of what some suggest is the emergence and evolution of a new field of scientific inquiry.

In this dissertation, I employ an empirical approach to explore the emergence and evolution of the science of endocrine disrupting chemicals to uncover how an obscure issue evolved into one of such influence. In the remainder of this chapter, I provide an overview of the theoretical perspective and the analytical approach of this process. I describe how scientific information and knowledge are communicated through the scientific literature and how it is possible to analyze this process of communication and in doing so reveal the factors that have influenced not only the dissemination of the scientific knowledge, but its generation as well.

### **1.3 Studying Science**

#### **1.3.1 Definitions**

The general purpose of this dissertation is to better understand which attributes of the literature of endocrine disrupting chemicals have influenced how the issue emerged and developed. That such a study is even possible is because the knowledge generated within the scientific enterprise is written up and “offered for consideration or acceptance” to the outside world (1989, p. 944).

Callon (1995) eloquently expressed the framework from which this dissertation views the interactions of science “Putting the universe into words is the essential task of scientific knowledge. Science is thus developed in the form of a dual dialogue, first between scientists and Nature..., and second between scientists themselves” (Callon, 1995, p. 35). Many consider the scientific literature as a communal space in which scientists offer the products of their work to scrutiny by the community with the hope that the work will be considered robust and credible. This communal space has its own formalities and rituals and takes the form of journals, the primary literature of science.



That scientists disseminate their knowledge this way is a practice so central to modern scientific enterprise that the editors of scientific journals are referred to as the “gatekeepers” of science for their role in controlling the distribution of scientific knowledge (Zsindely, Schubert, & Braun, 1982). This literature of science is a rich resource that can be used not only for communicating the conceptual elements and advances within a field of interest, but also for uncovering dynamics within it.

Not all agree about what constitutes science, scientific knowledge, or the scientific process so some definitions are in order before proceeding. For the purposes of this work, science is both a process and a product. A scientific process is one that aims to be an unbiased, methodical, and reproducible approach to answering a question—it is a self-aware, transparent, and systematic approach to answering questions about the natural world. The answers obtained from this approach are the products of science. The communication of scientific knowledge has some unique characteristics which arise from the norms and traditions that establish what is considered acceptable conduct. For example, it is more likely than not that when the answers obtained from scientific investigation are communicated it is with qualification. The results obtained through scientific process are assumed to be provisional—the only certainty being that for each question answered, there is a “next” question that remains.

I define the scientific enterprise as those individuals and institutions engaged in the process of science, and thus generating the products of science. The scientific enterprise is therefore a multi-dimensional social entity in which scientists, administrators, and assorted other players interact to define the boundaries of inquiry, mobilize the resources necessary to engage in that inquiry, and negotiate the

dissemination of the knowledge produced. Science and the scientific enterprise each have been the subject of inquiry with considerable attention given to the sociological, cultural, and administrative attributes of the scientific enterprise. There is an extensive literature on the organization and mediation of the complex social interactions that exist within the various institutional settings of the scientific enterprise. In addition, the influences of financial, technical, logistical, and administration support of the scientific enterprise on the setting of norms and rules, the formal and informal channels of communication, and the structures of accountability within its institutions have all been well studied.

Far less clear however is what effect, if any, do the products of science—the results of scientific inquiry—have on any of this. It appears that the lack of attention to this question might be because studying how the work of one scientist impacts the work of another requires the interest and ability to study “science” at the very junction of process and product. This task might have fallen to the scientist, but in the modern world “scientists are not trained to think about science, they are trained to do science” (Marks, 2002, p. 266). As such, thinking about science and its relationship with culture, politics, and even itself does not generally fall within the scholarly realm of the scientist *per se*, but rather within that of the philosopher or the social scientist. Yet, in the modern world, social scientists and philosophers are not as likely to be as interested in the products of the science as they are in its social, cultural, or political aspects. Therefore, and most likely because of such disconnects, we know little about what influences the path of scientific information once it leaves the laboratory and accordingly little about what influences whether any given product of the scientific enterprise becomes a dead end, or the basis for additional inquiry. These disconnects have led some scholars to conclude

that currently accepted notions about the role of science in decision making may be flawed because they have ignored the importance of the cognitive path of the science and thus have developed out of a misunderstanding of both the “science” and the scientific enterprise. As such, scholars have begun to call for work which incorporates the cognitive aspects of the science—the products of science - along side their social, political, and cultural attributes (Jasanoff, 1990; Layzer, 1999; Shrader-Frechette, 2002).

### **1.3.2 Frameworks for Studying Science**

The theoretical underpinnings from which this study emerges span a range of discipline, none of which provide a dominant theory to explain the role of the citation in the production of scientific knowledge or the use of that knowledge in decision making. It may well be however that all of the hand-wringing about the absence of theory is the result of having asked the wrong questions of science and the scientific enterprise. The social and political scientists that have examined the enterprise of science have generally done so from the perspective that there are a variety of internal and external factors (social and political) that influence its intellectual trajectory. Accordingly, choices about what to study, methodologies to employ, who is selected to conduct studies, and how results are communicated are all under the influence of some combination of these factors. But what about the *concepts* under study by the scientists? If one is to understand how and to what extent the trajectory of a specific scientific domain is shaped by social and political factors, it must follow that this cannot be done without considering the cognitive aspects of the science.

At minimum, there are three perspectives from which to examine the dynamic features of emerging knowledge domains. The first is from within the scientific

enterprise—the domain from which scientific propositions emerge. Examining the knowledge domain from this perspective prompts questions such as “how has a scientific proposition been received by the community from which it has emerged?” In modern times, the sciences are often highly specialized; which has resulted in the development of closely connected communities of scholars engaged in related work. Often working at a handful of institutions, these communities hold conferences, read the same literatures, and are members of the same professional societies. By examining the literature of a given discipline or specialty it is possible to assess whether an emergent proposition has been ignored, criticized, or embraced by its core community.

A second perspective from which to examine emerging science is that of its communication and assimilation. Expanding outward from its core community, it is possible to assess where and how new knowledge gains the attention of a wider scientific audience and becomes assimilated into other related disciplines or how it impacts more remote scientific communities. It is possible to trace how far new ideas migrate from their core intellectual community of their origin by determining where and how they are used in subsequent literature.

The third perspective from which to examine the propositions which emerge from the scientific enterprise is to gauge the manner and extent to which the propositions are modified or distorted as they move outward from their core community to the wider scientific community and into the public sphere. How does a scientific proposition withstand interpretation by other disciplines and are there characteristics that can predict the degree to which its findings are distorted? Are certain characteristics of a study predictive of its likely impact on future studies?

I submit that the most direct approach to unraveling all three perspectives of the intellectual trajectory of the particular science of endocrine disrupting chemicals is through its scientific literature, as it is through this communal archive that scientific propositions become accepted (or rejected) as “knowledge” (Ziman, 1998). A retrospective examination of the communal archive (scientific journals, books, proceedings, etc.) will reveal which propositions have inspired and formed the basis for subsequent work, as well as those which were largely ignored, or ignored altogether. This “uptake” or “translation” of propositions by others in the scientific enterprise can be observed and measured. This uptake sometimes occurs within the core community where the propositions originated, but oftentimes propositions have a reach beyond this core influencing the wider scientific community outside of their specialized areas. When such propositions (in the form of a published journal article) stimulate the production of new knowledge, they receive credit—in the form of a bibliographic citation.<sup>1</sup>

Citation analysis can be used to understand intellectual history. Citations are the traditional means by which the author of an article acknowledges the origins of the information or knowledge presented. Over the past few decades, citations have taken on a new level of significance in parallel with the development of computer technology and information systems. It is not uncommon to see citation analyses used for tracing back in time to establish the intellectual history of a topic. First, citation analysis can be used to determine which attributes of a study impacted its influence on subsequent developments in a field of study. The significance of such a determination is in finding whether there are certain attributes that make it more likely for a scientific study to have impacted other

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<sup>1</sup> A detailed history of the use of citations to track the progression of scientific propositions is found in Chapter II.

scientists and ultimately decision makers and public policy. Moreover, predictable patterns may be found in the emergence and evolution of the science that help to explain which findings have gained traction and which did not.

The written record of science has been well archived and its bibliographic features offer a rich source for analyses. This dissertation's inquiry into the scientific literature employs citation analysis to systematically examine the output of the scientific enterprise in the matter of endocrine disrupting chemicals. This study proceeds from models that depict science as a competitive enterprise, steeped in socio-cultural practices, and from which rational empirical knowledge is produced. Once produced, this knowledge emerges from the control of its founders to the scientific community and beyond through a series of rituals formalized within the scientific enterprise. These rituals include the creation of scientific papers—submitted in acceptable standardized formats to journal editors who then send the selected papers for review by recognized practitioners in the applicable field. Using a bibliometric model to deconstruct the progression of scientific concepts concerning endocrine disrupting chemicals enables not only a demonstration of the growth of the field over time, but the influence that each added knowledge statement (proposition) has had on subsequent submissions to the field. Deconstruction of the scientific literature using bibliometric (citation analysis) facilitated inquiry into how various attributes of scientific output influenced how this issue emerged and which attributes contributed to its prominence and acceptance among scientists and others. What made this study unique was its use of “the science” as a unit of analysis.<sup>2</sup>

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<sup>2</sup> Technically, this study employs the “document” or published paper as its unit of analysis. Theoretically, the document is where the cognitive “science” is proposed, explained, and transmitted.

Briefly, modern science advances as researchers publish the results of their work in the scientific literature. Generally, these results can be distilled into one or two propositional knowledge statements (e.g., the results of this study indicate that under a defined set of circumstances treatment X may result in effect Y). It is the path such statements follow, and the changes they undergo as they are taken up by others and amended that are of major concern to this dissertation. It is known that certain attributes of studies contribute to their acceptance and publication. What is not known is what factors contribute to their subsequent citation and further dissemination throughout the literature. Do some studies have attributes that make them more influential than others? Are there certain characteristics of scientific propositions that can be used to predict the extent of their reach?

Retrospective analysis of science is facilitated in part by the formalities of scientific publication, among which is the custom of citation. The use of citation as we know it was thought to have begun in the early part of the 20th century and involved authors acknowledging through reference the authors of previous related work (Wouters, 1999). This custom of “citing”—acknowledging previous work by others—was the primary manner by which the results that made their way into the scientific archive were distinguished, validated, and given credibility.

Citations can also be used to uncover the intellectual relationships that exist between the scientific papers that comprise the written archive of science. That citations provide useful insights into the intellectual origins of a work stems in part from the simple fact that it is standard practice to physically locate a citation near the thought to

which it relates. Using the citation as the link between the generations, it is possible to unearth the genealogy and intellectual history of a thought, proposition, or method.

The technological advances of the mid 20th century enabled an insightful few to begin storing information pertinent to the scientific literature in electronic format and to develop methods for unearthing the relationships between and among them. Among the more formidable results of this work was the Science Citation Index<sup>TM</sup> (SCI) which included not only the information needed to locate a particular reference, but information about many of the unique attributes of each study, including reference lists (the previously published works on which the authors relied) and all of the papers that refer to it (the subsequent works which reference them). Much can be accomplished by illuminating these linkages, including the construction of a genealogic map of the intellectual space.

In many ways, the scientific literature, or archive, is an entity unto itself, replete with its own protocols, formalities, politics, and personalities. Submitted works are prepared in the format of the journal in which publication is sought and generally includes an abstract, description of methods employed, the presentation of results, a discussion of the results, and references to the previously published studies or ideas on which the work relies.

Also, the process of having a research paper published in a journal is competitive and as such there are social implications for those whose work is selected for inclusion. Because not all submissions are selected for publication, an elevated stature is conferred upon those that are. Inclusion is meant to be an indication of the merit of the work and not other factors, so to ensure this there is a process by which submitted works are



reviewed by established members of the scientific community in the relevant field. This peer-review process entails journal editors sending the papers they receive to anonymous reviewers who critique and evaluate papers for publication. Papers may be either accepted or rejected outright, or may be returned to their authors for revision. Reviewers are competent actors within a given field who are tasked with examining papers for the value of their contribution as well as their credibility. Reviewers determine whether appropriate statistical tests have been used, and look for shortcomings that may impact the reliability or validity of the work.

The dissemination of scientific information that is depended upon for understanding complex human health issues is also influenced by the decisions and actions of those outside the scientific enterprise *per se*. A journal editor must decide whether to accept a paper for consideration by peer reviewers. Reviewers decide whether to accept, reject, or require revisions to a paper. Others within the enterprise of science decide which among the published works available they will cite as bases for their own work. Many factors influence each of these decisions, some of which are more subjective than others. For example, editors decide how appropriate a given work is for their journals. Among those factors which are far more subjective and political include the prestige of the institution with which the authors are affiliated, personal preferences of the reviewers for certain methods, even the settling of old grudges.

When new knowledge claims emerge in the literature they may be met with a variety of responses, both passive and active. The range of responses includes being ignored- not providing the stimulus for further discussion or for further investigation. Some newly published knowledge claims may be met with active resistance manifested

by complementary research (and citations), or by dispute, opposition, or by the publication of counter claims which question their reliability (Bauer, 2003).

Not only is the publication of scientific work important for the expansion of a scientific field, but authorship has important professional implications for scientists. Since the technology for generating citation frequency became available, the results have been used for a wide variety of purposes, some of which are of questionable value and validity. In intense “publish or perish” environments, the frequency with which publications are cited by others has been used to evaluate professionals status, the assumption being that the more often a work is cited by other, the more significant its impact. Authorship, the “primary currency” of science (Biagioli, 1999, p. 18), thus can fuel the same desires as money, being valued in quantity, sometimes at the expense of quality. The number of publications attributed to a scientist is sometimes a critical factor in promotion or for receiving research funds. It is suggested that these pressures have generated practices such as subdividing study results so that the work will generate more than one publication. In certain highly competitive fields within the biomedical sciences it is not uncommon for a scientist to barter for the inclusion of his/her name in the publications of others.

#### **1.4 The Analytical Approach**

The unit of analysis for this study was the published scientific work (i.e., document, article), each of which is assumed to represent a specific result, proposition, or knowledge claim and each of which is represented by its citation. Each published work has a set of attributes that distinguish it from others. Some of these attributes are bibliographic. Bibliographic attributes pertaining to scientific literature can be located,

retrieved, enumerated, sorted, and classified using electronic databases. Thus, it is possible to acquire the pertinent bibliographic information (e.g., article, author, and journal attributes) and to apply relevant bibliometric tools (e.g., citation analysis) to reveal how the current state of our knowledge about a topic such as endocrine disrupting chemicals has developed. This accomplished, it is then possible to examine the factors that have influenced how this knowledge domain developed as it did.

For the purpose of this dissertation, the attributes of each unit of analysis were assigned a descriptive value to enable comparisons. The complexities associated with assigning values to the attributes of each unit of analysis varied considerably depending upon whether the attribute concerned the article, the author, or the journal. Author attributes were straightforward, including only author names and institutions both of which were available in electronic bibliographic databases. Journal attributes were similarly determined. Article attributes presented a few more challenges. Certain article attributes such as length (measured by number of pages), publication dates, language, or type (e.g., review, research, editorial) were strictly bibliographic and provided by electronic databases. Assigning bibliographic values left little room for subjectivity or interpretation. Assigning non-bibliographic article attributes (those not available in electronic databases) required an reading each document or its abstract. Despite the subjectivity, time, and expertise involved, assigning values for attributes such as the investigative model (species, in vitro, in vivo), study topic, and support or negation of the EDC hypothesis, there is currently no other method for characterizing the cognitive aspects of a study other than reading the article itself (or its abstract) and applying professional judgment.

Among the bibliographic attributes of articles are those pertaining to citations—the reference to previously published works upon which the current study relies. These references (citations) are generally alluded to in the body of the text and then followed with a listing containing the bibliographic information that one would need to acquire that reference for oneself. Electronic databases capture summary information about the size of the reference list of each published article, and also the detailed bibliographic information for each reference cited. Current electronic databases also provide summary data that reveal the extent of the influence that any particular article has had on others in its, or other, fields by calculating the number of times an article of interest has been cited by others in subsequent works.

The value of having this information in electronic format is that it facilitates analyzing the unwieldy datasets containing the citation relationships between thousands of scientific publications. Existing databases have made it possible to fulfill the objectives of this study, which are to assess and compare the attributes of scientific documents, track the trajectory of their influence, and determine the characteristics that have most likely contributed to its influence.

Electronic tools also exist that use citations as the links with which to create visual representations of the relationships between documents in the scientific literature. In this dissertation, these representations or “maps” will reveal how various studies, disciplines, specialties and subspecialties that have published articles concerning endocrine disrupting chemicals have evolved and are related. It is anticipated that the information gleaned will be sufficiently rich to allow the kind of spatial orientations that one might find in a geographical map—a means to finding one location relative to any

other location. As a case, endocrine disruption provides the possibility of looking across a range of scientific disciplines and specialties, thus ensuring observations covering a range of perspectives and increasing the validity of findings.

This study seeks to determine how attributes (the independent variables) of a published scientific paper such as topic, experimental outcomes, investigative model, and document type impact its influence (the dependent variable) over time. The independent variables are attributes of emerging knowledge statements and consensus associated with EDC science. “Influence” which is conceptually defined here as intellectual authority or persuasiveness (having ability to sway the thinking of others) is quantified as the number of times an knowledge statement subsequently makes its way into the work of others as measured by the frequency with which it is cited. It is assumed that works more frequently cited possess attributes which contribute to the extent and direction of their influence on the evolution of a knowledge domain.

It is generally agreed that the issue of endocrine disrupting chemicals became salient in both the political and scientific domains upon the convergence of three lines of research: findings of increasing reproductive anomalies in the human male; reports that wildlife reproductive and behavioral abnormalities might be associated with pollutants; and increasing evidence of the intergenerational impacts of diethylstilbestrol (DES) (Krimsky, 2000). Wildlife biologist Theo Colborn is generally credited with directing the attention of scientists and policymakers to these findings through the publication of her own observations and by organizing interdisciplinary conferences (Colborn, von Saal, & Soto, 1993; Krimsky, 2000). I submit that through the retrospective deconstruction of

citation patterns we can also identify which attributes of the scientific literature of endocrine disruption have influenced the trajectory of its intellectual history.

This exploratory study hopes to shed light on several important and timely questions. There are times when one sets out to study a topic with a clear goal to answer a single question with a well circumscribed empirical study. Such was the case here. I was interested in knowing something about how the scientific knowledge generated by *scientists* was communicated between scientists, and whether there were biases inherent in that communication as there once the science reached the political realm. What I was surprised to find was that very few people had ever looked at the issue. Why not? The best answer I could find was that this is a problem that interests social scientists, but the tasks involved to do the studies requires the skills from other types of scientists.

There is no question that the propositions emerging from the scientific literature can have significant impacts on individuals and society. With the increasing transparency and access to scientific literature it is likely that the reach and impact of influential papers will increase. In this study I hope to demonstrate that the skeptical characteristic of the scientist should not be overshadowed by the popularity of a given hypothesis. The need for a full picture of the science is as important as a full picture of the politics. Specifically for EDC science the question is one of how much of the notion of an “EDC hypothesis” is a social construction.

## **CHAPTER II**

### **REVIEW OF THE LITERATURE**

#### **2.1 Introduction**

This dissertation is predicated on the assumption that it is possible to explore the intellectual progress of a scientific proposition in much the same way that one might trace back in time to uncover a family tree. Scientific propositions are published and their relationships to previous work are made apparent through the practice of bibliographic citations. Tools now exist that make it possible to track citations back through time and to create both visual and conceptual representations of their relationships to one another.

The review which follows focuses on four critical areas of work which together form the bases of the questions that are asked in this dissertation. These areas of work include: the research frameworks for studying scientific progress; the use of citations and bibliometric methods for studying scientific progress; the elements that impact the role science in policy decision making; and finally, the case of the science of endocrine disrupting chemicals and its associated issues.

## **2.2 The Science of Science**

### **2.2.1 Frameworks**

In this section I trace how various frameworks for thinking about science have evolved—not scientific content *per se*, but science as an enterprise, a process, and a social system. The desire to understand the enterprise of science, the products of science, and the function of science in society is not modern but has attracted thinkers throughout history. This interest however grew rapidly as access to science and to scientific thinking grew. Scientific societies began appearing in the 17th century as did the growth of a group of publishers specialized in producing books by scientists and books about science. The 19th century saw the establishment of more formal scientific institutions and importantly, the acceptance of the practice of science as a respectable profession. There is no doubt that the most rapid and extensive growth in science took place in the 20th century and with this expansion came the growth of interest in its social, cultural, technological, and economic properties and impacts. The exponential growth in the visibility of scientific advancement, and availability and access to information of all sorts make it not at all surprising that a body of scholarly work would evolve to study these phenomena.

Fueled by post-war affluence and political resolve, the end of WWII brought an unprecedented infusion of money and talent to science and scientific institutions worldwide. This rapid expansion of the scientific enterprise that took place in the post Sputnik-1950s and early 1960s generated debate among some who felt that such growth was unsustainable, and this debate in turn created a supportive environment for those interested in developing empirical methods for research about science. Scholars of the



1960s argued the need to study science as an entity and government funding for a fledgling “science of science.” These early scientometricians, social scientists, and policy makers saw value in creating a body of empirical knowledge with which to make rational decisions about how to finance science and direct its efforts to practical ends (Price, 1961). This discussion was not unique to the U.S. and the “science of science” movement may have been much more prolific in Eastern Europe and China. Organizational procedures, systems of reward, and questions of production, control, and distribution of science were all hot topics for investigation.

Studies about science do not fit within a single canon. As Callon (1995) has explained, “science studies” is an area of interest the goal of which is to understand science and its facets by examining them through various perspectives. This examination has involved the use of several methodologies most of which were borrowed from the disciplines of history, philosophy, sociology, and political science.

Thackray (1977) observed that the measures of science conducted prior to the mid-20th century derived from an array of discrepant traditions and assumptions. Yet despite having been so derived, Thackray neatly categorizes the similarities between these discrepant approaches into four basic genres (Thackray, 1977). The first is the category of studies that have examined the development of scientific knowledge through geopolitical or temporal frameworks - an approach that might be used by historians of civilization. Thackray refers to the second genre as “genius studies” because the focus of these works was on outstanding individuals and their work. The third genre encompasses a body of work focused on social, cultural, and political issues associated with the use and function of science in society (Thackray, 1977).

Most significant to this dissertation is the genre of science studies that Thackray described as focused on the sociology of progress, which in retrospect might be seen as the intellectual foundation of the sociology of scientific knowledge movement. Studies in this genre included the works which set the stage for sociologist Robert K. Merton and others who would later investigate the social and cultural dynamics at work in scientific enterprises.

Robert K. Merton is generally credited as the founder of the field of the sociology of science. With a body of work dating back to the late 1930s, Merton legitimized pursuing the study of science from a sociologic framework, and sociology from a scientific framework. In 1942, Merton characterized the traditions and practices to which scientists adhered as a condition of their professional status and described them as “norms.” The norms of science thus described were communalism, universalism, humility and disinterestedness, originality, and skepticism. Regardless of the fact that these norms were not formally encoded, Merton proposed that scientists nonetheless endeavored to adhere to them as the prevailing standards of their profession.

Today, some consider Merton’s norms of science a bit too moralistic and idealistic; however, yet they still explain characteristics that are not only unique to the practice of science but still very much alive and well (Ziman, 1998). Communalism, for example, underlies the practices that converge to make scientific findings public goods. It is the fact that scientific findings are distributed into the public domain that permits the access to new methods and emerging knowledge upon which the development of science relies. Without communalism there would be no objective way to understand the intellectual pathways by which scientific propositions have emerged. That this norm is

still extant is demonstrated by the enormous value still placed on scientific publishing, the consistent growth of published matter, and by the ever-increasing interest in, and growth of, electronic access to scientific propositions.

When it first emerged in the 1970s, scholarship in the sociology of scientific knowledge was not so much practiced by sociologists, but by those concerned with how social factors were influencing the scientific enterprise. These scholars were concerned with answering questions about the extent to which scientific knowledge was socially constructed, and by the 1980s there was a sizeable body of empirical study predicated on the assumption that the study of science was the same as the study of any other cultural or social phenomena (Barnes, 1974; Shapin, 1982).

While the emphasis of early science studies was on scientific productivity, an independent and sometimes antagonistic area of science studies emerged in parallel which focused on science as a social system. By 1970, the large collection of work that had been carried out in the sociological tradition was being criticized as weak because it “took for granted the essentially positivistic view of science that was also implied in the drive for a rational science policy” (Edge, 1995, p. 7). A strictly sociological approach to the study of science failed to satisfy given the atmosphere of the times. Thus, among the many “radical” changes that occurred in the 1970s was an expansion in the way that sociologists applied their methods to the study of science.

Eventually, the multidisciplinary fields of science studies and science and technology studies (STS) achieved formal recognition, becoming

the modern academy’s most centrifugal, most argumentative (at times uncivil), as well as most vital terrains because what is at stake is nothing less than the proper interpretation of our culture’s most highly valued form of knowledge—its truth. (Shapin, 1995, p. 291)

Edge (1995) posited three elements that were critical to the mid-century evolution of science and technology studies (STS) into a distinct discipline. The first was the perceived need to understand the relationship between science and economic growth for the purpose of making “rational decisions” about the expanded availability of public financing for science post WWII. The second element critical to the growth of science studies was the perceived need to analyze science as a social system. The 1970s saw the emergence of a relativistic and interdisciplinary sociology of scientific knowledge and pivotal writings such as that of Kuhn (1970). At the same time studies were emerging which applied anthropological and sociological methods to the study of science. These included ethnographies of research laboratories, analyses of scientific rhetoric and technical discourse, and the application of actor-network theory to the enterprise of science and scientific programs (Edge, 1995).

The third element Edge (1995) posited as instrumental in the emergence of science and technology studies was the attention paid to reforming and liberalizing science education. This was in part a product of Cold War paranoia. Caught off guard by displays of Soviet technological prowess epitomized by the launch of Sputnik, U.S. policy makers began to focus on the educational and research strategies that would ensure the U.S. did not lag behind the Soviets in science literacy.

Collins and Evans (2002) viewed the development of social studies of science from the perspective of the roles given to experts. The “golden age” of expertise they assert was during the 1950s and 1960s, a time when the sciences were soaring in growth and awash in admiration. During that time scientists were held in high esteem, “science” was imbued with a paternalistic authority, and positivism was appreciated. This adoration

began to fade however in the latter 1960s as the authority of many institutions, especially those associated with the government, was being challenged. The advent of social constructivism mirrored this trend as it acknowledged the increasingly apparent reality that scientific knowledge itself was insufficient to bring parties to agreement in matters of controversy. Scientific knowledge, it appeared, was just like other forms of knowledge and not immune to the influences of bias, greed, or political ambitions.

### **2.2.2 Science as Extended Translation**

Callon (1995) suggested four perspectives from which to examine the bulk of science and technology studies that have explored not only the dynamics of science's cultural and political organization, but the dynamics of its cognitive content. In the first, science is an activity from which rational empirical knowledge is generated, and as such is distinct from other forms of knowing. From this perspective, the products of scientific research are both knowledge statements and networks of knowledge statements. The second perspective proffered by science and technology studies according to Callon, is one in which science is viewed as a competitive enterprise, and thus its organizational forms are of chief concern. The third perspective is one which focuses on science as a sociocultural practice.

It is from the perspective of science as the "extended translation" of knowledge that underlies this dissertation. Knowledge, the product of science, is generated from the scientific enterprise and is disseminated in the form of statements which are then published. Publication in the archives of science -the communal domain - enables the uptake, influence, use, modification and disappearance of knowledge statements to be observed and examined. This archive provides a rich source for answering questions such

about how knowledge statements prevail over time, and the factors that influence their circulation and popularity (Callon, 1995). It is from this perspective that this dissertation attempts to more fully understand the characteristics of extended translation by examining the emergence and evolution of the science of endocrine disrupting chemicals in the environment.

Callon (1995) explained extended translation as the process through which provisional knowledge statements may achieve influence in spheres both within and outside of their place of origin. Drawing from Callon's work, it is useful to conceptualize the scientific enterprise as a network which evolves over time as links are established between knowledge statements. Through the process of extended translation links are created when a statement or proposition is read and assimilated by its reader who then modifies, uses, and/or incorporates it in new proposition(s). The network of linkages grows as each new translation confirms, modifies, contradicts, or strengthens a previous statement and in the process confers a tacit agreement about either its value or importance.

Extended translation, therefore, is the process through which the knowledge statements introduced into the communal domain (i.e., the literature of science) morph over time as each link is added to the network. Later in this chapter, I will demonstrate how the scientific literature can be used to represent this network, and how each individual scientific paper can be used as a surrogate for what I have been calling propositions or knowledge statements. Furthermore, each scientific paper can be represented by its citation—the bibliographic information that uniquely identifies it within the entire body of scientific literature. Callon's model can be used as the basis

with which to examine how statements (ideas or propositions) change over time, and for determining the types of propositions that are more likely to influence the entire network. Through this model it is also possible to examine not only the propositions themselves, but the relationships or linkages between them, and the characteristics of those that translate them.

Callon's model of extended translation gives weight to the notion that the ability of a statement to influence future statements may depend on its location in the network relative to other statements. Callon's model also makes it possible to argue that the characteristics of the network are critical for determining the strength of any particular statement found within it. Callon theorized that statements which stand alone in a network, without links to others, have no authority. Accordingly, the most authoritative statements are those which have been widely translated and thus have many links. If we can observe the network formed by the statements that exist in the literature about endocrine disrupting chemicals, then perhaps we can determine which statements have had authority and have influenced the differentiation of the network. And, perhaps more importantly, we can determine whether there are shared characteristics among the most influential statements.

In Callon's model of science as extended translation, social organization is viewed either in terms of the overall dynamics of the network, or the internal management of the network. The extent to which translations proliferate and networks grow is a function of network dynamics which include factors that implicitly or explicitly limit statements. For example, situations may exist in which aspects of research must remain confidential, either to protect the privacy of human subjects or to contain the

transmission of intellectual property, The development of statement networks may also be limited by other social dynamics that designate the authority to transmit statements. The network of writing that is generated in the course of scientific research only emerges from it and into the public space of the scientific enterprise in accordance with the prevailing institutional and disciplinary norms. A laboratory technician does not (and probably cannot) publish test results from his or her laboratory, the norm being that published results are authored by credentialed scientists with institutional affiliation.

In fairness to Callon, he does not operationalize extended translation in the bibliographic sense that I do here, but he does mention that the concept of translation is *close* to that of “reference.” The statements that Callon refers to are not the propositional statements that I assume as equivalent to a reference citation, but are more loosely described as the links in a chain of translations (he uses the term “micro-references”) (Callon, 1995, p. 53) that lead to the propositional statements of knowledge that we accept as scientific. In essence, while we should not forget that the propositional statements published in the scientific literature have a complex lineage; it is not unreasonable to assume that they can be represented conceptually in the same manner they are often referred to—as a bibliographic entity. It was a surprising that the work described here has not been recognized for its conceptual linkage to the field of bibliometrics.

Latour and Woolgar (1986) and Latour (1987) have also observed and written widely that the propositions which ultimately comprise a network of scientific literature are themselves the products of a web of writing that includes everything from grant



proposals, columns of numbers in laboratory notebooks, graphs, and eventually published propositional statements—the writing of each with its own unique place and format.

## **2.3 Citation Analysis**

### **2.3.1 Citations as Metrics of Science**

The norm of communalism in the scientific enterprise remains viable because those working in scientific fields are governed by institutionalized systems of reward which are closely tied not only to the number of publications credited to them, but to the subsequent visibility that publications confer on their authors. Publishing is important, but publishing works that are cited by others is better still. Thus, science remains a body of interrelating texts, the relationships between which tell us something about how science changes over time. A network of the intellectual history of scientific propositions has been created because scientists published their propositions in a communal literature, and because they formally acknowledged (through citation) the previously published knowledge upon which they relied. This network of intellectual history can be explored retrospectively in several ways.

Citations represent the relationships of ideas between documents (texts). They are acknowledgement of the intellectual origin of an idea, statement, or proposition. Citations therefore provide a relatively objective means for deconstructing the network of extended translation of propositions over time—when the written record of science is deconstructed, a network of citations is revealed. As used here, “citation” refers to the written reference made to another text within the network of scientific literature. By convention, the “citer” refers to a distinct (generally written and published) entity such as a journal article, book, letter to the editor, or to some sort of personal communication

(e.g., a letter from the “citee” to the “citer” or some other individual). An abbreviated citation generally appears in the body of the text near the relevant thought and a more substantive entry generally occurs in a footnote or in a list at the end of the article. The format for citations in journal articles (which represent the majority of the works in consideration here) may vary slightly in format from one journal to another, but will include author names and institutional affiliation, keywords, the title of the journal article or book, and other information that provides the reader with enough information to locate that reference should he or she choose to do so (e.g., date of publication, volume number, page numbers).

Citations are predominately an innovation of the 20th century although the concept of legitimizing scholarly discourse and argument by reference to established texts has a much longer history, generally thought to trace back to Middle Age scholasticism. At that time, reference to previous related work was essential for establishing one’s credibility among scholars. In the 19th century, “science” underwent significant transformation including the establishment of institutions and professional societies of science. It was during this time that references became increasingly used in scholarly writing. The references made however were not to specific (or dated) works, but to individuals and their entire body of work. By 1900, about 50% of the references in written materials were dated and referred to materials that were within six years of the citing articles date of publication (Leydesdorff, 1998). It was not until after 1910 that citation began to represent reference to specific propositions as they do today (Leydesdorff, 1998; Wouters, 1999).

As the enterprise of science and its literature were rapidly evolving in the post WWII era, Eugene Garfield saw the value of creating an index of scientific citations (Garfield, 1955). Garfield outlined an ambitious plan for creating a complete listing of all periodicals, their articles, and all the articles that made reference to them. In *Science*, Garfield wrote that such an “association of ideas” would “clearly be useful... when one is trying to evaluate the significance of a particular work and its impact on the literature and the thinking of the period” (Garfield, 1955, p. 109).

Garfield was anxious that this tool be used to its fullest and rallied hard to convince others of the value of his idea for a science citation index. He sought the input of noted scholars, among them Derek de Solla Price. Price was intrigued with the concept of using science to measure itself and wrote in 1961 that examining the relationships found within the literature of science would surely reveal patterns, and perhaps even “laws” that govern the production of knowledge. Price recognized citation indexing as more than a bibliographic resource for locating documents, and saw its potential as a quantitative—bibliometric—tool for measuring the structure of scientific development (Price, 1961).<sup>3</sup>

The Science Citation Index (SCI) became available in 1962 following what was nearly a decade of persistent efforts by Garfield and his colleagues to foster interest and acquire funding (Wouters, 1999). The SCI, a compilation of bibliographic information, made it possible to identify and enumerate citations as well as the relationships between them. By deconstructing the network of connections between scientific propositions in

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<sup>3</sup> Bibliometrics is a set of quantitative tools which can be used to deconstruct a body of literature by its bibliographic attributes. It thus enables a qualitative assessment of the production and dissemination of knowledge that may not otherwise have been possible.

the literature, both the social and cognitive frameworks of scientific development could be revealed.

By 1963, Garfield saw the possibility of using citations to create maps for tracking the historical path of scientific development. Garfield, Sher, and Torpie (1964) mapped the progression of DNA studies using bibliographic coupling (a technique in which references shared between articles are compared). Price (1965) demonstrated that patterns of citations could be used to reveal the trajectory of research over time and to illuminate foci of interest. Price also expressed hope that the Science Citation Index, and the quantitative study of science that it enabled, would become foundational for policymaking. Garfield and Price hoped it could provide decision makers with a visual depiction of the cumulative work of all the science on any particular issue (Price, 1965; Wouters, 1999).

However, the focus of scientometrics was not on its use as a policy making tool, but on finding evidence within the structure of bodies of scientific knowledge revealed through the study of citations. The hope and expectation was that this would lead to the discovery of generalizable principles and laws. In general, the work entailed the use of descriptive statistics to compare the distribution of papers across disciplines and over time. But there was much interest in developing indicators that could be used to understand the intellectual and social impacts of science (Wouters, 1999).

One of the ideas that took hold in the 1970s was that highly cited documents become “concept symbols” for the specific discoveries or methods found in the document itself. In some cases these would come to represent the concept itself and become symbols for the citing author (Small, 1978). Using the bibliographic details (e.g., author name,

cited references) of research papers as surrogates for concepts, Small (1978) demonstrated that citation links represented meaningful assertions about science. Clusters of such links could be uncovered which would reveal an even greater network of scientific statements. For example, the dual nature of citations might be used to elucidate both cognitive systems (links between texts) and social systems (links between authors) (Cozzens, 1989). Citations provided documented insight into how concepts evolve and how they are valued within the scientific community. Moreover, the links between citing and cited texts uncovered through citation analysis revealed much more than cognitive relationships; they also embodied cultural, social, and political influences (Cozzens, 1989).

That the citation network depicted in databases such as Thomson's Science Citation Index (SCI) was a valid representation of science was based on the assumptions that 1) that it represented all of the science that has been published through the peer review process; 2) that citation practices are substantive and consistent; and 3) that the relationship between SCI and the scientific literature is not subjective (Small & Griffith, 1974).

Techniques for visualizing networks of scientific texts have been under development at least since the 1960s. Several pioneering scientists and historians of science saw value in being able to represent the progression of, and relationships between, scientific advancements. As computer processing speeds and storage capacity increased, so too did the availability of large bibliographic datasets such as those

constructed by Thomson's Institute. The first historical maps were soon constructed for developments in physics and genetics (Doyle, 1961; Garfield, 1963; Price, 1965).<sup>4</sup>

Another advance came from Small's technique for representing scientific domains (Small, 1973) through the process of co-citation analysis, a method for locating and quantifying the relationships between researchers in a given field. Co-citation analysis establishes the frequency with which two published entities are cited together in subsequent works, the assumption being that co-cited documents are conceptually related. Therefore, if an analysis finds that certain works are more frequently cited together than others, it can be inferred that they may be of greater relevance in a field than other works less frequently co-cited. The more cited works in common between groups of papers, the more thematically related they are likely to be, and we can assume that the cited works in common between groups can be used as a measure of their intellectual relationship.

Small and Griffith (1974) and Griffith, Small, Stonehill, and Dey (1974) created maps of the natural sciences which illustrated areas of shared intellectual history between the fundamental concepts unique to subdisciplines. The following year Aaronson (1975) showed that it was not only possible to map the scientific enterprise, but that the variability between the clusters and the differences within clusters over time provided useful insight into the intellectual landscape of the scientific domain being analyzed.

There have been bibliometric studies that demonstrated the value of co-citation clustering for exploring both the social and cognitive structure of a scientific field. Small

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<sup>4</sup> Those active in the science of science movement of the 1960s were unaware that they had been "scooped" in 1923 by unnamed Polish scholars who announced the emergence of a new field *wiedza a nauce* or "knowledge about science" which was distinct from perspectives of epistemology, logic, or descriptive histories of science (Krause et al., 1977, p. 198 as quoted in Wouters, 1999, p. 82). This movement became known as a "science of science" by 1928 and was described in the journal *Organon* by 1936 (Ossowska and Ossowska). Unfortunately, the work of this group was halted when the Nazis invaded Poland in 1938.

(1986) constructed co-citation clusters to create synopses of scientific fields. Using both the ISI data and the literature itself, he extracted the “consensus passages” that linked the citation clusters. He was then able to diagram the conceptual linkages in a knowledge domain with very much the same logic that a scientist might use when writing a review of that field. Small recognized that method would also be useful for identifying areas of agreement (or disagreement) among the scientists that have contributed to the literature within a knowledge domain (Small, 1986).

As electronic methods for information retrieval advanced in the 1990s so did the sophistication of citation analyses. Since the early 1980s a steady progression of citation analyses have incorporated statistical and multidimensional scaling techniques with which to better reveal and represent various knowledge domains. With the application of multidimensional scaling techniques, it became possible to situate clusters in more visually meaningful ways. Specifically of use was the frequency of co-citation represented by the size of the clusters (density) and the distances between them representing relative cognitive relatedness (centrality). However, the increasing sophistication of bibliometric analyses has not addressed some of the more fundamental issues concerning the value and meaning of citation analyses.

Small (1978) also demonstrated that there was agreement between the use of terms in a cited passage and the citing work. His analysis of the actual text in which citations were used revealed shared patterns of language between authors. Through such analyses Small asserted that there was conceptual agreement in cited passages that traversed multiple citing authors over time. Thus, patterns of citations provided a unique path to understanding the conceptual connections between authors over time.

Another critical aspect of the role and value of citations as attributes of the scientific literature involve the process by which scientists decide what they will cite and how they will cite it. Aksnes (2003) suggests that there are two overarching dynamics at play in this decision. The first is a “quality” dynamic in which the cognitive content of an article is considered. The second is a “visibility” dynamic in which social aspects of the decision to cite are considered. The visibility dynamic is demonstrated by a phenomena referred to as the “bandwagon effect” in which the more a paper is cited the more visible it becomes and therefore, the more it is cited over and over again. This is similar to Merton’s (1968) Matthew Effect which in essence suggests that there is a bandwagon effect in science - that the level of recognition scientists receive is skewed in favor of already recognized scientists.

### **2.3.2 Validity of Citations as Measures of Science**

Valid criticisms have been made about using citations as data, with most concerning the ever popular practice of using the number of citations to an author or institution as a measure of quality and as a tool for evaluation. It is not uncommon for citation counts to be used for evaluating individual scientists (e.g., for tenure) or institutions (e.g., for grants). The basic argument for this use of citation analysis is that the many confounding variables involved in the decision to cite or not cite make citations highly unreliable indicators of either influence or quality. Moreover, as MacRoberts and MacRoberts (1986, 1987, 1997) assert, the relationships between the true influences on an author’s work and what appears in his/her bibliography have never been adequately studied despite the nearly two decades in which the need for such data has been voiced.



Questions about the validity of using citation analysis are clearly testable despite the dearth of such data. MacRoberts and MacRoberts (1986, 1987) conducted a few simple experiments to test the claim that scientists accurately cited the actual influence for their work. Reading randomly selected papers in fields with which they were familiar, MacRoberts and MacRoberts found that the number of references cited in the works examined typically failed to represent influences that should have been cited. Their findings revealed that authors cited only about 30% of the literature that influenced their work.

In addition, MacRoberts and MacRoberts (1996) found evidence suggesting that author selection of citations is biased. In a test in which they traced 13 “facts” (knowledge claims), they found that 63% of the time these facts were inaccurately attributed (not credited to the correct source). They also found that credit (in the form of citation) tended to be disproportionately allocated to certain facts over others. The sources of some facts were nearly always given proper credit (88%) while others were never credited. They also observed that citation rates tended to vary by discipline, nationality, as well as across generations.

MacRoberts and MacRoberts (1996) also found that credit was often not correctly attributed to the source of a knowledge statement but was instead credited to a secondary source or to a review article, thus giving credit to an author having nothing to do with the actual generation of the scientific proposition. Critics of using citation counts to compare or evaluate the quality of an individual’s work have also argued that an author’s decision to cite any particular work may be biased by political or social purpose. Brooks (1985, 1986), Liu (1993), and MacRoberts and MacRoberts (1988, 1989) all stress that when

citations are used in empirical studies it behooves the investigator to evaluate whether psychological and social factors may have affected how citations were included or excluded.

There are additional issues with the use of citation analysis that must be considered as well. The development of citation analysis as a tool of the scientometrician has clearly advanced in both use and presumably utility because fast and inexpensive processing combined with an explosive growth in the availability of data. Yet despite these technical advances there is still a considerable void in the theoretical understanding of what these data and subsequent analyses mean. The scientometric literature is largely devoid of theory (Cozzens, 1986; Leydesdorff, 2001). Hence, there is a clear need for the type of systematic examination of the relationships between quantitative measures (e.g., bibliometrics) and qualitative measures such as those provided in this study.

### **2.3.3 The Case for Citation Analysis**

An important, but controversial, voice in scientometrics, Leydesdorff (2001) explains that the best approach for understanding how science works involves acknowledging it as a multidimensional phenomenon that is comprised of texts, scientists, and cognitions. Originally focusing his attention on words, Leydesdorff shifted the focus of his study to the information generated by science, or what he considered the fundamental concept or claim. Hence, “[t]he systematic processing of information in order to reduce uncertainty about the environment is the core process in scientific developments that the scientometrician attempts to map” (Leydesdorff, 2001, p. 5). Leydesdorff (2002) saw that the bibliometric ranking of papers and journals also revealed a hierarchy of the relevant actors (e.g., journals, individuals, institutions) and that by

examining the relationships between clusters, nodes and links, the communication structure between those actors was also revealed. Based on this, Leydesdorff turned his attention to examining whether the citation relationships between and among journals might be good indicators of structural change within the organization of science.

What is unique about Leydesdorff's schematic interpretation is that it offers theoretical support for linking the cognitive and textual elements of science. Whereas citation analysis might enable a look at the relationships between scientific claims made in the literature, they do not tell us much about the claims themselves. For that it is necessary to apply other means. The cognitive dimensions of important issues must be revealed for there to be sound decisions made (Leydesdorff, 2001).

Underlying the research described in this dissertation is the assumption that the relationship between a citing document and a cited document is meaningful. Maps based on citation relationships are informative because they reveal the historical developments occurring in a field. Those who value applying bibliometric tools to the study of science often see citations as quantifiable surrogates for concepts within a network of scientific claims. However, these relationships have not been sufficiently studied. In recent publications on the theoretical implications of citation practices in science (Cronin, 1998; Leydesdorff, 1998), law (Talley, 1999), and technology (Meyer, 2000), there was little attempt to extend work on the citation as concept symbol (Small, 1978). Even in some recent work creating longitudinal maps of specific knowledge domains, little attention is given to this underlying assumption.

While bibliometrics is a powerful tool, its use is not without its challenges and bibliometrics alone are insufficient to fully appreciate the intellectual history of an area of

knowledge. The first challenge in identifying the emergence and evolution of the science of a particular issue is the scale and complexity of the relationships that exist. A citation links one article to another—the new with the old—and the citations received by a paper may vary from zero to several thousand. There may be many reasons that an author chooses to include or not to include, any given citation. It is not sufficient to assume that two papers linked through citation are in agreement with each other. A paper may be cited because it supports the citing paper’s arguments, or because it contests them.

Most of the criticisms that have been leveled at the use of citations as data are not relevant for the purposes of this dissertation. The study undertaken here is not concerned with evaluating research quality or its impact per se. Nor does it make any normative assessment of the value of a given work. The criticisms leveled at the use of citation analysis as a tool for evaluation seem almost self evident. It is not at all difficult to imagine citations being made or not made for any variety of reason including ignorance, conceit, ingratiation, or obligation; however they are the most trusted and visible record that exists for tracing the intellectual history of science.

#### **2.3.4 How the Attributes of Scientific Literature Impact Citedness**

Is it possible to relate the value of the content of a scientific paper within a specific area of science to the amount of attention (i.e., citations) it receives? According to Franck (1999), the amount of attention received by a theory is “not necessarily related to its scientific value.” The characteristics that Franck postulates as contributing to the attention a theory receives include “looks suggestive,” “rebels against convention,” and “matches the *zeitgeist*” (Franck, 1999, p. 54). While all of these characteristics are as elusive to controlled measurement as is the basic concept of “scientific value,” the notion

that clearly expressed, but provocative ideas have as great an impact as do the mundane is an intriguing proposition.

While none of the factors affecting citation patterns in science have been extensively studied, existing studies indicate that an author's decision to cite previously published work is influenced by several factors, some of which have little to do with scholarly context. Factors that have been studied for their ability to influence citation frequency include article length (Leimu & Koricheva, 2005), collegiality (Leimu & Koricheva, 2005), journal impact factor,<sup>5</sup> nationality (Aksnes, 2003), gender, and whether study findings support or dispute existing hypothesis (Leimu & Koricheva, 2005).

In one of the very few studies of its kind, Leimu and Koricheva (2005) looked at the factors influencing citation rates of ecology papers concerned with three different hypotheses for which there are competing schools of thought. They found that citation rate was influenced by the direction of study outcome; for example, whether findings supported or disputed generally accepted hypotheses, and that the direction of the effect varied with the hypothesis being considered. Studies supportive of widely accepted hypotheses were more highly cited than studies that did not. Studies that were critical of hypotheses that were widely criticized were more highly cited than articles arguing that the critics had erred. Authors tended to cite articles that they agreed with. Leimu and

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<sup>5</sup> Journal *impact factor* is a metric invented by Eugene Garfield and associates in the 1960s that has been shown to influence the citation rates of journal articles. A journal's impact factor is calculated by dividing the number of citations to current year documents by the number of documents published over the previous two years. Thus, the journal impact factor is the frequency with which the average document in that journal has been cited in a particular year. An annual list can be purchased from SCI. This factor was developed to eliminate bias that results from simply counting citations which would give preference to large journals or journals that publish more frequently, it seems to have become a marketing tool and surrogate for journal prestige.

Koricheva opined that was an indication that citations might be more often employed as tools of persuasion than linkages to background information.

While the direction of research findings (i.e., the support or negation of hypotheses) has been shown to impact citation rates, the statistical significance of the reported results apparently does not (Koricheva, 2003; Murthaugh, 2002). However, while attributes such as the magnitude of the reported effect or statistical significance of the reported findings did not correlate with citation rates, they were shown to correlate with the publishing journal's citation rates. This indicated that papers with "better" statistics tended to be published in journals with more highly cited journals. Aksnes (2003) also tested the hypothesis that highly cited papers are typically found in high impact journals—those which in general have higher than average citation rates. Also, while it has been shown that statistical power may not influence an article's citation frequency, citation rates have been related to sample size in the medical literature (Callahan, Wears, & Weber, 2002; Peritz, 1994), although not the ecology literature (Leimu & Koricheva, 2005).

Leimu and Koricheva also found a significant positive correlation between the length of a paper and the number of citations it received. In explaining why this might be, they credited the increased visibility of a longer paper within a journal and the possibility that longer papers have more potentially citable text. They also found that papers authored by those for whom English is the national language were more highly cited than papers written by those from non-English speaking countries. Likewise, American authors were more highly cited than European authors. Many of Leimu and Koricheva's findings underscore the significance of the very hard to measure attribute of "prestige" in

evaluating the prominence of a research paper. The prestige of the author's academic institution was shown to influence citation rates, authors from more prestigious universities being more highly cited.

Taken together, this body of work, though small, gives credence to the idea that there are variables other than cognitive content and relative scientific merit that influence citation rates. This is significant because of the social importance given to the authors of highly cited papers, and the real possibility that highly cited papers have greater influence on the evolution of scientific literature. Highly cited papers may also have greater influence within the scientific enterprise or beyond, although few have attempted to test this hypothesis by looking beyond the bibliographic data provided by SCI databases to examine the cognitive content of the papers or the context of the citations.

Aksnes (2003) and Leimu and Koricheva (2005) explain the correlation between the number of authors and the rate of citation in a number of ways. First, having a large number of authors suggests a well-funded study that has been conducted in either a large institution or through a collaboration of several institutions. In addition, having more authors suggests that there will be a greater pool of potential citers simply from the combined networks of the authors and their institutions. Well-funded studies conducted at large institutions or involving the collaboration of several institutions are also more likely to reach a greater pool of potential citers because their completion and publications are more likely to be publicized by either the funding institution and/or the research institution itself.

Several studies have found a disproportionate number of review articles among highly cited papers (Aksnes, 2003). In Aksnes study of Norwegian papers review articles

represented 2% of all papers reviewed, but comprised 12% of the articles classified as highly cited. The manner in which these papers were cited was not examined so it is not known whether review articles are cited in the context of providing background material or whether they are used as secondary sources of data that would be more appropriately cited from their primary sources.

The studies relying on citation analysis often refer to the effect of author self-citation on the citation frequency for determining an article's impact (MacRoberts & MacRoberts, 1989). Aksnes (2003) found that roughly 15% of the citations for highly cited papers were self-citations compared to a 21% in the entire data set. Aksnes did however observe a wide range of self-citation with one paper being cited 136 times by one or more of its authors out of a total of the 237 total citations the paper received.

Callaham et al. (2002) found that the impact factor of the publishing journal was a stronger predictor of citations per year than either methodology or research quality. They determined that a weak paper published in a strong journal might receive more attention than a strong paper published in a weak journal. They found no relationship between study design and impact of the journal. After accounting for journal impact factor they found that the only other predictors of citation frequency were newsworthiness, sample size, and the presence of a control group.

In a study of papers submitted in 1991 for publication to an emergency medicine journal, Callaham et al. (2002) found that of the 204 papers accepted for publication the mean citation rate for these papers in a 3.5-year period was 2.04 (in 440 different journals) and approximately 9% were never cited. Using regression analyses, they were able to only weakly predict the attributes of this group of papers that influenced citation



( $R^2 = 0.14$ ). Nonetheless, the factors determined to influence whether a paper would be cited were the impact factor of the publishing journal; a subjective determination of the newsworthiness of the paper; the presence of a control group in the study being reported; and a study's sample size. They found that with the exception of the use of a control group, neither methods nor study design influenced the likelihood of citation frequency.

Accuracy in the data field of SCI is often given as the primary cause in the use of citation analysis. Using papers published in the journal *Occupational and Environmental Medicine*, Gehanno, Darmoni, and Caillard (2005) determined the percentage of inaccurate citations in the fields of environmental and occupational medicine. The authors chose this particular journal because it had the highest journal impact factor of the journals in these fields. Errors that could affect the citation count such as the spelling of the author name, inaccurate first page number, or errors in the title were found in 3.35% of 3,347 papers.

Ravnskov (1995) studied the accuracy of reviews that had been written by distinguished scientific bodies concerned with the effect of diet on coronary health. This study was driven by concern that the dissemination of the faulty knowledge contained in these expert reports would have essentially the same "disastrous effect in science as a data virus in a computer" (p. 717). Ravnskov (1995) focused his investigation on how the expert bodies managed and explained discordant results in the literature by comparing passages from relevant papers with opposing findings to the three authoritative reviews that had been published. Ravnskov found that the citations provided in the expert reports were biased in the way they represented the discrepant results from the scientific literature reviewed. Ravnskov divided the literature on diet and heart disease by the

hypotheses tested (five groups) and looked at the evidence and counter evidence available for each. Quotes were classified as “correct” if they impartially referred to the controversial finding in a paper contradicting the hypotheses. Quotes were classified as “irrelevant” if they gave meaningless or misleading information from the cited paper without mention of its contradictory findings. Quotes were considered “inflated” if statistically insignificant results were exaggerated. And finally, quotes were considered contrary if the contradictory paper was quoted as if it were supportive.

In comparing the cited literature to the expert reports, Ravnskov (1995) found that only two of the twelve papers reporting evidence counter to the hypotheses were correctly quoted, and half of the papers presenting contradictory information were completely ignored. Ravnskov also found that even insignificant papers were cited if they supported the hypotheses, thus inflating the appearance of the actual level of support that existed for these papers in the literature. It was also determined that evidence from papers that disputed hypotheses was incorrectly quoted, and studies supportive of hypotheses were favored even when the studies with counter evidence were stronger; for example, non-randomized trials with positive outcomes were more frequently favored over randomized trials with negative outcomes. All of the biased citations found were those that favored the heart/diet association. These findings were troubling for many reasons, among which was the apparent tendency for scientists to become enamored with “fashionable” hypotheses, thus creating a sort of scientific “groupthink” phenomena (Ravnskov, 1995).

## **2.4 The Role of Science in Decision Making**

### **2.4.1 Policy Making**

The environmental movement has relied almost exclusively on scientific claims to justify its calls for protectionist policies, and yet environmental controversies have been studied primarily from the perspective of the relationship and influence of science on policy making and not from the perspective of policy making on science or from the perspective of influences within science. Basing arguments for protectionist environmental policy on scientific knowledge (as opposed to spiritual, moral, or ethical claims) has not proved as powerful a determinant as might have been anticipated given the perceived authoritative power of science. Indeed, the very norms that serve the growth of science so well also make it vulnerable to those who oppose its influences. The norm of disinterested objectivity demands empirical data, but for many of the complex questions of environmental science data may be unavailable, or insufficient to counter the skeptics. Alternatively, research findings that make their way into science's communal repository are often attributed with value that they may not deserve.

The focus of this dissertation, however, is on the intellectual history of an emergent and controversial area of science which has both motivated public policy and been fueled by public policy. While interdisciplinary science studies methods such as citation analysis provide a framework for understanding the social and cognitive dynamics of its science, it is important to consider that these developments have been, and are being, played out in a political context. A discussion of how the issue of endocrine disrupting chemicals gained political salience is found later in this chapter, but suffice it to say here that this issue acquired a degree of political significance that quickly

pushed it up the policy agenda. Therefore, it is worthwhile to consider the interactions between science and policy decision making.

Among the reasons compelling scholars to better understand how the scientific enterprise works, is that in the United States and elsewhere governments have chosen to use science to inform public policy decision making. They have incorporated science-based criteria into the regulatory infrastructure through which the impacts of industry and technology are managed. Often the history of how government came to acquire these responsibilities is omitted from discussion and replaced by criticism of the unwieldy web of law and regulation that has evolved, thus overlooking that this infrastructure resulted from both the inability and unwillingness of the private sector and states to reign in or control the hazards of industrialization. With no motivation other than altruism or fear of litigation, industry did not adequately protect its workers, the public, or the environment from the impacts of its activities. As a result, most governments in the developed world were forced to seize the authority to control hazards or potential hazards and did so through a vast framework of methods that included issuing regulations, supporting research, granting incentives, and disseminating information. While each of these tools employs different strategies for decision making, some generalizations can be made about the complexities of using scientific information in a political framework.

Scientific knowledge claims are dynamic and subject to revision, expansion, or falsification, and these ambiguities often do not suit the needs of those outside the scientific community. Politicians and interest group leaders who must argue convincingly for a particular course of action are stymied when science is unable to offer a definitive knowledge claim. In accordance with the norms of science, the debates that ensue

between scientists as provisional knowledge develops and matures occur in public. While such debate is normal and accepted within the scientific enterprise it tends to undermine the authority of science in other spheres where the admission of provisional knowledge is seen as weakness. Even after mounting evidence clarifies and validates a claim, opponents to a particular course of action have no trouble reaching back and alluding to past disagreements between scientists as testimony to the uncertainty of science. A good example of this phenomenon is the issue of global warming. Opponents to precautionary and protective strategies continue to argue that the science is not convincing by ignoring how the cumulative developments of the science have made it robust, instead focusing on statements made in the past, when indeed, the science was less certain.

Of course, it is naïve to blame all of the conflict about environmental issues on how the characteristics of science make it vulnerable in the public realm. In the final analysis, science alone is not sufficient for resolving debates that are essentially about values, morals, and ethics. Regardless, the body of U.S. environmental law provides a forum for debates about science because it contains provisions for parties to assert their interests, argue claims in the courts or through processes of judicial review, and by requiring agencies to consider public comments in creating or modifying regulations. Parties with an interest in determining the level at which standards and thresholds are set for particular pollutants can all bring their scientific evidence to the attention of decision makers and attempt to make their case and discredit those with opposing positions. The result of this adversarial system has been to significantly slow, and often to halt, decisions that are needed to establish standards and thresholds that by law are to be determined by science.

The degree to which science is afforded epistemic authority in the decisions made by governments, industry, and the public has been the topic of much discussion in the policy and science studies literature. Much of the reporting in the policy literature concludes that science plays only a small role in the decisions made by those who come to argue an issue with opposing points of view. Hence, science plays only a small role in informing public policy decision making. Collingridge and Reeve (1986) contend that the decisions made in cases of controversial environmental issues have had much more to do with political compromise than with scientific evidence and would have been similarly constructed without the technical details.

Perhaps as the result of this regulatory infrastructure, it has become the norm of environmental disputes to debate technical details such as whether investigators have used a valid model, than it is to argue opposing values. In essence, science provides the justification for the positions taken by those with opposing values (Collingridge & Reeve, 1986; Nelkin, 1984).

Another quagmire in the role of science in political decision making is that the norms of science such as skepticism, so essential to the “healthy” functioning of the scientific enterprise may be vulnerabilities in a political arena. It is the rare piece of scientific literature that does not temper its reported findings with a cautionary statement to readers about the preliminary nature of the work, its limitations or uncertainties, or more commonly, the many related questions that remain to be answered. However, policy makers operating in the political realm seek unqualified answers from science that science cannot provide without qualification. Even studies in which the findings are

highly significant include caveats about the need for more confirmation, or the choice of dose.<sup>6</sup>

Since the explosion of environmental regulation of the 1970s, the use of scientific information has become an integral part of the decisions made concerning human health and the environment. The regulations promulgated for the major environmental laws required the establishment of limits, standards, and assessments which were built upon a negotiated understanding of critical natural resources and the hazards faced by citizens. This understanding, in turn required the input of people with expertise in an array of scientific and technical fields. While it is tempting to take comfort in what was intended to be a rational process, the data indicate that science may have had very little impact on how we prevent or mitigate the impacts of modernity on human health and the environment. While enacted to make rational the multitude of choices facing a society dealing the impacts of technology, it soon was apparent that “science” was not a panacea—neither for precisely identifying hazards, nor for clearly illuminating mitigation or prevention.

The system of rational policy making to which many environmental regulations aspire derives from an ideal that policies should be logical extensions of scientific understanding of the issues. Improving both the science and the use of science in making environmental policy decisions is still a mantra in policy circles regardless of point-of-

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<sup>6</sup> A good example of the qualified manner in which scientific findings are reported can be found in a recent paper by Anway, Cupp, Uzumcu, and Skinner (2005). In a laboratory study linking endocrine disruptor chemical exposure to effects seen in more than 90% of male offspring two generations removed from the exposed parent, the authors still concluded with a caveat by stating “... [t]his study shows that environmental factors can induce an epigenetic transgenerational phenotype [changes which appear in the offspring of exposed animals] through an apparent reprogramming of the male germ line. It should be noted that the exposure levels used in these studies are higher than anticipated for environmental exposure; hence, future toxicity studies would be needed to ascertain the possible impact on animal populations” (Anway et al., 2005, p. 1468).

view. As the regulatory infrastructure for environmental issues took shape in the 1970s many believed that the various standards and thresholds required would be developed through a rational process that took available science into account. Scholars hoped that some of the tools developed for the science of science could serve as the foundation for such policymaking as they provided a way to visualize the cumulative work of the science available for a particular problem (Jasanoff, 2003; Price, 1965). This ideal persists because it makes sense that consensus should be possible when there are objective data available to inform our understanding of a problem, identify alternatives, and implement solutions. It makes sense that agreement can be reached about any given hazard if there are enough data with which to assess it.

The problem is that reaching an agreement in this way requires that the decision makers and their advocates agree on just what constitutes the scientific understanding of any given issue, and the thirty-year history of U.S. environmental regulation shows that such agreement is rare. Despite claims to the contrary, the science by which we had hoped to understand and manage environmental hazards, has, is, and will continue to be disputed, dissected, disparaged, and denied as interested parties argue their positions and decision makers grapple with the hard choices that must be made.

Environmental issues in particular tend to be divisive with most disputes distilled into two camps: those arguing for protective or precautionary policies and those arguing that such approaches are unnecessary. When an issue involving environmental contamination is identified, each camp mobilizes to influence the public and government decision makers and science is used as the source of supporting evidence. Disputes tend to then become focused over whether protective strategies are warranted and what those



protective strategies should be. Expertise and scientific knowledge play important roles in how arguments are framed and evolve and policy scholars have focused much attention on these phenomena over the past 30 years. Less explored, however, is the extent to which science actually informs the decisions that are ultimately made.

The integration of science into public policy decision making has proved difficult to manage. Science generally cannot provide clearly defined actions and alternatives; not all interested parties can agree on the interpretation and use of the available scientific information; and it is common for parties to disagree on how the scientific processes should be undertaken. Even when scientific findings are relatively uncontroversial, there are disagreements about how to translate these findings into actions, or how much weight they should be given compared to economic or other considerations.

The task of decision makers is to acquire, assess, and aggregate the available information so that the impacts of complex issues can be managed to the satisfaction of stakeholders. There is no dominant theory of the use of science in policy making. The use of science in public policy decision making has proved difficult to study, in part due to the sheer complexity of the issues at hand (i.e., there are no simple solutions available to satisfy all of the interested parties). The development of a central theory to explain the influence and use of science in policy making would require a cross-disciplinary mindset along with an understanding of how we endeavor to understand the natural world as well as the sociocultural, political, and philosophical forces that shape our perceptions of that natural world. The information needs of policy makers differ from the information needs of the scientific enterprise. The process of science entails simplifying the natural world—

to unravel complex issues or systems in a way that facilitates answering distinct questions.

The literature suggests that more science, or “better” science, or the politically loaded concept of “sound” science, is immaterial, because there are other factors which prove far more significant in the ultimate outcome of decision making. It is widely held that although the body of science about human health and the environment has grown tremendously over the past 30 years, most environmental policy has been far more influenced by political elements and prevailing social values than it has by science (Layzer, 1999). In the typical controversy involving a suspect hazardous agent, proponents of policy that would limit or ban the use or production of the material generally provide justifications that include the scientific evidence of adverse impact caused by the agent, or scientific evidence that implies a connection between the agent and an adverse impact. Opponents of the policy generally argue that such actions are unwarranted given the lack of evidence demonstrating adverse impact, the negative economic consequences of discontinuing or limiting production, and/or the net positive benefits that result from the use of the suspect material.

Collingridge and Reeve (1986) asserted that contrary to the presumption that the availability of scientific information would narrow a dispute, more science actually widened the political debate by including dispute about technical issues as well as the interpretation of data. They noted as well that rather than a moderating influence, appeals to science in the context of policymaking resulted in “endless technical bickering” over voluminous and often irrelevant scientific material the result of which were compromises

that were often totally “insensitive to any scientific claims” (Collingridge & Reeve, 1986, p. 32).

(Healy & Ascher, 1995) looked at the role of information in natural resource policymaking and found results similar to those found in the studies that concerned toxic chemicals. They looked at how the policies adopted by the U.S. Forest Service incorporated scientific information and found that more information did not lessen political conflict or change decision making, rather it conferred political advantage to the participants who held information.

In general, several conclusions can be drawn about the function and impact of scientific information in policymaking. First, in conflicts involving the use of the power obtained through scientific information generally shifts away from the non-expert to the designated expert (the one with the information). In addition to this shift of power, the discourse shifts as well from discussions about values and rights to discussion about technical points. The debate about effective courses of action is then likely to become polarized, the effect of which is often an inappropriate delay in making decisions about mitigation measures.

Currently available literature “confirms the conventional wisdom” that because science is uncertain it can be manipulated and is vulnerable to exploitation. However, there are some predictable impacts that result from the use of science in policymaking. For example, it is accepted that science is useful in narrowing the range of alternatives among those under consideration, and that science influences the balance of power among those advocating for disparate outcomes. While information and expertise seem to have become increasingly important in the scholarly assessment of the political bases of

environmental policy, there is little work on how emerging scientific evidence of hazards is identified.

Does science contribute to making “better” decisions about complex issues about environmental health and the environment? Some studies have shown technical expertise is not always an asset, and may actually be of little value in advocating for a particular cause. According to Layzer (1999), the literature on the use of science in policymaking suggests that science has greater influence when the hazard is clear and incontrovertible, but the extent of the influence depends on the policy making context, and the influence of the advocates. Unfortunately, by the time a hazard becomes fully understood the options for managing the risks from it may be limited. Combining what was known about the influence of science in policymaking with general theories on policymaking Layzer (1999) proposed four factors which explained the extent to which policies reflect the scientific understanding of environmental problems: 1) the institutionalization of competing interests, 2) the salience of the environmental problem, 3) the legal leverage available to competing advocates, and 4) the certainty of the science.

Layzer contended that while scientific understanding is critical to determining the balance of power between the interested parties, their relative power tends to be “mediated” by their respective advocacy skills. Power struggles are an inherent part of the use of science in policymaking and power hinges on the abilities of involved parties to manipulate knowledge and to challenge evidence. On power, Beck (1992) wrote “[so] long as risks are not recognized scientifically they do not exist-at least not legally, medically, technologically, or socially, and they are thus not prevented, treated, or compensated for” (p. 71). Those professing a particular point of view and desiring a

specific outcome use “scientific consensus as a shield against” criticism. This shield assumes the prestige associated with scientists and also presumes their objectivity.

It is difficult to find studies in which the details of the science of an issue are rigorously assessed alongside its political and social contexts and this is especially apparent in the study of issues of environmental significance. Nonetheless, a clear need for substantial multidisciplinary examination of the science critical to environmental health policy has been demonstrated. Although the processes by which science influences policy have been examined by both political and social scientists, studies which synthesize these approaches with those of the environmental health sciences have been lacking (Jasanoff, 2003; Shrader-Frechette, 2002).

#### **2.4.2 Decision Making for Environmental Health Policy**

The focus of this dissertation is on that part of the scientific enterprise from which our understanding of environmental health emerges - specifically, the collective activities of those engaged in the study of chemical, physical, and biological phenomena relative to the chemical contaminants that have become part of the ecosystem as the result of human activity. A relatively recent phenomenon, environmental health research presents some very unique challenges among which is that the complexity of the systems under study require a multidisciplinary approach which is at odds with the tradition of specialization that had been the direction of scientific work for nearly a century.

Ever since the advent of the current regulatory scheme there have been battles waged in courtrooms and in the legislature over efforts to eliminate or reduce the use of chemicals suspected of causing acute or chronic health impacts. The focus of these fights has been over the value, certainty, and interpretation of the available science. There are

many unique attributes of the environmental health sciences that complicate their use in making public policy decisions. First, the types of questions investigated involve complicated systems and ultimately interdisciplinary approaches. More times than not the questions asked about the impacts of exposure to chemicals are not conducive to controlled experimentation for the obvious ethical reasons, which means that the data are less robust and more vulnerable to criticism. For example, without controlled experimentation the dose to which a subject is exposed must be extrapolated from the concentration in surrounding environmental media. In cases where the contaminant is present at very low levels the methods used for measuring exposure may be at or beyond the threshold of their sensitivity. It may thus be difficult, if not impossible, to determine actual exposures. In addition, determining the types of data needed to definitively determine the degree of hazard associated with a specific chemical exposure would require a significant sample size and for certain end points such as cancer may require long-term observation.

That science cannot always offer strong, conclusive, and specific answers to politically salient questions about environmental health makes it especially vulnerable in the political arena. Because toxicity experimentation in humans is not conducted, decisions must be made from a variety of other sources. These include the scientifically less robust epidemiologic and occupational health studies and extrapolating the results of animal studies to humans. Because studies in animals tend to be quite costly, it is also common practice to conduct animal studies using high doses of chemicals over a short period of time and then to extrapolate these findings to predict the results of chronic (long-term) low dose exposures. These practices introduce additional degrees of

uncertainty which increase the likelihood that the conflict gets locked into bickering about technical issues.

In situations where the science does not bring consensus of opinion but rather conflict and uncertainty some social and political scientists have suggested alternative resolutions. Once such resolution is based on the application of various models of conflict resolution, conceptual and methodological analyses, as well as for tools and procedures for “analyzing the scientific concepts, uncertainties, models, and inferences associated with methodological value judgments” (Shrader-Frechette, 2002, p. 369).

Nearly everything associated with the science that tries to explain the relationship between human health and the manufactured environment is complex and contested. Conflicts ensue between social groups with disparate interests such as scientists, clinicians, industry representatives, governmental entities, interest groups and individuals. Sometimes these conflicts become mired over which claims should be considered in identifying or responding to hazards, and other times these conflicts center on which claims are to be considered scientific (valid) knowledge.

#### **2.4.3 Endocrine Disruptors or Hormonally-Active Agents?**

The case selected for this dissertation is one in which many of the common characteristics of environmental conflicts are present. The chemical agents implicated as harmful are for the most part synthetic and commercially important. The impacts suggested to result from exposure to these chemicals of concern involve many systems, many outcomes, and a wide variety of species. The mechanisms by which these chemicals of concern exert their impacts and the exposures at which harm may occur have not been conclusively identified. There is conflict about the nature and extent of the

hazards of these chemicals and of the probability that harmful effects have, or will, occur. Finally, even the naming of the potential threat – endocrine disrupting agents *vs.* hormonally active agents—has been contested.<sup>7</sup>

Among the chemicals suspected of disrupting endocrine function are many that represent significant commercial undertakings and investment and some, such as those found in plastics, are so intimately ingrained in the modern world that it is almost impossible to imagine life without them. On the other hand, it is equally difficult to imagine life in 20 years if it is true that exposure to minute amounts of certain chemicals may disrupt endocrine function and reduce sperm counts, cause reproductive failures, increase the risk of hormonally mediated cancers, or disturb normal neurological development.

While no serious scientist among the various stakeholders in this issue considers this a trivial issue, some do contend that the endocrine disruptor issue is similar to other policy debates that have occurred through the years and represents the struggles between science and ideology. Critics have argued that the theory of endocrine disruption is not based upon sound scientific evidence, but upon anecdotal evidence uncovered by researchers who then tried to find additional data that were consistent with their theory. Congress, they would add, acted in haste, and under pressure, at the first sign of a theory and did not wait for the science. The result is a congressionally mandated testing program that could not reach its intended goals because the necessary science and technology was

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<sup>7</sup> My decision to use the term “endocrine disrupting chemicals” is based on the fact that it is still the most common in use to describe this group of agents. That there are many problems with this term (its inflammatory tone and technical inaccuracy) was discussed in the National Research Council’s (1999) report which suggested that the term “hormonally active agents” be used instead. Despite this suggestion, these hormonally active agents are still generally referred to as endocrine disruptors.



not yet available. How then does a society determine the correct action to take when faced with uncertain hazards and conflicting interests?

Hormones are the chemical messengers through which organisms respond to external stimuli (e.g., danger, adrenaline) and through which the glands (e.g., ovary, testes, thymus, pituitary, etc.) direct distant cells to turn on the genes which direct growth and sexuality. Hormones may also impact the production of chemicals that modulate heart rate and blood glucose levels. As appropriate to their function as chemical messengers, hormones are classified by both their chemical structure and by whether they are released directly in the bloodstream or fluids. Endocrine and neurosecretory cells (in the hypothalamus) release hormones into the circulatory system where they may be transcribed by the applicable target cell. Other hormone-producing cells target local tissues through secretion to interstitial spaces.

Hormones are also grouped by chemical structure and related factors such as whether they are fat- or water-soluble. Among the fat soluble hormones are the steroids which have chemical structures related to cholesterol. Steroids bind to receptor sites on cell surfaces where they then direct the nuclei of target cells in the production of proteins. There are three major groups of these sex hormones, all or which are found in both males and females, these are; estrogens, androgens, and progesterones.

Environmental estrogens are organic compounds which are hypothesized to function in much the same way as the estrogen hormones that are naturally found in animal species. Environmental estrogens may be either synthetic chemicals that have entered the environment from the production, use, or disposal of manufactured goods or may be produced naturally in various plant or animal species. Synthetic environmental

estrogens are also referred to as xenobiotics because they are clearly out of place in the tissue of living things. They are generally considered to be long-lived in both environmental media and living organisms, slow to break down and readily bioaccumulative.

Despite that the chemical structures of the synthetic molecules suspected of being endocrine disruptors are often not at all like the structure of the natural hormones that they mimic, EDCs appear capable of interacting with the natural functioning of the endocrine system in a variety of ways. For example, it has been postulated that upon binding to a receptor site, an environmental estrogen can stimulate hormonal response in much the same way as a natural hormone, or at an increased or decreased intensity. Environmental estrogens may also act as an anti-estrogen by inhibiting normal hormonal responses. Some believe that environmental estrogens might also be capable of binding to other types of cell-surface receptors and disrupting normal cell function or triggering novel reactions within the cell. It is through such mechanisms that EDCs have been implicated as a cause of cancer. In addition, it has been hypothesized that environmental estrogens may interfere with the normal processes by which hormones are created and released into the circulation in response, thus further disrupting biochemical functions in the organism (Hessler, 2000).

It is generally agreed, though not previously tested, that it was the convergence of several lines of inquiry that led scientists to draw the connection between the abnormalities observed in animals and humans on one hand, and exposures to environmental contaminants that hormonally active and chemicals on the other (Colborn et al., 1993; Hester & Harrison, 1999; Krinsky, 2000). Investigators had reported

disturbing observations in human male reproductive health; decreases in sperm counts and increased incidences of testicular cancer, hypospadias (misplaced opening of the urinary tract), and cryptorchidism (undescended testicles). There were also similar reports of abnormalities reported in wildlife populations and, not surprisingly, an association with exposures to environmental chemicals was suggested as an explanation for these effects. Soon, experimental evidence emerged which demonstrated that some chemicals which were widely prevalent were capable of binding with and activating estrogen receptors.

Some of the studies and observations which are commonly referred to throughout the literature of EDCs include the following: There have been reports of male fish living near sewage outfalls in England which exhibited male and female secondary sexual characteristics as well as biochemical characteristics typically found only in females. The effects appeared to be dose dependent as indicated by their distance downstream from the source of the contaminated water. The feminine effects observed were attributed to alkylphenols, compounds associated with the degradation of plastics and detergents (Jobling & Sumpter, 1993).

Another often cited example of the impact that estrogenic compounds may be having on wildlife comes from observations made of the alligator population in Lake Apopka in Florida. Guillette et al. (1994) and Guillette (1995) concluded that an extensive contamination of the lake by dicofol and dichlorodiphenyltrichloroethane (DDT) and its metabolites resulted in the significant population declines witnessed ten years following the spill which led to the contamination. Furthermore, the inability of the alligator population to rebound was attributed to reductions in successful hatchings and

increases in mortality in newly hatched animals that were the offspring of exposed animals. Adolescent females were observed to have highly abnormal ovarian structure and function and elevated blood estrogen levels. Adolescent males were described as hyper-feminized with deformed testes and penises, elevated levels of estrogen, and low levels of testosterone. In short, the normal biological processes of reproduction of the alligators living in Lake Apopka had been severely disrupted.

Sharpe and Skakkebaek (1993) released a study which suggested that environmental estrogens were responsible for falling human sperm counts and male reproductive tract disorders. This study set off a flurry of media attention. Subsequent studies have called into question the sperm count results; however there is still ongoing concern about what appears to be an increase in male reproductive cancers and abnormalities such as cryptorchidism and hypospadias.

The story of diethylstilbestrol (DES) is also widely cited as an example of the potential potency of synthetic estrogens and the damage they can cause. DES is a very potent synthetic estrogen that was given to women in the 1950s and 1960s with the thought that it would prevent miscarriages. Although the exposed women themselves appear to have suffered no ill effects, their offspring have had increased incidences of reproductive abnormalities, and DES daughters have had increased occurrences of a very rare type of vaginal cancer (clear cell carcinoma). The effects observed in humans have been replicated in both male and female mice. The DES case therefore differs significantly from the others because it has clearly demonstrated the direct causal relationship between exposure to a synthetic estrogen and adverse outcomes. That offspring could suffer serious abnormalities while their exposed mothers exhibit no ill

effects was powerful evidence of the vulnerability of the developing fetus to synthetic agents. Such findings also call into question conventional wisdom of the common methods by which chemical hazards have been assessed.

The importance of the DES experience to the story of the EDC issue is that there is clear “cause and effect” evidence of a sort generally not possible in research concerning the exposure of humans to toxic agents. Because natural estrogens have many functions, there is dispute about which laboratory studies should be used to determine estrogenicity (the ability to function as an estrogen in an intact organism) of suspect chemicals. Chemicals may be tested to determine if they can bind to an estrogen receptor site, activate estrogen-specific genes, cause cell proliferation, or to determine their bioavailability (whether they are likely to be taken up into the tissues of living organisms).

In the mid-1980s, Theo Colborn began gathering scientific papers on the health of humans and wildlife living in and around the Great Lakes. Her goal at that time was to assess the recovery of these ecosystems in the aftermath of the Clean Water Act and other Great Lakes restoration efforts. Colborn compiled data from a collection of scientific papers which had reported adverse effects in wildlife populations including reproductive abnormalities, tumors, immune suppression, population declines, and behavior. She found that the organisms at the top of the food chain, those that had fed on fish, were the most impacted. Once consolidated into a single data set it became clear to Colborn that although contaminant levels in the lakes themselves had dropped, the impacts of bioaccumulation and biomagnification were still widely apparent in these creatures. She noted that that the serious effects observed were not so much apparent in the adults of the

impacted species, but in their offspring. She found developmental anomalies across a diverse array of species; birds who failed to protect their nests, gulls nesting in same sex arrangements, and birth defects. Colborn concluded that the common thread linking these aberrations in development and mating behaviors was that they were all hormonally mediated. Thus far, the bulk of the scientific work conducted by both industry and government on the impacts of environmental chemical contaminants was focused on acute toxic effects and cancer—not endocrine disruption. But Colborn found ample evidence to support her proposition that synthetic chemicals could profoundly influence hormonal function.

Colborn sought support for her hypothesis by looking beyond her own scholarly niche for corroboration. Included in her book are studies of *position effect* that Frederick vom Saal, a reproductive physiologist, conducted to determine the cause of some of the behavioral differences he was observing in mice specifically bred to be similar. vom Saal showed that when a female was positioned in utero between two males, she received a greater exposure to testosterone than did a female pup positioned between two females, or between a male and a female. That exposure resulted in characteristics such as increased territorial and aggressive behaviors more commonly attributable to males. The opposite effect was observed in males positioned between two females (vom Saal & Bronson, 1980; vom Saal, Grant, McMullen, & Laves, 1983).

Other work that raised the public profile of the EDC issue was that of Sonnenschein and Soto (Soto, Justicia, Wray, & Sonnenschein, 1991; Soto & Sonnenschein, 1987) who accidentally discovered that the unregulated growth of human breast cancer cells in tissue culture dishes was being stimulated by p-nonylphenol

leaching from the plastic culture tubes that they used in their laboratory. P-Nonylphenol is a member of a class of synthetic compounds (the alkylphenols) that are added to plastics such as polyvinylchloride (PVC) and polystyrene to make them less brittle. This serendipitous finding corresponded with a change that had been made in the manufacturing of the culture dishes that they had routinely purchased and was the culmination of an intense effort to determine why the protocols used in their laboratory were no longer predictable.<sup>8</sup>

Researchers at the Stanford University School of Medicine also made a serendipitous discovery at about the same time as Soto and Sonnenschein. Krishnan, Stathis, Permuth, Tokes, and Feldman (1993) found that a contaminant was binding to an estrogen receptor in their experimental system. The determination was eventually made that this estrogenic substance was bisphenol A and was leaching from the polycarbonate flasks that they were using to sterilize water for their studies.<sup>9</sup>

The political impacts of Colborn's book started well before its release date as it received wide-spread pre-release media attention and because industry groups readied their critiques and counter arguments in anticipation of its release. Colborn's book raised the level of awareness about the concept of endocrine disruption as a function of exposure to man-made chemicals and counseled readers how to minimize their exposure. *Our Stolen Future* was written and marketed for a broad audience, reaching many more people than a review would have if published only in the scientific literature. Even before its release, the media began hyping the risks addressed and highlighted the controversy

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<sup>8</sup> For a dramatic account of this investigation see: Colborn, Dumanoski, and Myers (1996).

<sup>9</sup> Because among other items, polycarbonate is the material used to make clear baby bottles, it is not surprising that this finding drew a considerable amount of media attention. Attempts to replicate these findings by the FDA and others have been unsuccessful (Nagel et al., 1997).

that existed both within the scientific community and between scientists and industry groups. The book and its authors were both praised and maligned. Of particular interest, is that unlike other environmental hazards this quickly gained importance on the public policy agenda. In turn, this stimulated agencies to release research funds for further investigation, and led to panels to study the existing science and examine whether current standards for the testing of chemicals in commerce were sufficient to identify potential EDCs.

Krimsky credits Colborn with stimulating the challenge to long-held premises of toxicology and thus expanding the perspectives from which chemical hazards are identified. Colborn's efforts to highlight the EDC issue resulted in three important U.S. government reports that were prepared between 1996 and 2000. The first was issued in November 1996 by the Committee on Environment and Natural Resources (CENR) of the National Science and Technology Council, a cabinet-level council chaired by the President with membership that includes the Vice-President, Cabinet Secretaries, and the heads of executive agencies with "significant science and technology responsibilities." The CENR report *The Health and Ecological Effects of Endocrine Disrupting Chemicals: A Framework for Planning* contains a review of the available science and develops a framework for coordinating Federal research.

The second was the *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* released by the U.S. Environmental Protection Agency (USEPA) Risk Assessment Forum in February 1997. This report was prepared by USEPA scientists with the stated objective of promoting scientific consensus on risk assessment issues and to "ensure that this consensus is incorporated into appropriate risk



assessment guidance” (USEPA, 1997, p. vii). The third was the August 1999 report of the National Research Council (NRC), Commission on Life Sciences entitled *Hormonally Active Agents in the Environment*. The NRC report was the product of a multi-disciplinary expert commitment.

The question of how to define this issue has a history all of its own and became a significant factor in the analysis conducted by the NRC (1999) study. The NRC panel was charged with evaluating the EDC hypothesis and reaching consensus. They were to 1) interpret the hypothesis, 2) decide on which of the available facts were relevant to their evaluation, 3) decide which sources of available information would be included in their evaluation, 4) differentiate between and assign weights to conflicting information, 5) offer alternative scenarios for patterns observed in the data, 6) decide on acceptable errors, and 7) come up with a set of criteria for developing conclusions and recommendations based on their understanding of the hypothesis and their evaluation of the data (NRC, 1999).

The NRC panel encountered serious difficulties not only in trying to reach consensus in framing the EDC hypothesis, but to define and name the issue. The panel convened to assess the science and to make recommendations for future research found that the name that had been in use was troublesome on several fronts. They expressed discomfort that the existing name (endocrine disrupting chemicals) was overtly emotional and suggestive of outcomes and mechanisms of action that had not been demonstrated. The panel agreed on the name “hormonally active agents” because it did not imply either a potential outcome or a biological mechanism of action. Defining this issue became a serious factor in the analysis conducted by the NRC panel and while they were concerned

about the power of their semantic compromise to either expand or contract the issue the impact of their report seems to have been minimal if any.

Shifts in actions and attitudes occur from time to time within scientific circles as they do elsewhere in social and political realms. The thinking about an issue, how it should be studied, and what could, and should, if anything, be done about it—may remain in a lag phase until some combination of events coincide which brings the issue to the forefront. These events may in fact be quite similar to those which have been shown to open policy “windows”—the convergence of focusing events such as a crisis, increased media attention, or the attainment of legitimate status by an authoritative source.

In general, there are three viewpoints which have emerged about the EDC issue and how to appropriately respond to it. The first viewpoint is one of skepticism based on the inconclusive findings and the lack of obvious cause and effect data. The second viewpoint among scientists is one of skepticism modified by curiosity and the acknowledgement that a better understanding of the issue is needed. This view includes the position that the most harmful substances should be identified. A third opinion among scientists is that existing evidence is convincing enough to warrant reducing exposures and precautionary steps to mitigate future consequences.

Past efforts to visually depict the development of science are impressive and the techniques developed offer a unique way to examine what the role of these attributes are, if any, in the development of the science of a particular topic of interest. As I will demonstrate, there is an impressive body of work which suggests that it is possible to reveal the cognitive structure of science by the examination of its literature. Furthermore, techniques available to visualize the relationships that exist within and between subsets of

this domain can be used to facilitate an understanding of both the social and cognitive attributes that have defined them over time.

The scientific enterprise has been studied from a variety of perspectives using the analytic and/or descriptive methods of historians, anthropologists, sociologists, political scientists, and philosophers. As the result of this work it has become clear that a valid approach to the study of science is through its literature. It is possible to use the scientific literature to follow the way that specific knowledge emerges and evolves. That is because specific knowledge (i.e., a concept) is represented in the scientific literature as a citation. The STS, SKS, and scientometric communities as well as the scientists themselves are in agreement that citations are useful representations of concepts. Citation analysis is a valuable tool for assessing the intellectual relationships between past events.

The objective of this dissertation is to understand how the science of endocrine disrupting chemicals evolved over time, and the attributes that shaped its evolution. Using the published scientific paper as the unit of analysis, bibliometric analyses of the scientific literature will enable a charting of the progression of the science of endocrine disrupting chemicals and the characterization and classification of knowledge statements and networks of knowledge statements.

## **2.5 The Research Question**

This study attempts to better understand if, and to what extent, certain characteristics of published scientific studies have contributed to their influence within the community of scientists studying endocrine disruption in the time period from 1980 to 2004. It is generally accepted that the intellectual influence of a research paper published in the scientific literature can be measured by the extent to which it is cited by

others. Furthermore, the influence of papers deemed important by this measure is likely to extend beyond the scientific enterprise, to other spheres. What is less clear, however, is whether this influence is solely a function of scholarly strength, or whether other attributes might contribute to the likelihood that a paper gains influence through citation.

That such phenomena are worth evaluating is ultimately related to their role in the generation, selection, and assessment of the science that is used in decision making. Knowledge of these phenomena should ultimately contribute to a better understanding of the way that scientific knowledge evolves in a complex society. It should also lead to a better understanding of the nuances at play when selecting the scientific literature on which to rely in making policy decisions, and a better understanding of the factors that influence the availability, longevity, and reach of the literature in which the knowledge is communicated.

Therefore, while there is an academic value in understanding how science evolves over time, and how the development of knowledge starts and stops, there is practical value to this understanding as well. The practical value of this understanding is that the better we understand the factors at play in the production, dissemination, and use of scientific knowledge the better we can make sound decisions from among the available alternatives and guard against making poor ones. The importance of this becomes particularly apparent when considering the value often placed on the citedness or citation frequency of an article.

Which factors tend to propel research in any particular direction or which attract the attention of decision making bodies or the public? Answering such questions first requires examination of the distinguishing attributes of the contributions to scientific

literature as well as of the content of this literature. In part, because of the numerous social, cultural, and political forces which shape the scientific literature we are still far from having a comprehensive understanding of how any particular attribute is likely to affect the acceptance or influence of a research article. This dissertation attempts to fill in a bit of the gap in our knowledge of these complex relationships by examining the features of one particular knowledge domain as it emerges and evolves over time.

Citations can be used to gain perspective about a given knowledge domain or to uncover its development over time. Citation analysis is a methodology based on the assumption that the references cited in scientific papers have some relevance to the work in which they are cited—they are consciously selected by the author to augment an argument or to give appropriate credit to an idea or method. Through the use of citation analysis it is possible to track both the recognition and influence of a particular scientific proposition over time throughout the scientific literature. The dynamics of citation are such that once the results of a scientific study have been published it is possible for these results to have influence throughout a range of social worlds including other scientists in closely related scientific communities, the broader scientific community, industry, elected officials, government agency decision makers, interest groups, a variety of media outlets, and the public at large.

The endocrine disrupting chemical issue involves the question of whether certain chemicals in the environment are capable of disrupting normal hormonal function appears to have acquired its moniker in 1993. This is confirmed by findings here which indicate that the terms endocrine disruption, endocrine disruptor, or endocrine disrupting chemical (searched as endocrine disrupt\*) appear nowhere in the scientific literature prior

to a publication which appeared in the journal *Environmental Health Perspectives* in October of 1993 (Colborn et al., 1993). Prior to this, there were studies looking at the impact of environmental chemicals on vertebrate endocrine function, but none use these terms. However, after 1993, the use of these terms grows steadily with each subsequent year, not only in the scientific literature, but in government documents, and in the lay press.

The scientometric literature suggests that it is possible to test assumptions about the emergence and evolution of scientific interest in endocrine disruption by using bibliometric techniques (e.g., citation analysis). Furthermore, by using such techniques to deconstruct retrospective citation patterns it should be possible to identify whether there are attributes of individual documents which correlate with their ultimate influence on the direction of this contested area of science. The decision to use the issue of endocrine disruption as a case was made based upon several factors. First, the temporal boundaries of interest in endocrine disruption science are readily apparent as the term does not appear in the literature until 1993. Also, while the temporal boundary of attention by scientists to the issue of EDCs is quite clearly demarcated, the disciplinary boundaries of the scientists engaged in its study are much less so. It is possible therefore to divide this particular domain into several topic categories, in turn making it possible to test the proposed hypotheses across several fields while controlling for the impacts of time and external events. Another feature of the EDC issue is that its political salience appears to have been driven primarily by the scientific community rather than interest groups and politicians.

## 2.6 Hypotheses: The Science Matters

This study explores the development of the science concerned with endocrine disrupting chemicals in the environment through the use of bibliometric methods. This body of knowledge is composed of thousands of individual studies. Some of these studies are connected to each other through citation and the resultant network created by these relationships can be explored. There were two primary objectives to this study:

1. To identify the literature of endocrine disrupting chemical science for the period 1980 to 2004 to examine influential documents and their attributes.
2. To create visual representations of the science of endocrine disrupting chemicals and examine them for salient features that help explain the emergence and evolution of the domain.

Scientific hypotheses seek to make sense of phenomena, and are communicated through provisional statements. These statements put forward the possible relationships that exist between variables (for example,  $x$  and  $y$ ) and attempt to answer the question “in what way does  $x$  influence  $y$ .” Although this is an exploratory study, it is nonetheless driven by hypotheses that make sense of the forces in the scientific literature that influence the direction of its growth. In this study, the variables that are considered are attributes or characteristics of studies published in the scientific literature and which concern the topic of endocrine disruption by chemical contaminants in the environment. In this study, the question asked was—how did the attributes ( $x$ ) of the scientific literature influence the development of the scientific knowledge domain concerned with endocrine disruption ( $y$ ). The attributes ( $x$ ) pertained to characteristics of the articles, journals, or authors. The variable  $y$  represented the influence of an article within the

scientific domain and was operationalized by citation counts; a metric widely regarded as valid measures of influence—the more citations a paper receives, the greater its influence.

**H<sub>0</sub> (the null hypothesis):** The extent to which any given paper, and thus its proposition, published in the endocrine disrupting chemical literature influences the direction of this literature (as determined by its citation frequency) is unrelated to its bibliographic or non-bibliographic attributes.

**H<sub>1</sub>:** It is expected that the development of endocrine disrupting chemical science has not been random; rather certain documents have greater influence because they have attributes that increase the likelihood that they will be cited.

The attributes hypothesized to impact citation frequency are categorized into three groups depending upon whether they pertain to the author (H<sub>1a</sub>), document (H<sub>1b</sub>), or journal (H<sub>1c</sub>).

#### *Author Attributes*

**H<sub>1a</sub>:** Authors have names, national origins, and institutional affiliations. Authors have influence as measured by the number of times their work is cited by others. It is expected that citation frequencies will be influenced by the institutional affiliation of the author attribute.

#### *Document Attributes*

**H<sub>1b</sub>:** Documents (also referred to as articles or papers) have titles, genre or document type, topics, subject matter, propositions, and conclusions. A document's influence can be measured by the extent to which it is cited in subsequent documents. It is expected that citation frequencies will be influenced by document attributes.

#### *Journal Attributes*

**H<sub>1c</sub>:** Journals publish have titles, publication dates, and publishers. A journal's influence can be measured by the extent to which it is cited by authors in subsequent journals and documents. A journal may also confer influence if a citing document gains status by citing it. It is expected that citation frequencies will be influenced by journal attributes.



## **CHAPTER III**

### **ANALYTICAL METHODS**

#### **3.1 Introduction**

This study is predicated on the assumption that each unit of analysis (paper/article) published in the scientific literature represents a cognitive contribution to the overall knowledge domain of science. The focus of this dissertation is on the areas concerned with the effects, or lack thereof, of environmental chemicals on endocrine function.

As previously described, progress in modern science is communicated through a formal network of texts (i.e., journal articles) and this progress can be measured by mining the bibliographic elements (journal citations and their attributes) that form this network. Thanks to advances in information science and large bibliographic databases, there are now tools for revealing the production of knowledge over time. These tools have been applied in attempts to find patterns in the communication between disciplines; to determine the impact of authors, institutions, or the scientific enterprises of geopolitical regions on scientific fields; and to visually depict specific scientific fields for the purpose of identifying the depth and breadth of its available literature. As previously noted however, few studies have considered the scientific content of the literature being

processed. The application of quantitative methods to bibliographic data (bibliometrics) can facilitate not only the acquisition and analysis of large scientific literatures and their salient features, but the cognitive relationships that exist between each paper in this literature. The use of such methods reduces some of the complexity embodied in a network of scientific literature so that the influences of a select group of attributes on the whole can be examined. It is possible to determine and compare the attributes pertaining to the journal in which an article is published, the author of the article, or the article itself.

In the first section below, I describe the process used to explore the trajectory of the scientific literature concerned with endocrine disrupting chemicals (EDCs), including the process of acquiring and constructing the database which contained the citation history of EDCs from 1980 through 2004. Theoretically, this data set represents the intellectual history of EDC science within this timeframe and contains all of the investigations conducted as well as when, where, how, and by whom. Methods used to determine whether certain attributes of individual articles in the literature of this domain contributed to their influence are also described.

In the second section, I describe the process of creating visual representations of the intellectual history of EDC science using the proprietary software tool HistCite<sup>TM</sup> to depict aspects of the literature which may have been pivotal in its development.

### **3.2 Endocrine Disrupting Chemical Science**

Identifying and acquiring the relevant scientific literature was made possible through the use of the Web of Science® (WoS) which provides World Wide Web access to the Science Citation Index Expanded<sup>TM</sup> (SCI) of the Institute for Scientific Information (ISI) Web of Knowledge<sup>SM</sup>. All of these are products of the Thomson Corporation

([www.thomsonscientific.com](http://www.thomsonscientific.com)). These resources were made available through the subscription held by the Cleveland State University library and were available for remote on-line access. The citations acquired from SCI keyword searches provided the database for subsequent analyses.

A static longitudinal analysis of the dataset was prepared by creating a year-by-year comparison of the attributes of published papers that were identified by keyword searches of the SCI database. Accomplishing this required identifying and acquiring all of the literature that has been published on the subject between the years 1980 and 2004, as well as all of the unique bibliographic information associated with this literature. Locating the scientific articles published within the relevant time period (1980-2004) was accomplished using the *General Search* function of the Thompson Web of Science on-line interface. The search terms used are: *endocrine disrupt\**, *hormonally active agent*, *xenoestrogens*, *hormone mimic*, *estrogen mimic*, *hormone disrupt\** and *environmental estrogen*.

Each paper (unit of analysis) identified by a keyword search has a set of distinct attributes, some of which have been hypothesized both here and elsewhere to impact how influential a paper might ultimately be in the development of the knowledge domain. The initial keyword searches generated a list of published papers for the years requested—in this case 1980 to 2004. Once this list was retrieved, records for which additional information is required were “marked” and electronically resubmitted to the database for additional data. This included details pertaining to the paper’s cited reference list, papers in which it is subsequently cited, and the article’s abstract as published in the literature. The results of citation searching were downloaded in both ASCII text (.txt) and Excel

(.xls) formats. The files were used for analyzing the relationship between article attributes and the number of times the article is cited (.xls) as described in this section, and are also used as the base data upon which historiographs are constructed (.txt).

Static longitudinal analyses of the dataset are presented in tabular and graphic format in Chapter 4. The influences of all bibliographic attributes were measured by both citation and publication counts for the entire dataset for the period between 1980 and 2004. The influences of both bibliographic and non-bibliographic attributes were measured by both citation and publication counts for the highly cited subset of documents published between 1980 and 2004.

All of the bibliographic attributes of interest were available to this study through the SCI databases. Those non-bibliographic attributes that not defined or captured by SCI databases included the study topic, investigative model, and whether the study supported or negated the EDC hypothesis. Determining the values for these attributes was accomplished by reading the each article abstract. On the occasion when an abstract did not provide sufficient information to determine these attributes, the article itself was acquired and read. The criteria used to assign non-bibliographic attributes are listed in Chapter IV.

### **3.3 Mapping Intellectual History**

It may be that the most important contribution of this study was revealing the intellectual history of the way the scientific enterprise attempted to understand the EDC hypothesis since the topic became politically salient. To understand how a topic evolves over time requires finding and exploring its literature and observing the changes that

occurred in 1) the frequency with which key works were cited over time and 2) the citations relationships between these works.

While the use of automated mapping software is convenient, it is not necessary. That having been said, automation is clearly preferable given the extensive volume of material to be considered and the difficulty of being objectively inclusive. The development of automated tools has made it possible to breeze through thousands of published documents as well as to applying algorithms and scaling techniques that can generate graphic representations of the literature in a matter of minutes. The ease with which these materials can be searched, clustered, and displayed, however, belies the complexity of the relationships that they represent. While there are numerous scholars working on advancing visualization methods, most needed are researchers willing to glean the meaning out of these data and representations.

The primary goal of creating visual representations of the endocrine disrupting chemical literature is to identify and describe its overall structure and to determine whether there are “hubs, pivots, or landmarks” that help explain development in the field (Chen, 2003). These visually salient features of these visual representations (maps) are then examined both for the overall network and for the specific time intervals. Temporal changes in the attributes of salient nodes and major changes between adjacent time series will be described.

Such methods have been an increasingly popular area of interest since the 1980s and are now frequently encountered in bibliometric and scientometric research. Such maps provide visual representations of an area of interest and can be constructed using any number of bibliographic elements or attributes such as words, authors, or citations.

Maps can be constructed qualitatively or by using any number of algorithms that have been derived for determining relationships within a knowledge domain and then placing the bibliometric elements into a meaningful array. For example, the relationships between cited and citing documents in the scientific literature can be mapped, and thereby enable the user to view the relative size and similarity of areas of interest. In addition, the connectedness between scientific contributions to the entire knowledge domain can be visualized. Maps representing the structure of endocrine disrupting chemical science at various periods of its development were prepared using the hierarchical software tool HistCite<sup>TM</sup>.

### **3.4 Domain Mapping Based on Direct Citation Links**

Maps of science can be created by identifying relevant documents and then plotting the relationships that exist between cited and citing pairs. Iterative thresholds enable the investigator to adjust the resolution of data-rich maps so that they are meaningful. HistCite<sup>TM</sup> automates the steps involved in creating a type of citation map known as a historiograph which is similar to the depiction of a family tree. This particular software is under development by Eugene Garfield and the *beta* version was made available for this work through a written agreement. The real-time historiographs created by HistCite<sup>TM</sup> enable a year-by-year examination of the intellectual development of a field and are created by uploading the ASCII text files extracted from SCI databases which contain the list of articles identified by keyword searches and their selected attributes, including citation history. To retrieve the citation history of a document the user selects from among the *meta* data available, marking the fields (bibliographic attributes) desired for future analyses.

While visual representations can be produced using other units of analysis such as authors or words, visual representations of intellectual development within a field are best constructed using documents. By using citation counts it becomes possible to set thresholds which permit adjusting the map resolution to a manageable level. When tied to the use of graph drawing algorithms such as the GraphViz program on which HistCite<sup>TM</sup> relies, articles are clustered according to their association strengths. Each citation link (usually depicted as lines of various widths or lengths) provides an indication of the strength of the association between the cited articles which are geographically placed together in a node, the size of which varies with the number of articles it contains.

HistCite<sup>TM</sup> also generates Local Citation and Global Citation Scores (LCS and GCS, respectively). The LCS is the frequency with which a given article is cited within the collection of articles that have been retrieved through the keyword searches performed (the dataset), and the GCS is the frequency with which the article is cited in the entire SCI. By comparing the LCS with the GCS it is possible to appreciate the extent of influence of an article both within the dataset of interest as well as its influence in other domains.

The process by which HistCite<sup>TM</sup> calculates the similarity between units to create maps involves the creation of a matrix populated with cited and citing documents obtained from an automated search of the SCI databases for the time period specified. The program removes duplicates that result from co-authorships and the raw data are stored in a correlation matrix. This matrix of co-occurrence then becomes the input for standard hierarchical agglomerative cluster analysis. Multidimensional scaling algorithms in turn position the clusters.

Analyzing the maps generated was a dynamic and iterative process. The fundamental problem faced in mapping any scientific domain by any process is that often to make a map visually meaningful its resolution must be minimized. This is especially troublesome when depicting a large dataset such as the one generated for this study (the citation relationships between and among at least 3,000 individual papers). However, the mapping programs generated maps in real time so it was possible and necessary to adjust several parameters. The size of nodes was automatically determined and was relative to either the local citation score (LCS) or global citation score (GCS) score as determined by the user when creating a map. However, it was possible to experiment various thresholds with each subset of the data to generate the most meaningful characterization of the data.

Scholars agree that the maps constructed of complex networks such as the scientific literature are a rich resource. However, the most all of the work done on the visual representation of knowledge has focused on the development of methodology. Sorely lacking in the literature are attempts to glean, interpret, and apply the information that these maps must contain. Among the strengths of HistCite is that it automates the comparison of influential documents over time. This combined with the descriptive analysis of the relative importance of each group of highly cited documents over time should reveal the evolution of the field and the relative importance of bibliographic and non-bibliographic attributes on that evolution.



## CHAPTER IV

### RESULTS

#### 4.1 Introduction

The results reported here are based on a subset of the peer-reviewed scientific literature concerned with the science of endocrine disrupting chemicals (EDCs) that was published between the years 1980 and 2004. Access to this literature and the unique attributes of each individual paper was made possible through the use of comprehensive and multi-disciplinary electronic databases of scientific literature. The Web of Science® (WoS) is a group of commercial databases which provide World Wide Web (www) access to the Science Citation Index Expanded™ (SCI) of the Institute for Scientific Information (ISI) Web of Knowledge™, all of which are products of the Thomson Corporation ([www.thomsonscientific.com](http://www.thomsonscientific.com)).<sup>10</sup> For the sake of brevity, these databases are collectively referred to herein as the Science Citation Index or simply as SCI.

The electronic version of SCI provided identifying information for each individual article that had been published in the peer-reviewed scientific literature since about 1972, the year for which electronic records are first available. By 2004, the SCI databases contained records from well over 16,000 international journals, books and

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<sup>10</sup> For a more thorough discussion of the SCI databases was presented in Chapter II.

proceedings in the sciences, social sciences, arts, and humanities. Approximately 9,000 of these sources are international scientific journals (Thomson Scientific, 2007). The SCI data facilitated not only the location of articles of interest, but also provided the reference lists (cited references) for each retrieved article and the number of times that the article had been cited whether or not that citation was in an SCI-indexed source.

The data acquisition methods described in Chapter III proved more than sufficient for generating a sizeable dataset for exploration. Given the more than 20 million articles currently in the SCI database, the data available for analysis was potentially enormous, so perhaps not surprisingly the dataset obtained by the initial keyword searches for this dissertation, and upon which this study relied, was large. The results presented here were derived from over 3,400 individual articles and any significant article not captured by keyword searching was connected to the broader literature via the articles cited in its reference list (list of cited references). Thus, the 3,400+ articles in the dataset were connected by first degree citation relationships to nearly 200,000 other papers. The original dataset of 3,412 cited 129,958 articles. The dataset identified by keyword searching also had links to the papers in which they themselves were subsequently cited (times cited). The 3,400 papers in the original dataset were linked by subsequent citation to more than 60,000 other papers, and again this information was captured through SCI database searches.

The breadth and depth of the available information created nearly limitless opportunities for analysis. The results reported here, however were focused on exploring the attributes of journals, authors, and documents. They relate to citation frequency and the influence of an article over time. To accomplish this, the bibliographic attributes

described in Chapter III were analyzed first for the entire dataset, and then for a subset of the dataset containing the most highly cited papers. The non-bibliographic attributes (described in Chapter III) were analyzed only for the subset of highly cited papers. Section 4.2 presents all of the summary data for the bibliographic attributes of the entire dataset for the period from 1980 through 2004. Section 4.3 presents the bibliographic and non-bibliographic results from the subset of the data ( $n = 276$ ) that was determined to contain the most influential articles (cited  $\geq 45$  times) published during the period between 1980 and 2004.<sup>11</sup> The publication and citation counts for bibliographic attributes for the four sequential *chronological* sub-units: 1980-1995; 1995-1998; 1998-2000; and 2000-2004 are included as an addendum and presented as Table XIV through XXXVIII in Appendix A. Section 4.4 contains visual representations of the dataset for different time periods: 1980-2004; 1980-1995; 1995-1998; 1998-2000; and 2000-2004.

## **4.2 Summary Data for the Period 1980 -2004**

### **4.2.1 Keywords**

The software tool used to create the dataset upon which this study relies was the General Search function of the SCI which, with the proper subscription, can be accessed through the Web of Science<sup>TM</sup> page of the Science Citation Index Expanded<sup>TM</sup>. This function enabled searches of all SCI databases using keywords, author names, journal names, titles, or any combination thereof. Using this function, each keyword was searched individually for each year. Once each list was retrieved, the records were marked to indicate the data desired for retrieval. The attribute data acquired from SCI included SCI-unique identification numbers, the article abstract, author names, author

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<sup>11</sup> The large size of the dataset necessitated the creation of this subset for assigning non-bibliographic attributes to articles that required reading.

institution and addresses, journal names and addresses, beginning and ending pages, volume, issue, publication date, publication year, times cited, list of references cited, number of references cited, document type, and language. The data files generated from the SCI were saved for further analysis in both ASCII (.txt) and Excel<sup>TM</sup> spreadsheet (.xls) formats. The results generated from these keyword searches are detailed in the following sections.

Table I summarizes the keyword searches of the SCI that were conducted in December, 2006. A variety of related words were searched to ensure that all relevant work was acquired. The search terms used were: “endocrine disrupt\*” (ED), “hormonally active agent” (HAA), xenoestrogen\* (XE), “hormone mimic”<sup>12</sup> (HM), “estrogen mimic” (EM), “hormone disrupt\*” (HD), and “environmental estrogen” (EE).

**Table I. Publications Identified by Keyword Searches for the Period 1980-2004**

<b>Keyword</b>	<b>Publications Count by Keyword</b>	<b>% of Total</b>
ED	2,844	76.53%
EE	158	4.25%
EM	15	0.40%
HAA	17	0.46%
HD	85	2.29%
HM	0	0.00%
XE	597	16.07%
<i>Sum</i>	3,716	100.00%

Legend: ED-endocrine disrupt\*, EE-environmental estrogen, EM-estrogen mimic, HM-hormone mimic, HAA-hormonally active agent, HD-hormone disrupt\*, X-xenoestrogen

As seen in Table I, the terms “xenoestrogen” and “environmental estrogen” were both well represented within the dataset and generated 4.25% and 16.07 % of the identified articles, respectively. The term “endocrine disrupt,\*” designed to capture

<sup>12</sup> The keyword “hormone mimic” did not appear in any of the searches conducted and was dropped from inclusion in further analysis.

endocrine disruptor, endocrine disruption, and endocrine disrupting chemicals, resulted in the vast majority of the hits at 76.5%. There were several cases where a paper was identified by more than one keyword. In such cases, “endocrine disrupt\*” was (with few exceptions) also among the identifying keywords, and therefore the paper was added to the “ED” total.

The effectiveness of the launch of the EDC “issue” is evidenced by the sheer volume of papers published on the topic and the use of the term itself which consistently generated the most number of hits for each year in the study period. Arguing that the EDC term was unduly provocative and scientifically inaccurate the National Research Council (NRC) argued in its comprehensive report (NRC, 1999) that the subject should be renamed. As the results shown here indicate, their suggested alternative “hormonally active agent” (HAA) gained little traction and was found in only 17 articles in the entire SCI database, less than 0.5 % of all keyword hits for the entire dataset.

#### **4.2.2 Publication Counts**

After removing all of the duplicate records (from papers having been identified more than once by different keywords) the dataset consisted of 3,413 unique articles.<sup>13</sup> The attributes of the articles, their relationships, their topics, their impacts on future publications were available either by review of their non-bibliographic attributes from abstracts or contents as described in Chapter III, and their bibliographic attributes were available in electronic format.

The term “endocrine disrupting chemical” does not appear in the dataset until 1993, when it appears in three different published papers. The sudden appearance of the

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<sup>13</sup> It should be noted that this number may vary. As the literature was read, it became obvious that a few papers were totally unrelated to the issue at hand and were discarded from further analysis.

EDC term in the literature and its tremendous rate of growth between 1993 and 2003 are clearly visible in Table II. The elements surrounding the introduction of this issue and its 200-fold increase in nine years are discussed in detail in Chapter V.

**Table II. The Emergence of EDC Science in the Peer-Reviewed Literature**

<b>Publication Year</b>	<b>Count</b>
1987	1
1992	1
1993	3
1994	4
1995	31
1996	55
1997	121
1998	250
1999	252
2000	387
2001	480
2002	557
2003	641
2004	630
Total	3,413

### 4.2.3 Citation Counts

Table III reveals the range of citations for the articles within this dataset. Nearly 75% (2,662) of the papers in this dataset were cited twice or more, while only 15.8% (539) were never cited. It is important to note that 183 of these 539 uncited papers were published in the years 2003 or 2004 and thus were not as likely to have reached the peak of their potential influence. Table III also shows that about 40% of the articles were cited between 5 and 19 times (19.6% cited 5-9 times and 20.1% cited 10-19 times).

**Table III. Range of Citation Counts (1980-2004)**

Range of Citation Counts	%
0	15.8%
1	6.2%
2-4	15.3%
5-9	19.6%
10-19	20.1%
20-29	8.6%
30-39	4.7%
40-49	2.7%
50-99	4.8%
100-199	1.5%
200-299	0.4%
300-499	0.2%
500-1,000	0.1%
1,000 +	0.0%

### **4.3 Influence of Bibliographic Attributes (1980-2004)**

#### **4.3.1 Document Type**

To determine the relationship between the document type (DT) and the influence (citation frequency) of a published paper, the publications were grouped by the document type designation given by the SCI—review, (research) article, news item, or editorial. As shown in Table IV articles (research papers) made up the vast majority (81%). of the papers in the dataset. Articles also received the most citations (83%). However, the rate at which research articles were cited was less than that for reviews. The average global citation scores (GCS) for review articles (37.4 citations per paper) were twice that for research articles (17.4 per papers). The GCS is a count of the number of times a paper has been cited in the entire SCI databases ( $n \approx 20,000,000$ ). For most of the analyses performed, the GCS was more meaningful than the local citation score (LCS, a count of

the times that a paper was cited in the local collection) because it represented the entire EDC literature and therefore included even those papers that were not captured by the search strategies employed.

**Table IV. Influence of Document Type on Publication and Citation Counts**

Document Type (DT)	Publication Count Ranked by DT		Citation Count (GCS*) Ranked by DT		
	Number	Percent	Number	Percent	Average Times Cited per DT
Articles	2,762	81%	48,002	83%	17.4
Reviews	243	7%	9,112	16%	37.5
Meeting Abstract	157	5%	725	1%	6.7
Editorial Material	109	3%	56	0%	0.5
News Item	105	3%	35	0%	1.3
Letters	28	1%	15	0%	0.1
Corrections	8	0%	1	0%	0.1
Totals	3,412	100%	57,946	100%	

#### 4.3.2 Authors

To answer questions pertaining to the influence of authors on citation frequency, the global and local citation scores of authors in the dataset were compared. Table V presents the top twenty publications in the dataset by author, ranked first by GCS and then by LCS. There are two papers that are found ranked in the top four of both lists. The first is the paper by Colborn et al. (1993) (GCS = 1176; LCS = 364). It is in this paper that the case was made for concern about EDCs by discussing the range of findings from laboratory and to field studies that support the EDC hypothesis and raised the alarm for the need for continuing study. The second was the paper by Jobling, Reynolds, White, Parker, and Sumpter (1995) (GCS = 506; LCS = 172) in which the authors present findings of measurable quantities of endocrine disrupting chemicals in environmental media.



**Table V. First Authors Ranked by Publication and Citation Counts (1980-2004)**

<b>Top Ten 1st Authors Ranked by Global Citation Score, Pub Year, &amp; Source</b>	<b>GCS*</b>
Colborn T, 1993, ENVIRON HEALTH PERSPECT, V101, P378	1176
Toppari J, 1996, ENVIRON HEALTH PERSPECT, V104, P741	584
Jobling S, 1995, ENVIRON HEALTH PERSPECT, V103, P582	506
Jobling S, 1998, ENVIRON SCI TECHNOL, V32, P2498	400
Olea N, 1996, ENVIRON HEALTH PERSPECT, V104, P298	386
Nagel SC, 1997, ENVIRON HEALTH PERSPECT, V105, P70	378
Brotons JA, 1995, ENVIRON HEALTH PERSPECT, V103, P608	362
Kavlock RJ, 1996, ENVIRON HEALTH PERSPECT, V104, P715	358
Routledge EJ, 1998, ENVIRON SCI TECHNOL, V32, P1559	335
<b>Top Ten 1st Authors Ranked by Local Citation Score, Pub Year, &amp; Source</b>	<b>LCS**</b>
Colborn T, 1993, ENVIRON HEALTH PERSPECT, V101, P378	364
Jobling S, 1995, ENVIRON HEALTH PERSPECT, V103, P582	172
Nagel SC, 1997, ENVIRON HEALTH PERSPECT, V105, P70	168
Toppari J, 1996, ENVIRON HEALTH PERSPECT, V104, P741	150
Brotons JA, 1995, ENVIRON HEALTH PERSPECT, V103, P608	135
Olea N, 1996, ENVIRON HEALTH PERSPECT, V104, P298	130
Kavlock RJ, 1996, ENVIRON HEALTH PERSPECT, V104, P715	128
Steinmetz R, 1997, ENDOCRINOLOGY, V138, P1780	114
Jobling S, 1998, ENVIRON SCI TECHNOL, V32, P2498	108
Vom Saal FS, 1998, TOXICOL IND HEALTH, V14, P239	105

\*LCS: Local Citation Score = # of times article is cited within the dataset (n = 3412).

\*GCS: Global Citation Score= # of times article is cited in all SCI databases

### 4.3.3 Institutional and National Origin

Table VI contains a summary of the countries from which the papers in the dataset originate. As shown, the EDC issue attracted global interest with more than half of the papers in the dataset coming from outside the United States, primarily the United Kingdom (UK) and Japan. However, as the citation scores indicate, US sources tended to generate higher citation scores.

**Table VI. Countries Ranked by Publication and Citation Counts (1980-2004)**

Countries Ranked by Publication Counts			Countries Ranked by Citation Counts (GCS*)		
Country	Number	Count %	Country	Number	GCS %
USA	879	26.61%	USA	24762	38.98%
Unknown	690	20.89%	UK	8566	13.48%
Japan	431	13.05%	Japan	4668	7.35%
UK	247	7.48%	Germany	4281	6.74%
Germany	199	6.02%	Canada	3312	5.21%
Canada	135	4.09%	Spain	2782	4.38%
Spain	81	2.45%	Denmark	2447	3.85%
Italy	76	2.30%	Netherlands	2213	3.48%
France	73	2.21%	France	2020	3.18%
Netherlands	64	1.94%	Sweden	1609	2.53%
Denmark	62	1.88%	Italy	1399	2.20%
Sweden	50	1.51%	Finland	1017	1.60%
Belgium	47	1.42%	Belgium	881	1.39%
South Korea	40	1.21%	Norway	731	1.15%
Norway	31	0.94%	Switzerland	374	0.59%
Peoples R China	26	0.79%	South Korea	337	0.53%
Switzerland	23	0.70%	Australia	312	0.49%
Finland	18	0.54%	Peoples R China	236	0.37%
Australia	18	0.54%	Unknown	119	0.27%

\*GCS: Global Citation Score= # of times article is cited in all SCI databases

Table VII summarizes the institutional affiliations of the authors in the dataset for the years 1980 to 2004. While there were more than 1,400 distinct institutional entities represented, these counts include *all* author affiliations not just the affiliations of first authors. Therefore, the numbers shown are inflated by the institutional affiliation data provided for all of the authors of a single paper (generally from three to six per paper).

**Table VII. Institutional Rankings (1980-2004)**

<b>Institutions Ranked by Publication Counts</b>			
<b>Institution</b>	<b>Institution Type</b>	<b>Publication Count</b>	<b>% Pub</b>
Unknown	Unknown	690	46.91%
US EPA	Government	112	7.61%
NIEHS	Government	51	3.47%
University of Florida	Academic	49	3.33%
Brunel University	Academic	41	2.79%
Univ Missouri	Academic	41	2.79%
Univ Tokyo	Academic	41	2.79%
Univ Texas	Academic	36	2.45%
Environment Canada	Government	35	2.38%
Natl Inst Hlth Sci	Government	35	2.38%
Michigan State Univ	Academic	34	2.31%
CSIC	Government	33	2.24%
US FDA	Government	30	2.04%
Univ Calif Davis	Academic	28	1.90%
Texas A&M Univ	Academic	26	1.77%
Hokkaido Univ	Academic	26	1.77%
Tulane Univ	Academic	25	1.70%
Natl Ctr Toxicol Res	Government	22	1.50%
Univ Guelph	Academic	21	1.43%
Natl Inst Env Studies	Government	21	1.43%
Univ Granada	Academic	20	1.36%
World Wildlife Fund	Environmental Advocacy	19	1.29%
N Carolina State Univ	Academic	18	1.22%
Univ Utrecht	Academic	17	1.16%

<b>Institutions Ranked by Citation Counts</b>			
<b>Institution</b>	<b>Institution Type</b>	<b>GCS</b>	<b>% GCS</b>
US EPA	Government	3942	13.86%
Brunel University	Academic	3613	12.70%
Univ Missouri	Academic	2657	9.34%
Univ Florida	Academic	2406	8.46%
World Wildlife Fund	Environmental Advocacy	2077	7.30%
Tulane Univ	Academic	1866	6.56%
NIEHS	Government	1631	5.73%
Univ Granada	Academic	1305	4.59%
Michigan State Univ	Academic	1071	3.76%
Univ Texas	Academic	961	3.38%
CSIC	Government	843	2.96%
Texas A&M Univ	Academic	666	2.34%
US FDA	Government	665	2.34%
Univ Calif Davis	Academic	654	2.30%
Natl Ctr Toxicol Res	Government	644	2.26%
Environm Canada	Government	581	2.04%
Univ Tokyo	Academic	558	1.96%
N Carolina State Univ	Academic	522	1.83%
Univ Guelph	Academic	443	1.56%
Univ Utrecht	Academic	349	1.23%
Hokkaido Univ	Academic	319	1.12%
Natl Inst Hlth Sci	Government	305	1.07%
Natl Inst Env Studies	Government	252	0.89%
Unknown	Unknown	119	0.42%

GCS: Global Citation Score= # of times article is cited in all SCI databases

The SCI database lists the institutional affiliation provided by a paper's authors and therefore determining how to categorize an organization often required some detective work. Governmental agencies were not necessarily closely or clearly attributed. An example of this was that papers coming from the National Institute for Environmental Health Sciences (NIEHS) would be listed as U.S. Environmental Protection Agency (USEPA) or at other times as NIEHS. As indicated by the vast number of "unknowns" in the SCI data, determining institutional affiliation for the some authors was sometimes difficult if not impossible. There were occasions when even the information provided in a paper was insufficient to determine a document's institutional origins.

While the institutional affiliations of more than half of the authors could not be discerned from the SCI database, the impact of these "unknowns" was minimal (0.42% GCS). Of the remaining papers, the papers with academic institutional affiliations comprised about 29% of the dataset and 61% of the citations. The government affiliated papers (this includes all governments) comprises about 23% of the dataset and received about 31% of the citations.

An examination of the funding sources for the most highly cited papers revealed that only a small minority of the research was funded by other than government sources regardless of whether the research was conducted in the US, UK, Canada, or Japan or whether it was conducted in a government or academic setting. The only exception to this was the highly cited paper by Colborn et al. (1993), which was funded through the World Wildlife Fund through several not-for-profit organizations (Colborn et al., 1993). This impact of this paper is reflected by the fact that this category received 7.3% of the total citations with 1.2% of the publications.

#### 4.3.4 Journals

The papers identified by keyword searching were found in 572 journals, of which nearly half (295) contained only one (1) article. There were 58 journals which published ten (10) or more articles identified in the dataset. A ranking of the most influential journals in which articles were published as indicated by citation counts is shown in Table VIII. Approximately 450 of these journals were subsequently cited in other publications at least one time. Table VIII is divided into two sections. In the first section, journals are ranked by publication (number of publications found in the EDC dataset), and in the second section, the journals are ranked by their global citation scores (GCS).

An examination of the data revealed that the journal *Environmental Health Perspectives* (EHP) had published more than 200 papers that were captured in the keyword searches and another journal *Environmental Toxicology and Chemistry* (ET&C) had published over 100 papers. Together these two journals represent 12.6% of the total publications in the dataset, but 40% of the LCS, and nearly 30% of all global citations. Table IX shows the top five journals in the data set as indicated by publication count, local citation scores, and global citation score.

**Table VIII. Top Journals Ranked by Publication Count (1980-2004)**

<b>Journal</b>	<b>Publications</b>	<b>% Pubs</b>
ENVIRONMENTAL HEALTH PERSPECTIVES	233	7.9%
ENVIRON TOX & CHEM	140	4.7%
TOXICOLSCIENCES	80	2.7%
ENVIRON SCI & TECH	65	2.2%
PURE & APPLIED CHEMISTRY	62	2.1%
AQUATIC TOXICOLOGY	57	1.9%
CHEMOSPHERE	55	1.9%
REPRODUCTIVE TOXICOLOGY	54	1.8%
ABSTR OF PAPERS OF THE ACS	49	1.7%
J OF CHROM A	47	1.6%
TOXICOLOGY	45	1.5%
TOXICOLOGY LETTERS	43	1.5%
SCI OF THE TOTAL ENVIRON	40	1.4%
MARINE ENVIRON RES	40	1.4%
APMIS	40	1.4%
<i>Sum</i>		35.5%
<b>Journal</b>	<b>GCS*</b>	<b>% GCS</b>
ENVIRONMENTAL HEALTH PERSPECTIVES	11296	22.3%
ENVIRON TOX & CHEM	3823	7.6%
ENVIRON SCI & TECH	1999	4.0%
TOXICOLSCIENCES	1502	3.0%
SCI OF THE TOTAL ENVIRON	1332	2.6%
TOX & APPLIED PHARM	1325	2.6%
AQUATIC TOXICOLOGY	1276	2.5%
TOX & IND HEALTH	1240	2.5%
CRITICAL REVIEWS IN TOXICOLOGY	959	1.9%
CHEMOSPHERE	943	1.9%
ENDOCRINOLOGY	897	1.8%
J OF CHROM A	789	1.6%
J OF STEROID BIOCHEM & MOL BIO	670	1.3%
REPRODUCTIVE TOXICOLOGY	653	1.3%
MARINE ENVIRON RES	558	1.1%
<i>Sum</i>		57.9%

\*GCS: Global Citation Score=# of times cited in SCI databases.

\*LCS: Local Citation Score=# of times cited in dataset (n = 3412)

**Table IX. The Influence of Top Ranked Journals**

Journal	Pub Count	%	LCS*	%	GCS**	%
ENVIRON HEALTH PERSP	233	7.9%	3,210	30.7%	11,296	22.3%
ENVIRON TOX & CHEM	140	4.7%	948	9.1%	3,823	7.6%
TOXICOL SCIENCES	80	2.7%	239	2.3%	1,502	3.0%
ENVIRON SCI & TECH	65	2.2%	382	3.7%	1,999	4.0%
PURE & APPLIED CHEMISTRY	62	2.1%	63	0.6%	323	0.6%
<b>Sums</b>	<b>580</b>	<b>19.6%</b>		<b>46.3%</b>		<b>37.5%</b>

\*\*GCS: Global Citation Score=# of times cited in SCI databases.

\*LCS: Local Citation Score=# of times cited in dataset (n = 3412)

<b>Journal Rankings</b>	
Journal Name	Ave Citation Count/Paper
ENVIRON HEALTH PERSP	48
ENVIRON SCI & TECH	32
ENVIRON TOX & CHEM	27
TOXICOL SCIENCES	19

#### 4.2.2 Influence of Non-Bibliographic Attributes on Highly Cited Papers

A more thorough exploration of the influences on the EDC science literature required examining attributes such as study type and topic which are not captured in commercial databases, or anywhere for that matter. It was therefore necessary to reduce the dataset to a size which would make it possible to read and abstract the necessary elements from each paper. Examining the papers which had been cited 45 times or more resulted in a subset of 276 “highly cited” papers which together represented more than 50% of all the citations received by all the papers in the dataset. The selection of 45 citations as a threshold was validated by the thresholds set by SCI thresholds for highly cited documents, the average of which for the field of environment/ecology for the years 1996 to 2006 was 80.77 citations. The attributes examined within the set of highly cited documents were study type, investigative model, and support or negation of the endocrine disrupting chemical hypothesis.

#### 4.4.1 Study Type

All of the highly cited papers were read to determine the type of study that was undertaken. This was sometimes possible to determine from reading a paper's abstract, but at times it was necessary to obtain the entire paper to determine the study details. Review articles were generally classified as such by their authors or titles. If an article did not present the results of a study, but instead reviewed and discussed the work of others it was classified as a review article. Reproductive/developmental studies were research papers that involved any *in vivo* reproductive or developmental endpoint. Biochemistry/Molecular biology studies were research papers that were generally *in vitro* studies concerned with determining biochemical pathways, or gene expressions. Screening studies were defined as those research papers directed towards finding methods to determine whether a substance might be estrogenic or hormonally active. In many cases these were biochemical assays, however, the authors expressly mentioned their relevance as potential EDC screening methods. Monitoring studies were research studies that reported the concentrations of EDCs in environmental media, including consumer products; whereas exposure assessment studies reported the actual or calculated exposure of impacted populations. Carcinogenicity studies were research papers that specifically reported on the carcinogenic potential EDCs. This category did not include studies that used cancer cells (human breast cancer cells) as a model for testing estrogenicity.

Research directed towards finding environmental sentinels (e.g., sentinel species) were categorized as biomarker studies. Studies concerned with the effects of exogenous hormones on the nervous system were categorized in neuroendocrinology. Finally,



editorial and reviews of workshop proceedings were labeled as such by journal editors and by SCI. On one occasion, an article marked as editorial material was re-classified and placed into the review article category based on its content and size.

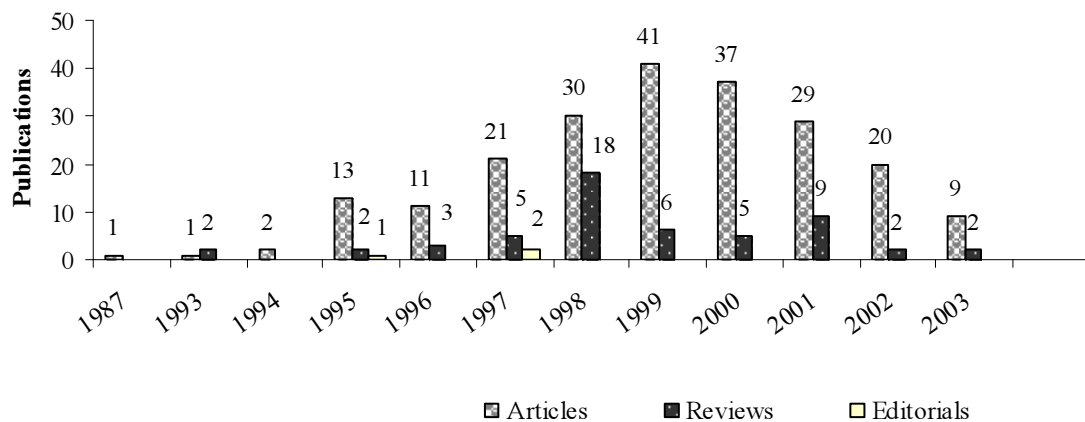
The results of the study type analysis are shown in Table X and in Figures 2, 3, 4, and 5. Of the 276 papers examined, four (4) were found totally irrelevant to the topic and were removed from further analysis.

**Table X. Study Type of Highly Cited Publications**

Study Topics	Papers Cited $\geq$ 45 Times	% of Papers (n = 272)	# of Citations (n = 27123)	% (TC) of Highly Cited (n = 27,123)	% (TC) of All Papers (n = 57,896)
Reviews	51	18.4%	6,422	23.7%	11.1%
Reproduction/Dev	78	28.7%	7,525	27.7%	13.0%
Biochem/Molecular Bio	43	15.8%	3,196	11.8%	5.5%
Screening Methods	37	13.6%	3,402	12.5%	5.9%
Monitoring Studies	28	10.3%	3,236	11.9%	5.6%
Exposure Assessment	10	3.7%	783	2.9%	1.4%
Carcinogenicity Studies	9	3.3%	527	1.9%	0.9%
Biomarkers of Exposure	7	2.6%	417	1.5%	0.7%
Neuroendocrinology	3	1.1%	525	1.9%	0.9%
Editorial Material	3	1.1%	304	1.1%	0.5%
Rev of Workshop Proc	4	1.5%	786	2.9%	1.4%

Among the 276 papers cited  $\geq$  45 times, there were 51 review articles. The close examination given to the highly cited papers revealed that the document type designation assigned by SCI was somewhat arbitrary and not entirely accurate for the purposes of this study. This inaccuracy was most evident in the classification of reviews as “articles.” Therefore, in the results presented here the study type designation was based not on the SCI designation but by a review of a paper’s abstract, or if the abstract was not sufficient to alleviate any uncertainty, by acquiring and reviewing the paper. This level of review

revealed that thirteen (13) papers designated as “articles” by SCI were more accurately described as reviews (i.e., they involved the review, synthesis, and discussion of the previously published work of others) and four (4) papers that had been designated by SCI as editorial materials which were better described as review articles. Figure 1 show the array of document types (reviews, research articles, and editorial materials) by year for the years 1980 to 2004.



**Figure 1. Highly Cited Documents: Document Type by Year (1980-2004)**

A more thorough examination was given to review articles and reviews of workshop proceedings because of their apparent importance in the trajectory of EDC science. A closer look at these papers revealed that they were not a homogeneous group. Table XI displays the titles, authors, and journals of the most highly cited review papers along with their citation counts. The most highly cited of the review articles is the oft-mentioned paper by Colborn et al. (1993) in which the term “endocrine disruption” is first used.

**Table XI. Most Cited Review Articles (1980-2004)**

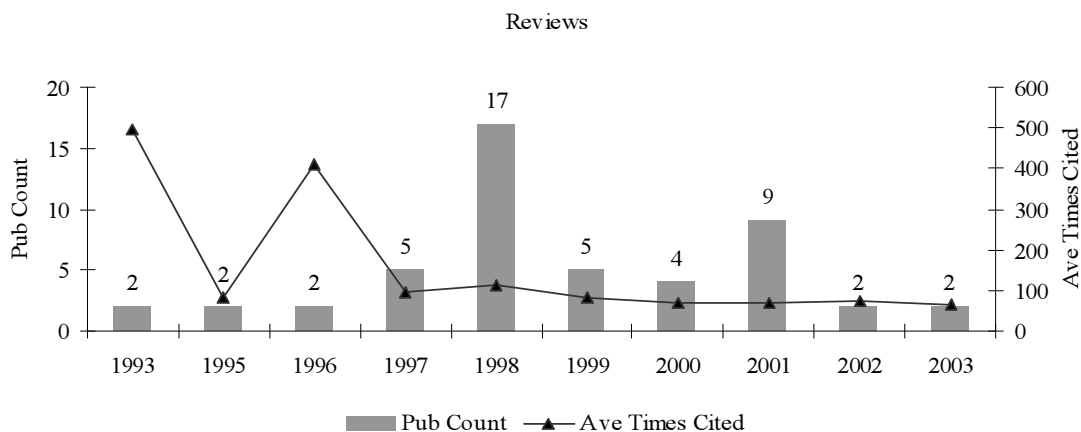
Authors	Times Cited	Journal	Article Title
Colborn et al. 1993	1163	EHP	Developmental effects of endocrine disrupting chemicals in wildlife and humans
Toppari et al. 1996	584	EHP	Male reproductive health and environmental xenoestrogens
Kavlock et al. 1996	358	EHP	Research needs for the risk assessment of health and environmental effects of endocrine disruptors: A report of the US EPA-sponsored workshop
Davis et al. 1993	328	EHP	Medical hypothesis: Xenoestrogens as preventable causes of breast cancer
Sonnenschein & Soto 1998	305	J of Steroid Bio & Mol Biol	An updated review of environmental estrogen and androgen mimics and antagonists
Tyler, Jobling, & Sumpter 1998	299	Critical Revs in Tox	Endocrine disruption in wildlife: A critical review of the evidence
Nimrod & Benson 1996	233	Critical Revs in Tox	Environmental estrogenic effects of alkylphenol ethoxylates
Matthiessen & Gibbs	194	ET&C	Critical appraisal of the evidence for tributyltin-mediated endocrine disruption in mollusks
Ankley et al. 1998	166	ET&C	Overview of a workshop on screening methods for detecting potential (anti-) estrogenic/androgenic chemicals in wildlife
Crisp et al. 1998	163	EHP	Environmental endocrine disruption: An effects assessment and analysis

EHP: Environmental Health Perspectives

ET&amp;C: Environmental Toxicology &amp; Chemistry

A comparison of the average citation count for review articles is plotted against the publication counts for study period in Figure 2. Highly cited review articles were available for 1993 to 2003. As the plot indicates, there was a steady number of highly cited review papers published on EDC science since 1993, with a peak of 17 highly cited reviews published in 1998. The most influential reviews however were those published in 1993 and 1995.

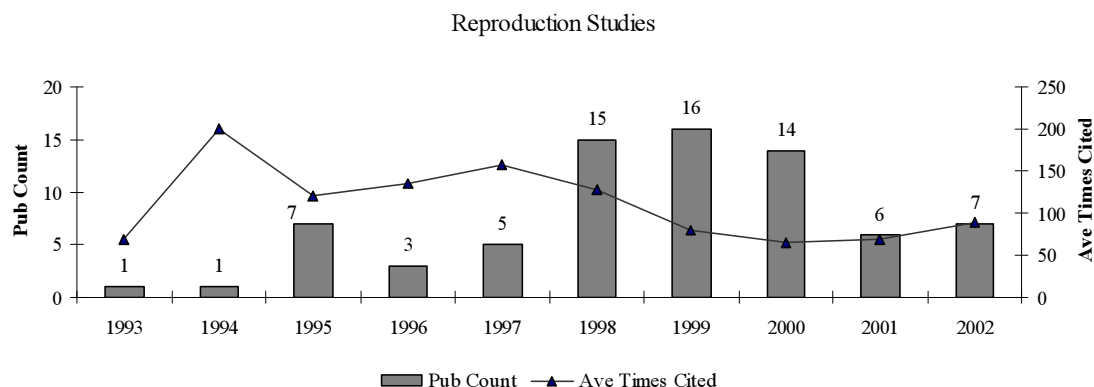
Clearly, papers concerned with reproduction and developmental toxicity ( $n = 78$ ) of endocrine disruptors are highly influential papers representing 28.7% of the highly cited papers and 13% all citations. Briefly, this group of papers is concerned with such topics as EDCs role in the feminization of male fish, declining male fertility and alterations in the reproductive behaviors of wildlife.



**Figure 2. Average Citation and Publication Counts for Highly Cited Reviews**

A comparison of the average citation count for reproduction/development articles is plotted against the publication counts for study period in Figure 3. Highly cited articles concerning reproduction and developmental effects attributable to EDCs were available for 1993 to 2002. As the plot indicates, there was one paper published in 1994 that had the highest average citation rate for the entire period. In 1998, 1999, and 2000 the number of publications in this area were nearly triple what they had been in the past and in 2001 dropped again by more than half. The corresponding average citation counts for this time period was not remarkable.

Screening studies ( $n = 37$ ) were found to be another important category of influential papers representing 13.6% of the highly cited papers by count and 12.5% of the citations received by the highly cited group. These figures indicate that these highly cited screening studies received nearly 6% of the citations for the entire dataset. The screening study topic concerns the development of laboratory methods that would enable scientists to determine whether a particular chemical was capable of inducing an estrogenic response. A more detailed description of factors impacting the emergence and influence of screening methods can be found in Chapter V.

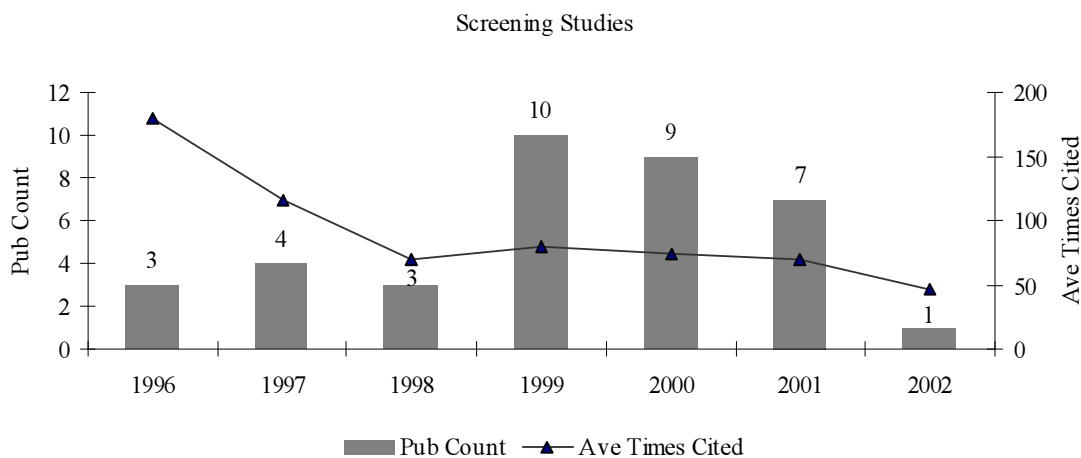


**Figure 3. Average Citation and Publication Counts for Highly Cited Articles Concerning Reproduction & Development**

A comparison of the average citation count for screening articles is plotted against the publication counts for study period in Figure 4. Highly cited articles that reported on the development of screening methods were available for 1996 to 2002. As the plot indicates, the three papers published in 1996 that had the highest average citation rate for the entire period. Highly cited screening studies peaked in 1999 after more than tripling from the previous year. In 1999, 2000, and 2001 the number of publications in this area were nearly triple what they had been in the past and in 2001 dropped again by more than half. The corresponding average citation counts for this time period were not remarkable and appeared to follow the same pattern seen in the previous study type groups where the early papers for each topic generated far more attention did than the later studies.

There were 43 papers among those cited  $\geq 45$  times which focused on the more mechanistic features of the EDC science and were assigned into the study topic “biochemistry/molecular biology” These papers included those that examined the binding of suspected estrogenic compounds or tried to elucidate the mechanisms that resulted in effects seen in the whole animal. The 43 papers in this category comprised 15.8% of all

the highly cited papers ( $n = 272$ ) by count, and received 3196 total citations of all citations for the entire dataset 5.5%.

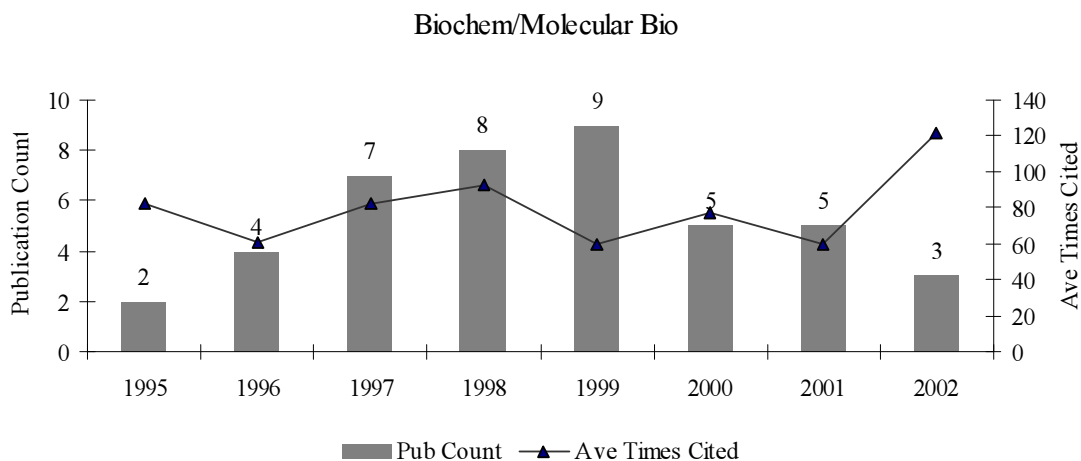


**Figure 4. Average Citation and Publication Counts for Highly Cited Screening Studies**

A comparison of the average citation count for biochemistry/molecular biology articles is plotted against the publication counts for study period in Figure 5. Highly cited articles that reported on developments in biochemistry and molecular biology were available for 1996 to 2002. Figure 5 is clearly different from the previous similar plots. Unlike the plots for reviews, reproduction, and screening studies this plot does not show a high initial peak in average citation count in the early years. Instead, after an introductory paper in 1995 there was a slight dip and then an increase in both the number of publications and their average citation counts. Overall, the average citation counts remain somewhat steady until a peak in 2002.

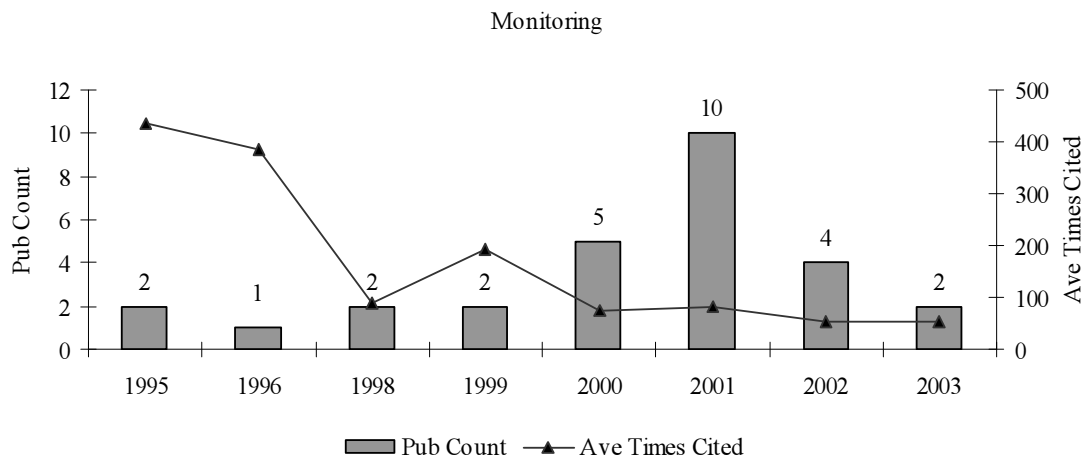
Monitoring studies were also well represented among the highly cited studies. This topic included papers that attempted to assess or measure the presence of potential

endocrine disrupting chemicals in a variety of environmental media. Studies in this category measured suspect chemicals in leachate from tin cans, in wastewater treatment plant effluent, in fresh water systems, and in dental resins. The 28 papers in this category comprised 10.3% of the highly cited papers ( $n = 272$ ) by count, and 5.6% of all citations for entire dataset.



**Figure 5. Average Citation and Publication Counts for Highly Cited Studies Concerning Biochemistry and Molecular Biology**

Highly cited monitoring studies were available for 1995 to 2003. A comparison of the average citation count for monitoring studies is plotted against the publication counts for the study period is shown in Figure 6. This plot indicates that in 1995 and 1996 there were highly cited papers with very high average citation scores, but following this period there was no comparable level of influence seen. In 2001, however, there was a peak in publication of monitoring studies.



**Figure 6. Average Citation and Publication Counts for Highly Cited Monitoring Studies**

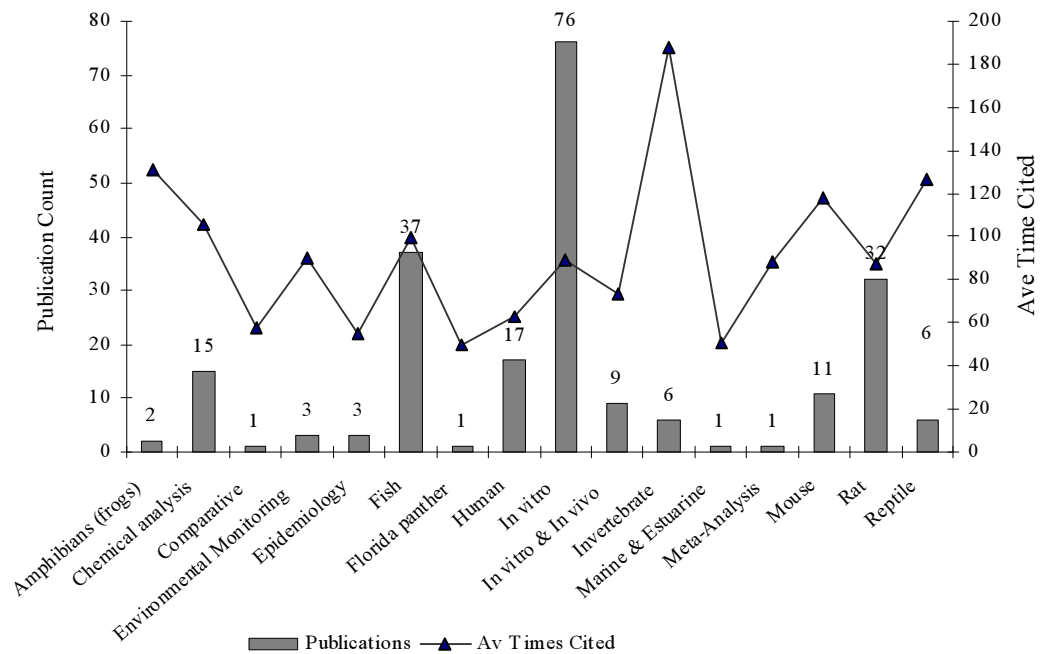
#### 4.4.2 Investigative Model

To characterize the investigative models of the highly cited dataset, the 50 review papers, the four “not applicable” studies, and three editorials were removed from the dataset ( $n = 276$ ) and the remaining 221 studies were examined for the influence of investigative model on citedness. Table XII and Figure 7 show that *in vitro* studies are the largest investigative model category within the group of highly cited studies with a publication count of 76 or 34.4% of all the relevant highly cited studies ( $n = 221$ ). Studies using fish (37) and rats (32) were next in importance when compared by number of studies published. As shown in Figure 7, however, there was little correlation between the investigative model category and the average citation count.



**Table XII. Influence of Investigative Model on Publication and Citation Counts**

Investigative Model Category	Publications	% (n = 221)	Avg Times Cited
Invertebrate	6	2.7%	188
Amphibians (frogs)	2	0.9%	131
Reptile	6	2.7%	127
Mouse	11	5.0%	118
Chemical analysis	15	6.8%	106
Fish	37	16.7%	100
Environmental Monitoring	3	1.4%	90
In vitro	76	34.4%	89
Meta-Analysis	1	0.5%	88
Rat	32	14.5%	87
In vitro & In vivo	9	4.1%	73
Human	17	7.7%	63
Comparative	1	0.5%	58
Epidemiology	3	1.4%	55
Marine & Estuarine	1	0.5%	51
Florida panther	1	0.5%	50



**Figure 7. Comparison of Average Citation and Publication Counts for Investigative Models**

#### **4.4.3 Support or Negation of the EDC Hypothesis**

Over 98% of the highly cited papers expressed some degree of outright support for the endocrine disruption hypothesis. Nowhere in the literature reviewed was there a strong dissenting opinion expressed. There were six studies that did not have outright statements endorsing or referring to the EDC hypothesis in their abstracts. Of these, three presented negative findings, two of which reported no significant reproductive abnormalities in fish exposed to suspect EDCs in waste water treatment plant effluent (Nichols, Miles-Richardson, Snyder, & Giesy, 1999; Nimrod & Benson, 1998). The third study failed to find estrogenic response in breast cancer cells treated with the hydroxylated metabolites of polychlorinated biphenyls.

Golden et al. (1998) wrote a lengthy review in *Critical Reviews in Toxicology* in which they compared then emerging EDC science with the mature science of potent drug DES. They concluded that while it may be reasonable to hypothesize that exposure to estrogen-like substances may be deleterious regardless of their source, it was not reasonable to compare the impacts of this estrogenicity to those of DES. In addition, they argued that “biological plausibility alone is an insufficient basis for concluding” that environmental chemicals have already adversely impacted humans (Golden et al., 1998, p. 109).

Another review appeared in 2000 which was specifically directed at an often-cited argument for the existence of EDCs in the environment; that is the increasing prevalence of male reproductive tract abnormalities. In this review, Safe (2000), a well known and highly published scientist from the Texas A&M countered these claims using what he considered more current studies. His opinion was that many of the effects attributed to

EDCs (sperm count decline etc.) had not actually occurred ... “[t]hus, many of the male and female reproductive tract problems linked to the endocrine-disruptor hypothesis have not increased and are not correlated with synthetic industrial contaminants” (Safe, 2000, p. 487).

In what was a rare finding among the 276 abstracts, in a highly cited review published in *Critical Reviews in Toxicology* Tyler, Jobling, and Sumpter (1998) caution their readers about extrapolating *in vitro* results

In fact, the evidence showing that such chemicals actually do mimic (or antagonize) the action of hormones in the intact animal is limited. In only a few cases have laboratory studies shown that chemicals that mimic hormones at the molecular level (in vitro) also cause reproductive dysfunction *in vivo* at environmentally relevant concentrations. In addition, the reported studies on wildlife populations are limited to a very few animal species and they have often centered on localized 'hot-spots' of chemical discharges (p. 318).

#### **4.4 Visual Representations of Citation Relationships**

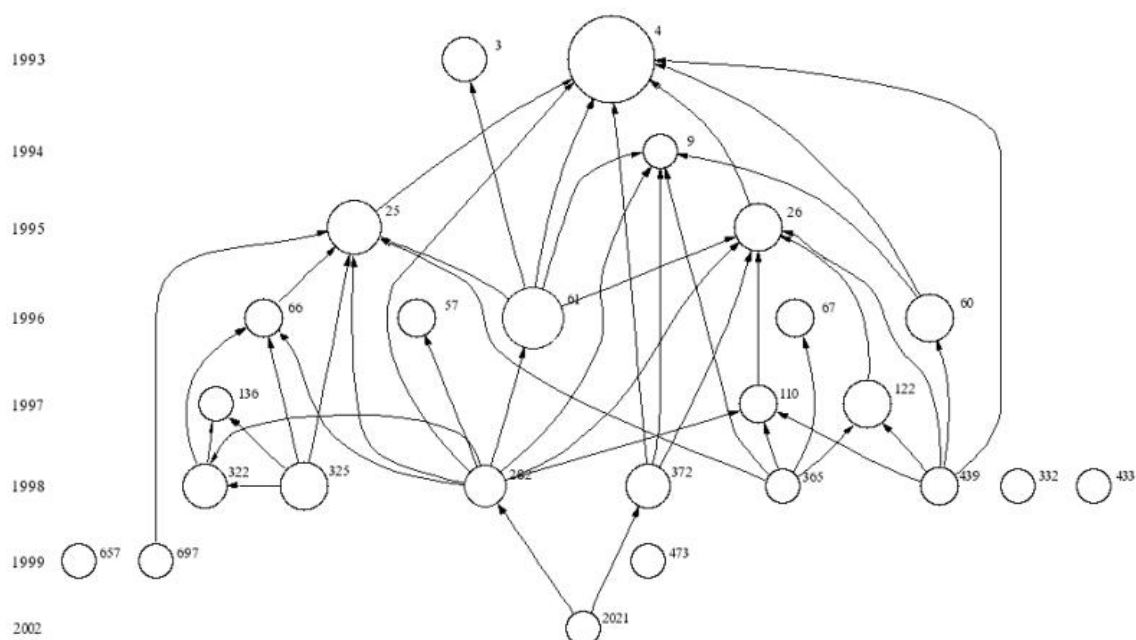
The value of representing citation information in a visual display becomes apparent in this section when the most highly cited documents are arrayed and their influences are visible. The citation relationships between the publications identified by keyword searches as well as their relative influence among all publications in the Science Citation Index are visually depicted in Figures 8 through 14 which follow at the end of this chapter. These visual representations, created with the software tool HistCite™ show which documents in the dataset are related by citation. Second, they depict the direction of the relationship by the positioning of the arrow head (i.e., the arrow points to the cited paper). Third, the maps depict the influence of a paper both within a specific dataset (the dataset used as input) and within the entire holdings of the Science Citation Index. This influence is depicted both by the links (and arrows) which illustrate relationships that

exist between papers within the dataset and the size of each node which is relative to the number of citations received. Thus, even when a paper has no citation relationships to other papers in the dataset, the size of its node reflects its significance, or lack thereof, elsewhere.

The biggest challenge of using HistCite<sup>TM</sup> and other map-generating citation analysis software is the difficulty in achieving a balance between the availability of data and the presentation of that data in a meaningful array. For example, it was determined that depicting citation relationships among more than 50 papers created a map too large to be meaningfully depicted on a sheet of paper. Since HistCite<sup>TM</sup> provided an interactive user interface it was possible to vary the thresholds for each subgroup to create maps that could provide insight into the relationships between papers in the dataset.

#### **4.5.1 1980 through 2004**

Figure 8 shows the citation relationships between and among the 25 most highly cited papers that were published between 1980 and 2004. Of these 25 papers the most highly cited paper (represented as Node #4) was cited 1,176 times and the least cited paper was cited 188 times (Node # 136). Node #4 is the 1993 paper by Colborn et al. (1993) and its importance within the dataset is immediately visible both by the size of the node and the number of links which point to it.



**Figure 8. Citation Relationships among Top 25 Papers (1980-2004)**

**LEGEND FOR FIGURE 8**

*Nodes: 25, Links: 43*

Node #	First Author, Pub Year, Source	GCS
3	DAVIS DL, 1993, ENVIRON HEALTH PERSPECT, V101, P372	328
4	COLBORN T, 1993, ENVIRON HEALTH PERSPECT, V101, P378	1176
9	KELCE WR, 1994, TOXICOL APPL PHARMACOL, V126, P276	200
25	JOBLING S, 1995, ENVIRON HEALTH PERSPECT, V103, P582	506
26	BROTONS JA, 1995, ENVIRON HEALTH PERSPECT, V103, P608	362
57	Nimrod AC, 1996, CRIT REV TOXICOL, V26, P335	233
60	Kavlock RJ, 1996, ENVIRON HEALTH PERSPECT, V104, P715	358
61	Toppari J, 1996, ENVIRON HEALTH PERSPECT, V104, P741	584
66	Folmar LC, 1996, ENVIRON HEALTH PERSPECT, V104, P1096	253
67	Shelby MD, 1996, ENVIRON HEALTH PERSPECT, V104, P1296	257
110	Steinmetz R, 1997, ENDOCRINOLOGY, V138, P1780	248
122	Nagel SC, 1997, ENVIRON HEALTH PERSPECT, V105, P70	378
136	Gray MA, 1997, ENVIRON TOXICOL CHEM, V16, P1082	188
282	Tyler CR, 1998, CRIT REV TOXICOL, V28, P319	299
322	Routledge EJ, 1998, ENVIRON SCI TECHNOL, V32, P1559	335
325	Jobling S, 1998, ENVIRON SCI TECHNOL, V32, P2498	400
332	Matthiessen P, 1998, ENVIRON TOXICOL CHEM, V17, P37	194
365	Sohoni P, 1998, J ENDOCRINOL, V158, P327	208
372	Sonnenschein C, 1998, J STEROID BIOCHEM MOL BIO, V65, P143	305
433	Brouwer A, 1998, TOXICOL IND HEALTH, V14, P59	191
439	Vom Saal FS, 1998, TOXICOL IND HEALTH, V14, P239	262
473	Larsson DGJ, 1999, AQUAT TOXICOL, V45, P91	211
657	Belfroid AC, 1999, SCI TOTAL ENVIR, V225, P101	211
697	Gray LE, 1999, TOXICOL IND HEALTH, V15, P94	209
2021	Hayes TB, 2002, PROC NAT ACAD SCI USA, V99, P5476	202

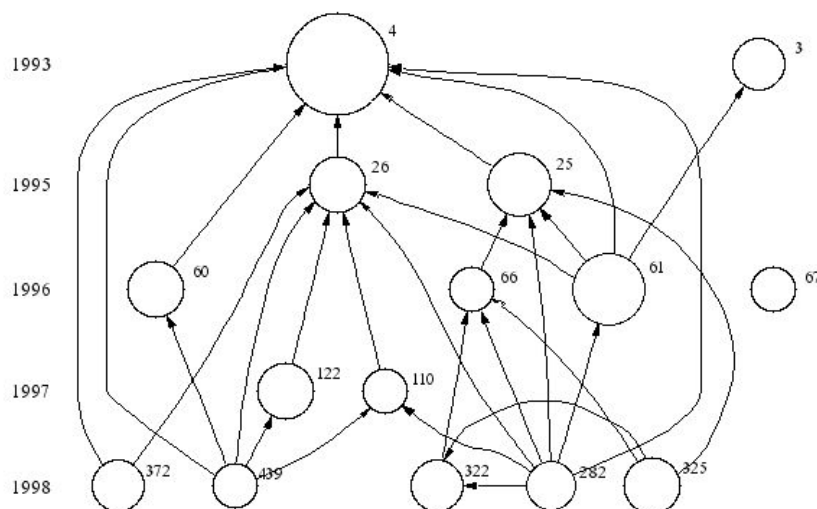
Nodes #25 and #26 were identified as hubs of influence and upon closer examination were found to be similar in content, both reporting findings that expressed strong concern about the EDC hypothesis and impacts to human and environmental health. The papers represented by these nodes each report finding estrogenic compounds in water and food, each of which one would expect to generate interest. Node #25 represents Jobling et al. (1995), entitled “A variety of environmentally persistent chemicals, including some phthalate plasticizers, are weakly estrogenic.” This paper reported the findings of a random screen of 20 effluent samples for the presence of estrogenic compounds. The results indicated that half of the samples interfered with estrogen binding. Node #26 was a paper by Brotons, Oleaserrano, Villalobos, Pedraza, and Olea (1995) in which the authors reported finding measurable concentrations of bisphenol A (a probable endocrine disrupting chemical) in canned vegetables. The bisphenol A was presumed to have leached from the inside plastic coating to the edible contents.

Also of note are the nodes which have no links such as #332, 433, 657, and 2021. Node #332 is a review article about the estrogenic effects of tributyl tin. It is cited 194 times in the overall literature, only 43 times in the dataset, but has no links to the highly cited papers. Node #433 is by Brouwer et al. (1998) from the journal *Toxicology and Industrial Hygiene* concerns the mechanisms and outcomes by which persistent environmental organohalogens might interfere with the thyroid hormone system and posits possible consequences for animal and human health. This paper had a GCS of 191, was cited 34 times in the dataset, but was not cited among the 25 most highly cited papers. Node #657 (Belfroid et al., 1999) reports on the development and testing of an

analytical method for measuring estrogenic compounds at concentrations in the nanogram per liter range. Testing of wastewater treatment plant effluent with this method detected extremely low levels of some estrogenic compounds. Belfroid et al. (1999) had a GCS of 211, was cited 43 times in the dataset, but was not among the top 25 highly cited papers.

Node #2021 in Figure 8 (Hayes et al., 2002) is interesting as it is the only post-1999 paper to appear among the top 25 papers. The Hayes et al. (2002) study found that a common herbicide impacted the sexual development of frogs. This paper had a GCS of 202 was cited 7 times in the dataset, but had no links to the top 25 highly cited papers.

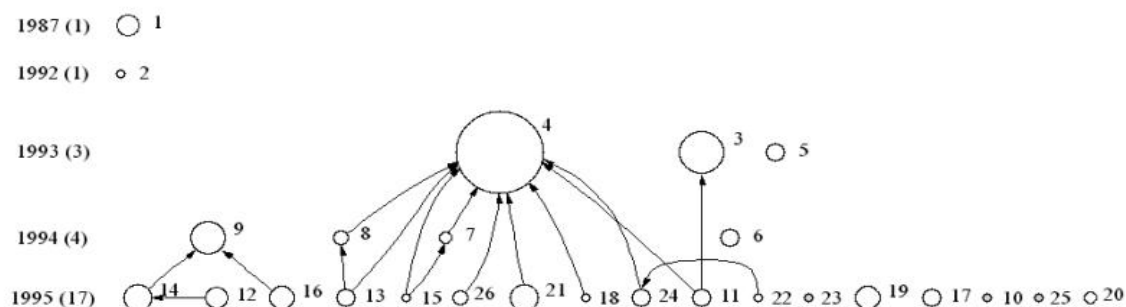
Figure 9 shows the same time period as Figure 8 (1980-2004) but focuses on the top 15 papers. From this perspective it is also evident that Node #67 had no links in the top 15 papers and only one link among the top 25. This paper reported the findings of a study by Shelby, Newbold, Tully, Chae, & Davis (1996) in which the authors used known or suspected estrogenic compounds to compare different methods of screening chemicals for their potential estrogenicity.



**Figure 9. Citation Relationships among the Top 15 Papers (1980-2004)**  
See Figure 8 for legend.

#### 4.5.2 1980 through 1995

Beginning with Figure 10, the citation relationships papers are examined within sequential chronological subsets. Figure 10 depicts the citation relationships for the period from 1980 to 1995. Visible are 26 nodes with citation counts ranging from 0 to 1,176. Sixteen links are also visible. Colborn et al. (1993) (Node #4, GCS = 1,176) is clearly the most significant node in this set, followed by Nodes #3 (Davis et al., 1993) (GCS = 328) and #9 (Kelce, Monosson, Gamcsik, Laws, & Gray, 1994) (GCS = 200).



**Figure 10. Citation Relationships (1980-1995)**

#### FIGURE 10 LEGEND

Nodes: 26, Links: 16

Node ID	First Author, Pub Year, Source	GCS (#rank)
1	WELSHONS WV, 1987, BREAST CANCER RES TREAT, V10, P169	76
2	MENA MA, 1992, BIOL REPROD, V46, P1080	6
3	DAVIS DL, 1993, ENVIRON HEALTH PERSPECT, V101, P372	328 (#2)
4	COLBORN T, 1993, ENVIRON HEALTH PERSPECT, V101, P378	1176 (#1)
5	FABER KA, 1993, REPROD TOXICOL, V7, P35	69
6	BECKAGE NE, 1994, ARCH INSECT BIOCHEM PHYSIOL, V26, P165	64 (n/a)
7	COLBORN T, 1994, ENVIRON HEALTH PERSPECT, V102, P55	23
8	SOONTORNCHAT S, 1994, ENV HEALTH PERSPECT, V102, P568	38
9	KELCE WR, 1994, TOXICOL APPL PHARMACOL, V126, P276	200 (#3)
10	HILEMAN B, 1995, CHEM ENG NEWS, V73, P30	0
11	SONNENSCHN C, 1995, CLIN CHEM, V41, P1888	70
12	JENSEN TK, 1995, CLIN CHEM, V41, P1896	88
13	BARRON MG, 1995, COMP BIOCHEM PHYSIOL PT C, V112, P1	54
14	FACEMIRE CF, 1995, ENVIRON HEALTH PERSPECT, V103, P79	132
15	COLBORN T, 1995, ENVIRON HEALTH PERSPECT, V103, P81	19
16	NEWBOLD R, 1995, ENVIRON HEALTH PERSPECT, V103, P83	107
17	BIRNBAUM LS, 1995, ENVIRON HEALTH PERSPECT, V103, P89	64
18	FOX GA, 1995, ENVIRON HEALTH PERSPECT, V103, P93	16
19	COLBORN T, 1995, ENVIRON HEALTH PERSPECT, V103, P135	119
20	LINDSTROM G, 1995, ENVIRON HEALTH PERSPECT, V103, P135	29
21	GUILLETTE LJ, 1995, ENVIRON HEALTH PERSPECT, V103, P157	144
22	LEBLANC GA, 1995, ENVIRON HEALTH PERSPECT, V103, P888	17
23	RENNER R, 1995, ENVIRON SCI TECHNOL, V29, PA494	0
24	BALDWIN WS, 1995, ENVIRON TOXICOL CHEM, V14, P945	69
25	[Anon], 1995, EUR CHEM NEWS, V63, P28	0
26	FRIES GF, 1995, J ANIM SCI, V73, P1639	40



Davis et al. (1993) was a review article published in *Environmental Health Perspectives* (EHP) entitled “Medical Hypothesis: Xenoestrogens as preventable causes of breast cancer.” In this article, the authors hypothesized that the majority of human breast cancer cases might be linked to exposure to environmental estrogens. Kelce et al. (1994) in *Toxicology and Applied Pharmacology* (“Environmental hormone disruptors: Evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metabolites”) presents results of experimental studies in rats in which the fungicide vinclozolin caused developmental malformations by impacting sex hormones.

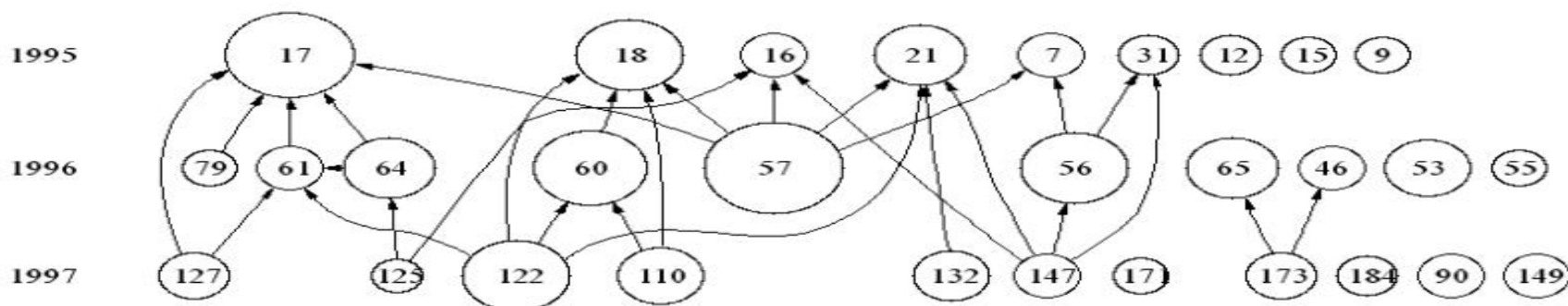
The visual representations bring to light several important characteristics of the dataset that may have been otherwise overlooked. In Figure 10 it becomes apparent that the publications with little or no influence on EDC science may have some shared characteristics. Faber and Hughes (1993) (Node #5) reported that genistein (isoflavonoid found in soy) mimicked the effects of estrogen when administered to rats. While this study had a GCS of 69 it had no links in this dataset.

Nodes #1 and #2 were published prior to the Colborn et al. (1993) paper but have no links to other documents in the dataset. Node #1, Welshons, Murphy, Koch, Calaf, and Jordan (1987) (GCS = 76) was published in *Breast Cancer Research and Treatment*. In this study, the authors evaluated the estrogenic and antiestrogenic activity of three plant-derived metabolites that are found in the urine of women, especially those consuming a vegetarian diet, and which had been thought to be protective against the proliferation of breast cancer cells. Using tissue culture methods, the researchers unexpectedly found that these compounds acted as weak estrogens which could promote and stimulate the growth of estrogen sensitive breast cancer cells.

Node #2, Mena, Arriaza, and Tchernitchin (1992) (GCS = 6) was an experimental study published in the *Biology of Reproduction* in which it was found that the timing of exposure of female rats to testosterone significantly impacted the type of effect that was seen as the rat developed. This study was supported by grants from the Third World Academy of Science and the University of Chile (Mena et al., 1992).

#### **4.5.3 1995 through 1998**

Figure 11 depicts the citation relationships among the top 30 papers for the period from 1995 to 1998. Because the nodes are scaled by citation counts, the most highly cited nodes are larger. For this period these nodes are #57, #19, #60, #122, #18, and #56 (ranked 1 through 6, respectively). All six of these highly cited papers were published in the journal *Environmental Health Perspectives*. Node #57 is a review article written by Toppari et al. (1996) (GCS = 584) in which the authors link reports of human testicular cancer, declining sperm quality, and other male reproductive abnormalities reported from clinical and laboratory evidence linking such abnormalities to exposure to estrogens. From this, the authors hypothesize that exposure to synthetic estrogenic chemicals during development may be the cause of such adverse reproductive patterns.



**Figure 11. Citation Relationships among the Top 30 Documents (1995-1998)**

**FIGURE 11 LEGEND** Nodes: 30, Links: 29

Node	First Author, Pub Year, Source	GCS (# = rank)
7	Facemire CF, 1995, ENV HEALTH PERSPECT, V103, P79	132
9	Newbold R, 1995, ENV HEALTH PERSPECT, V103, P83	107
12	Colborn T, 1995, ENV HEALTH PERSPECT, V103, P135	119
15	Bradlow HL, 1995, ENV HEALTH PERSPECT, V103, P147	94
16	Guillette LJ, 1995, ENV HEALTH PERSPECT, V103, P157	144
17	Jobling S, 1995, ENV HEALTH PERSPECT, V103, P582	506 (#2)
18	Brotons JA, 1995, ENV HEALTH PERSPECT, V103, P608	362 (#5)
21	Sharpe RM, 1995, ENV HEALTH PERSPECT, V103, P1136	261
31	Goldey ES, 1995, TOX APPL PHARMACOL, V135, P77	127
46	Waller CL, 1996, CHEM RES TOXICOL, V9, P1240	134
53	Nimrod AC, 1996, CRIT REV TOXICOL, V26, P335	233
55	Majdic G, 1996, ENDOCRINOLOGY, V137, P1063	99
56	Kavlock RJ, 1996, ENV HEALTH PERSPECT, V104, P715	358 (#6)
57	Toppari J, 1996 ENV HEALTH PERSPECT, V104, P741	584 (#1)

**FIGURE 11 LEGEND (continued)**

Node	First Author, Pub Year, Source	GCS (# = rank)
60	Olea N, 1996, ENV HEALTH PERSPECT, V104, P298	386 (#3)
61	Arnold SF, 1996, ENV HEALTH PERSPECT, V104, P544	147
64	Folmar LC, 1996, ENV HEALTH PERSPECT, V104, P1096	253
65	Shelby MD, 1996, ENVHEALTH PERSPECT, V104, P1296	257
79	Nesaretnam K, 1996, MOL ENDOCRINOL, V10, P923	93
90	Longnecker MP, 1997, ANN REV PUB HLTH, V18, P211	149
110	Steinmetz R, 1997, ENDOCRINOLOGY, V138, P1780	248
122	Nagel SC, 1997, ENV HEALTH PERSPECT, V105, P70	378 (#4)
125	Crain DA, 1997, ENV HEALTH PERSPECT, V105, P528	91
127	Coldham NG, 1997, ENV HEALTH PERSPECT, V105, P734	152
132	Gray MA, 1997, ENV TOXICOL CHEM, V16, P1082	188
147	Cooper RL, 1997, J ENDOCRINOL, V152, P159	133
149	Kelce WR, 1997, J MOLECULAR MED-JMM, V75, P198	133
171	Das SK, 1997, PROC NAT ACAD SCI USA, V94, P12786	106
173	Odum J, 1997, REGUL TOX PHARMACOL, V25, P176	163
184	Papadopoulos V, 1997, STEROIDS, V62, P21	130

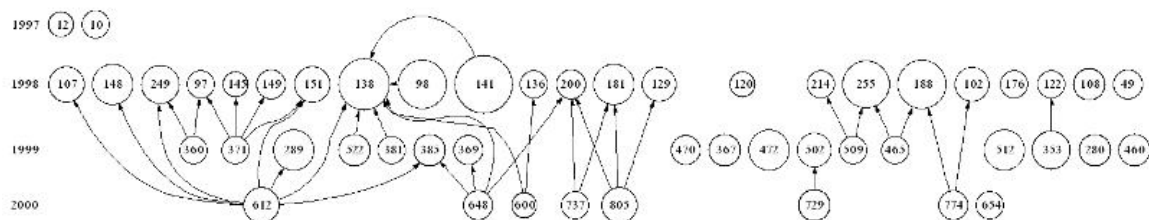
Node #17 was the paper by Jobling et al. (1995) discussed above (GCS = 506), in which the random screening of wastewater treatment plant effluent revealed the presence of estrogenic compounds in measurable quantities. Node #60 (GCS = 386) represents the paper by Olea et al. (1996) in which estrogenic compounds were found to have leached from dental sealants. Node #122 (GCS = 378) represents the paper by Nagel et al. (1997) in which report findings of comparative binding of various presumed EDC compounds. They conclude with the suggestion that very low levels of bisphenol A, such as those to which humans were exposed could induce reproductive abnormalities in the mouse.

Brotons et al. (1995) (Node #18; GCS = 362) presents data suggesting that the plastic lining of cans may leach estrogenic substances into food. Finally, Kavlock et al. (1996) (Node #56; GCS = 358) is a review of an Environmental Protection Agency workshop in which invited participants met to review data and discuss research needs.

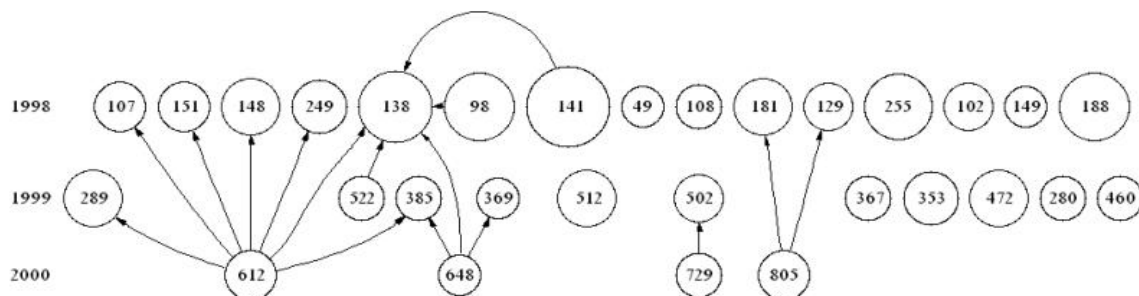
#### **4.5.4 1998 through 2000**

Figure 12 depicts the citation relationships among the 50 most highly cited papers from the period between 1998 and 2000 and Figure 13 depicts the 30 most highly cited papers for the same period of time. The most significant node is #141 (Jobling, Nolan, Tyler, Brighty, & Sumpter, 1998) (GCS = 400). Jobling et al. (1998) reported a high incidence of intersex condition among fish living near the discharges of sewage plants. Published in the journal *Environmental Science & Technology*, the authors contend that this

is the first documented example of a widespread sexual disruption in wild populations of any vertebrate [*fish*] and indicates that reproductive and developmental effects do result from exposure to ambient levels of chemicals present in typical British rivers (p. 2498).



**Figure 12. Citation Relationships among the Top 50 (1998-2000)**  
Nodes: 50, Links: 36



**Figure 13. Citation Relationships among the Top 30 (1998-2000)**  
Nodes: 30, Links: 16

**LEGEND for FIGURES 12 and 13**

Node	First Author, Pub Year, Source	GCS (#=rank)
10	Petit F, 1997, J MOLECULAR ENDOCRINOL, V19, P321	98
12	Green PS, 1997, J STEROID BIOCHEM MOL BIOL, V63, P229	86
49	Kramer VJ, 1998, AQUAT TOXICOL, V40, P335	111
97	Golden RJ, 1998, CRIT REV TOXICOL, V28, P109	100
98	Tyler CR, 1998, CRIT REV TOXICOL, V28, P319	299 (#4)
102	Steinmetz R, 1998, ENDOCRINOLOGY, V139, P2741	153
107	Crisp TM, 1998, ENVIRON HEALTH PERSPECT, V106, P11	163
108	Hansen LG, 1998, ENVIRON HEALTH PERSPECT, V106, P171	131
120	Milligan SR, 1998, ENVIRON HEALTH PERSPECT, V106, P23	88
122	Perez P, 1998, ENVIRON HEALTH PERSPECT, V106, P167	94
129	Bolger R, 1998, ENVIRON HEALTH PERSPECT, V106, P551	142
136	Rudel RA, 1998, ENVIRON SCI TECHNOL, V32, P861	100
138	Routledge EJ, 1998, ENVIRON SCI TECHNOL, V32, P1559	335 (#2)
141	Jobling S, 1998, ENVIRON SCI TECHNOL, V32, P2498	400 (#1)
145	Gillesby BE, 1998, ENVIRON TOXICOL CHEM, V17, P3	86
148	Matthiessen P, 1998, ENVIRON TOXICOL CHEM, V17, P37	194
149	Arcand-Hoy LD, 1998, ENVIRON TOXICOL CHEM, V17, P49	111
151	Ankley G, 1998, ENVIRON TOXICOL CHEM, V17, P68	166
176	Tong W, 1998, J CHEM INFORM COMPUT SCI, V38, P669	91
181	Sohoni P, 1998, J ENDOCRINOL, V158, P327	208
188	Sonnenschein C, 1998, J STER BIOCHEM MOL BIOL, V65, P143	305 (#3)
200	Gould JC, 1998, MOL CELL ENDOCRINOL, V142, P203	108
214	Nagel SC, 1998, PROC SOC EXP BIOL MED, V217, P300	90
249	Brouwer A, 1998, TOXICOL IND HEALTH, V14, P59	191

*Continued on the following page*

<b>LEGEND for FIGURES 12 and 13 (continued)</b>		
255	Vom Saal FS, 1998, TOXICOL IND HEALTH, V14, P239	262 (#5)
280	Baptista T, 1999, ACTA PSYCHIAT SCAND, V100, P3	134
289	Larsson DGJ, 1999, AQUAT TOXICOL, V45, P91	211
353	Andersen HR, 1999, ENVIRON HEALTH PERSPECT, V107, P89	186
360	Brouwer A, 1999, ENVIRON HEALTH PERSPECT, V107, P639	100
367	Cheek AO, 1999, ENVIRON HEALTH PERSPECT, V107, P273	121
369	Paulozzi LJ, 1999, ENVIRON HEALTH PERSPECT, V107, P297	114
371	Gronen S, 1999, ENVIRON HEALTH PERSPECT, V107, P385	91
381	Tyler CR, 1999, ENVIRON TOXICOL CHEM, V18, P337	96
385	Allen Y, 1999, ENVIRON TOXICOL CHEM, V18, P1791	121
460	Watson CS, 1999, PROC SOC EXP BIOL MED, V220, P9	125
465	Spearow JL, 1999, SCIENCE, V285, P1259	101
470	Kloas W, 1999, SCI TOTAL ENVIR, V225, P59	108
472	Belfroid AC, 1999, SCI TOTAL ENVIR, V225, P101	211
502	Nishikawa J, 1999, TOXICOL APPL PHARMACOL, V154, P76	137
509	Welshons WV, 1999, TOXICOL IND HEALTH, V15, P12	98
512	Gray LE, 1999, TOXICOL IND HEALTH, V15, P94	209
522	Servos MR, 1999, WATER QUAL RES J CAN, V34, P123	131
600	Korner W, 2000, CHEMOSPHERE, V40, P1131	88
612	Vos JG, 2000, CRIT REV TOXICOL, V30, P71	162
648	Safe SH, 2000, ENVIRON HEALTH PERSPECT, V108, P487	116
654	Colon I, 2000, ENVIRON HEALTH PERSPECT, V108, P895	90
729	Nishihara T, 2000, J HEALTH SCI, V46, P282	136
737	Diel P, 2000, J STEROID BIOCHEM MOL BIOL, V73, P1	101
774	Nadal A, 2000, PROC NAT ACAD SCI USA, V97, P11603	107
805	Laws SC, 2000, TOXICOL SCI, V54, P154	156

Routledge et al. (1998) was cited globally 335 times and appears in Figures 12 and 13 as Node #138. Also appearing in the journal *Environmental Science & Technology* and sharing some of the same authors as Node #141 above, this paper presents additional findings to link the feminization of male fish to the natural and synthetic estrogens found in waste water effluent from sites in the United Kingdom.

Sonnenschein and Soto (1998), Node #3 (GCS = 305), is a review article published in the *Journal of Steroid Biochemistry & Molecular Biology* in which the authors detail evidence to support the hypothesis that certain exogenous chemicals have been released into the environment which exhibit a range of disruptive effects on

hormone function. Tyler, Jobling, and Sumpter (1998) is represented by Node #98. With a GCS of 299 this is among the most highly cited paper within the dataset (also seen in Figures 12 and 13 as Node #282). Published in the journal *Critical Reviews in Toxicology* and thus far the only paper to explicitly acknowledge the limited evidence upon which the endocrine hypothesis is built. This review presents a critical assessment of available evidence from laboratory and field studies in which exposure to steroid hormones have been studied for their impact on reproductive function.

Node #255 represents Vom Saal et al. (1998), which was published in *Toxicology & Industrial Health* (GCS = 262). This paper is also shown in Figures 12 and 13 (where it was depicted by Node #439). In this study, fetal mice were exposed to very low doses (nanograms per liter) of suspected endocrine disrupting chemicals (bisphenol A or octylphenol). The results indicated that such “physiologically relevant” exposures altered sperm production, and the development and function of reproductive organs (vom Saal et al., 1998).

In Figure 8, Gray et al. (1999) is represented by Node #697. In Figures 12 and 13 it is represented by Node #512. This paper is of interest because it is one of several that was rather highly cited globally (GCS = 209), but not very highly cited within the dataset created by keyword searching. Thus, although this node appears in Figures 8, 12, and 13 it is not linked to any other nodes in these figures. This paper was published in a volume of *Toxicology & Industrial Health* devoted to the hormonal effects of herbicides and pesticides. The authors, all USEPA scientists, present results of experimental research in

which ten pesticides were shown to cause a variety of effects to the reproductive system in the male rat.<sup>14</sup>

#### 4.5.5 2000 through 2004

Figure 14 depicts the citation relationships among the 30 most highly cited papers published during the period 2000-2004. These papers are principally concerned with identifying chemicals that have the potential to disrupt endocrine function and with identifying and quantifying estrogenic chemicals that have made their way into wastewater treatment plant effluent and thus into fish habitat and potential sources of drinking water. Node #64 (GCS = 132) represents a paper by Parks et al. (2000) that was published in *Toxicological Sciences* and in which the plasticizer diethylhexyl phthalate was found to decrease the amount of fetal testosterone in male rats and thereby induce malformation. A study by McLachlan (2001) (GCS = 144) is represented by Node #220 in Figure 14 and is the 3rd ranked in citation frequency for this time period. This paper is a review published in the journal *Endocrine Reviews*. Conducted at a center of EDC research (the Environmental Endocrinology Laboratory in the Center of Bioenvironmental Research located at Tulane and Xavier Universities in New Orleans, Louisiana), McLachlan reviewed the science of the evolutionary biomolecular mechanisms in steroid receptors that might explain the inter-species and ecological impacts observed of endocrine disrupting chemicals.

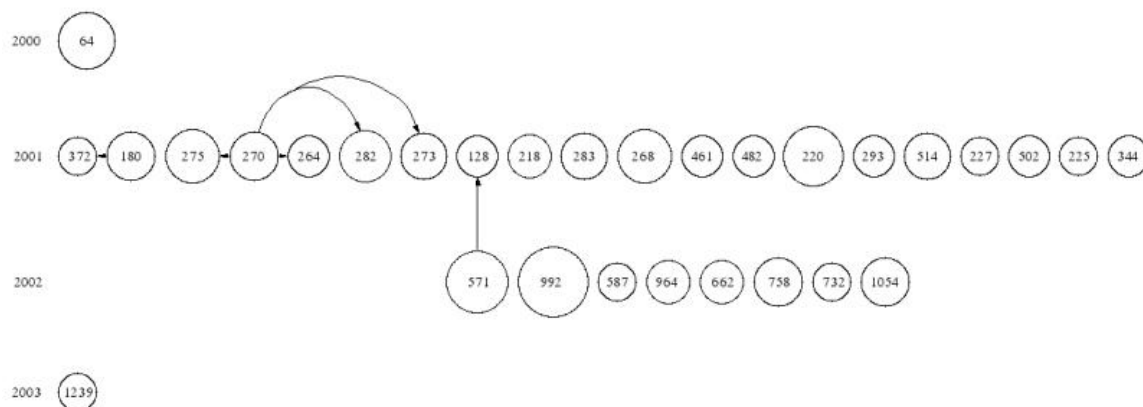
Kuch and Ballschmiter (2001) (Node # 268; GCS = 125) established a method for measuring the concentration of phenolic compounds and estrogens in both surface and drinking water at the picogram per liter range. Their results indicated that environmental

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<sup>14</sup> It is interesting to note that although this paper is attributed to Gray et al., the first author is actually Cynthia Wolf. This misattribution appears to be perpetuated throughout the citation databases and even on the online journal page through which one links to the article.



estrogens were not completely removed by sewage treatment processes but were measurable in effluent.



**Figure 14. Citation Relationship among the Top 30 (2000-2004)**

**LEGEND FOR FIGURE 14**

Nodes: 30, Links: 6; GCS, top 30; Min: 64, Max: 202 (GCS scaled)

Node #	First Author, Pub Year, Source	GCS
64	Parks LG, 2000, TOXICOL SCI, V58, P339	132
128	Piferrer F, 2001, AQUACULTURE, V197, P229	70
180	Fang H, 2001, CHEM RES TOXICOL, V14, P280	103
218	Moggs JG, 2001, EMBO REP, V2, P775	80
220	McLachlan JA, 2001, ENDOCRINE REV, V22, P319	144
225	Whitten PL, 2001, ENVIRON HEALTH PERSPECT, V109, P5	65
227	Snedeker SM, 2001, ENVIRON HEALTH PERSPECT, V109, P35	68
264	Jonkers N, 2001, ENVIRON SCI TECHNOL, V35, P335	72
268	Kuch HM, 2001, ENVIRON SCI TECHNOL, V35, P3201	125
270	Johnson AC, 2001, ENVIRON SCI TECHNOL, V35, P4697	98
273	Huang CH, 2001, ENVIRON TOXICOL CHEM, V20, P133	96
275	Metcalfe CD, 2001, ENVIRON TOXICOL CHEM, V20, P297	124
282	Lange R, 2001, ENVIRON TOXICOL CHEM, V20, P1216	113
283	Ankley GT, 2001, ENVIRON TOXICOL CHEM, V20, P1276	90
293	Spengler P, 2001, ENVIRON TOXICOL CHEM, V20, P2133	74
344	Foster PMD, 2001, HUM REPROD UPDATE, V7, P231	75
372	Shi LM, 2001, J CHEM INFORM COMPUT SCI, V41, P186	65
461	Rahman F, 2001, SCI TOTAL ENVIR, V275, P1	76
482	Zhou T, 2001, TOXICOL SCI, V61, P76	69
502	Gutendorf B, 2001, TOXICOLOGY, V166, P79	74
514	Ternes TA, 2001, TRAC-TREND ANAL CHEM, V20, P419	94
571	Devlin RH, 2002, AQUACULTURE, V208, P191	163
587	Hovander L, 2002, ARCH ENVIRON CONTAM TOXICOL, V42, P105	67
662	McDonald TA, 2002, CHEMOSPHERE, V46, P745	80
732	Turusov V, 2002, ENVIRON HEALTH PERSPECT, V110, P125	65
758	Silva E, 2002, ENVIRON SCI TECHNOL, V36, P1751	102
964	Hall JM, 2002, MOL ENDOCRINOL, V16, P469	79
992	Hayes TB, 2002, PROC NAT ACAD SCI USA, V99, P5476	202
1054	Andersen HR, 2002, TOXICOL APPL PHARMACOL, V179, P1	104
1239	Hunt PA, 2003, CURR BIOL, V13, P546	64

Metcalfe et al. (2001) represented by Node# 275 (GCS = 124) also concerned the possible exposures to the estrogenic compounds that may be present in wastewater treatment plant effluent which have been linked to high prevalence of female fish in urbanized areas and other abnormalities. In this study however, fish were exposed to known concentrations of known and suspected xenoestrogens and a range of dose and chemical-specific responses were observed. Also in this group is another study which looks more closely at the possible effects of estrogenic compounds on fish. Lange, Hutchinson, Croudace, and Siegmund (2001) (Node# 282; GCS = 113) used a known synthetic estrogen to study effects of various doses on developmental and reproductive outcomes.

Fang et al. (2001) (Node# 180; GCS = 103) used a technique called structure-activity relationships (SARs) to compare the possible estrogenicity of 230 chemicals. The purpose of this study was to aid in the setting guidance for the early identification of endocrine disruptors and to prioritize testing for existing chemicals.

The review by Johnson and Sumpter (2001) was also among the top ranked articles in this time period (Node #270; GCS = 98). In this paper, Johnson and Sumpter called attention to the endocrine disruptors that may be of greatest concern to human and environmental health by comparing the concentrations of xenoestrogens in wastewater treatment plant effluent with their biological potencies. The need for additional research into cost-effective treatment techniques was suggested.

The papers by Huang and Sedlak (2001) (Node# 273; GCS = 96) and Ternes (2001) (Node #514; GCS = 94) were also about the growing concern of the presence of

xenoestrogens in wastewater and how best to assess their presence of xenoestrogens and manage their removal.

The most highly cited paper in this time period was published in 2002 and is shown as Node #992 (GCS = 202). This is a paper by Hayes et al. (2002) and published in *Proceedings of the National Academy of Sciences*. This paper was funded by a National Science Foundation grant and examined the effects of atrazine (noted as the most widely used herbicide) on the sexual development of frogs. Atrazine exposure was shown to cause hermaphroditism, and decreased testosterone as well as other demasculinizing effects. In this study, the authors questioned whether exposure to low levels of atrazine might play a role in the worldwide declines in amphibian populations which were being discussed during this period of time (Hayes et al., 2002).

Devlin and Nagahama (2002) (Node #571; GCS = 163) is a review article which presents an overview of the genetic, physiological, and environmental factors that influence the determination and differentiation of sex in fish.

Andersen, Vinggaard, Rasmussen, Gjermansen, and Bonefeld-Jorgensen (2002) (Node #1054; GCS = 104) tested 24 commonly used pesticides for their interaction with the estrogen receptor and found a range of responses. Some of the pesticides tested were estrogenic and androgenic, others were estrogen or androgen antagonists, or combinations thereof. Various impacts on aromatase activity were also shown.

Silva, Rajapakse, and Kortenkamp (2002) (Node # 758; GCS = 102) studied the effects of exposure to multiple xenoestrogens and concluded that estrogenic agents acting together could produce significant effects when combined at concentrations which they would have exhibited an impact alone. They highlight the limitations of “the traditional

focus on the effects of single agents” which “almost certainly” result in an underestimation of hazard and risk (p. 1751).

## **CHAPTER V**

### **DISCUSSION**

#### **5.1 Introduction**

This study has explored the literature of endocrine disrupting chemical (EDC) science from 1980 to 2004, and has dissected the critical attributes that have likely contributed to its emergence and evolution. This study was predicated on the assumption that the influence of a scientific paper—and thus the proposition put forward by virtue of its publication—would be reflected by its citation frequency—the more highly cited the paper, the greater its influence on the development of the field. Thus, it was hypothesized that the emergence and evolution of the EDC scientific literature was not random, rather the likelihood that a paper would be influential was dependent upon these attributes.

To evaluate the path of EDC science that paralleled the issue's political salience during the period between 1980 and 2004, a dataset of over 3,400 publications was assembled through keyword searches of the SCI databases as described in Chapters III and IV of this dissertation. Bibliographic attributes included journal name, first author, publication year, times cited, nationality, institutional affiliation, and document type were determine for each of these publications and have been reported previously in Chapter IV. From this large dataset, 276 papers were identified as being “highly cited,” a

designation based upon a paper having been cited (times cited)  $\geq 45$ . Because this subset was small and manageable it was possible to read, at minimum, the abstract of each paper to determine its non-bibliographic attributes. Therefore, the influence of non-bibliographic attributes could be determined by citations counts for each paper in the highly cited group. These non-bibliographic attributes included study type, investigative model, and support or negation of the EDC hypothesis.

The remainder of this chapter is organized as follows. The first section discusses how the findings of this study met the expectations expressed in Chapters I and III that bibliographic attributes would influence both citation counts and publication counts in the dataset. Next, the discussion focuses on the findings that address expectations involving the influences of non-bibliographic attributes in the highly-cited group of documents. The final section presents a discussion of the visual exploration of the citation relationships between documents in the dataset as revealed through historiographs.

## **5.2 Influences of Bibliographic Attributes**

### **5.2.1 Journals**

The unit of analysis for this exploratory study was the published document. The individual unit of publication for which there was one author or group of authors, one title, and one article in which the author or authors make a claim and present their findings. The scientific enterprise as we know it has organized the distribution of such claims through journals. In this study, only a handful of journals were influential in the evolution of EDC science and this was not entirely unexpected as the literature has consistently supported the theory that most of what is known in science comes from only a small subset of the scientific literature. Recent citation studies have shown that for

science in general, only about 150 journals account for half of what has been cited and about one fourth of what has been published. This core of scientific journals however is not stagnant, but changes over time so that the journals that make up this central core of about 2,000 journals (85% of all articles published and 95% of all the articles cited) constantly shifts (SCI, 2001). As such, finding that journals differed in their relative importance in the evolution of EDC science had been expected.

Some journals were clearly more significant than others in pushing the field of EDC science forward. The dataset analyzed contained 572 different journals, but almost half of these journals contributed only one article to the total. Of these 572 different journals only 58 contributed ten or more articles. The dataset included over 200 papers from the journal *Environmental Health Perspectives* and more than 100 papers from the journal *Environmental Toxicology & Chemistry*. The influence of these two journals went beyond their contributions to the total number of articles published as together they accounted for nearly 30% of all citations that were made to the literature in the dataset. The three general topic journals covering wide subject areas and representing nearly 20% of all publications about 35% of all citations received were *Environmental Health Perspectives* (EHP), *Environmental Toxicology & Chemistry* (ET&C), and *Environmental Science & Technology* (ES&T).

The journal EHP was the most highly ranked journal in the dataset both by publication and citations counts. EHP published more than twice the papers of any other journal on the general topic of endocrine disruption (233 papers, 7.9%) and the papers it published were cited over three times more than its nearest competitor (GCS = 11,296;

22.3% of all citations). EHP also had the highest average citation count per paper at 48 citations per paper.

The top ranking of EHP in this study was consistent with metrics of influence from other sources. Using a more comprehensive set of factors including a process similar to that of peer-review, the SCI has grouped journals into 22 topic areas. According to these factors, EHP was placed into the “environment/ecology” topic area where it ranked among the top journals in the category based on number of publications and citations received (Essential Science Indicators [ESI], 2004). Between 1993 and 2003, the 3,569 papers published in EHP received an average of 13.21 citations each, for a total of over 47,000 citations. By comparison to other journals within the category of environmental/ecology, EHP ranked fourth in total citations, seventh in number of papers, and fifteenth in citations per paper.<sup>15</sup>

The journal EHP has played an important role in both the emergence and evolution of EDC science and the social scientist Sheldon Krimsky (who has written extensively on social and political aspects of the EDC issue) has referred to EHP as “the journal most sympathetic to the environmental endocrine hypothesis” (Krimsky, 2000, p. 36). Indeed, EHP published the pivotal article by Colborn et al. (1993) and unlike the two other pivotal journals does not have strong ties to industry.

First published in 1972, EHP is a publication of the National Institute of Environmental Health Sciences (NIEHS) (part of the National Institutes of Health [NIH]) whose mission is to provide a forum for dialogue about the interrelationships between the environment and human health. The NIEHS was created in 1969 in response to growing

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<sup>15</sup> Note that according to its own evaluation, EHP ranks “first among 132 environmental sciences journals and first among 90 public, environmental, and occupational health journals” ([www.ehp.org](http://www.ehp.org); accessed 3/13/07; [www.niehs.gov](http://www.niehs.gov); retrieved 3/13/07).



concern about environmental issues and human health, funds research, has its own research facility, and its scientists have published a significant body of work on EDC issues.

*Environmental Toxicology & Chemistry* (ET&C) is an international journal that contains scientific articles about environmental toxicology, chemistry and the application of these sciences to risk assessment. ET&C is the journal of the Society of Environmental Toxicology and Chemistry (SETAC) a global not-for-profit society made up of professionals and institutional entities concerned with assessing, managing, and regulating environmental problems. The stated mission of SETAC is to “support the development of principles and practices for protection, enhancement and management of sustainable environmental quality and ecosystem integrity” (Society of Environmental Toxicology and Chemistry [SETAC], 2007). The organization was founded in 1979 as an interdisciplinary forum for both individuals and institutions concerned with environmental issues and their management. Currently the board and membership of SETAC is a nearly equal mix of representatives from academia, business, and government.

*Environmental Science & Technology* is one of about 50 journals published by the American Chemical Society. ES&T is self-described as “...#1 in total citations and #1 in impact out of 35 journals in the category of engineering/environmental with 39,785 cites ... is also #1 in total citations and ranks #5 in impact factor out of 140 journals in the environmental sciences” (American Chemical Society, 2007).

### 5.2.2 Authors

It was also expected that authors would contribute to the influence of a paper and that this would be visible by both publication and citation counts. In the results reported here overall author influences as well temporal changes in author influence have been demonstrated. Overall, the work published by U.S. first authors were more highly cited than work originating from other countries, although several significant works have originated from outside the United States. Moreover, regardless of the country from which a paper originated, U.S. government funding was found to have at least in part supported nearly all of the work published. Therefore it was not surprising to see that greater than 90% of the highly cited articles were supported by government funding (United States, United Kingdom, or Japan).

There were several indicators that independently validated the credibility of this dataset among which were the bibliometric data available from SCI for scientific literature in the category of “environment/ecology” and the results here were validated by findings elsewhere. In a serendipitous discovery, it was found that the SCI had developed a listing of the most highly influential scientists in the category “environment/ecology” for the period between 1992 and 2002. Shown in Table XIII, ten of these top twenty scientists were also found among the highly-cited authors as determine here. Table XIII compares the average number of citations per paper between the scientists determined by SCI metrics as highly influential and those determined by this study to be highly influential.

Table XIII indicated that the keyword searching conducted for this exploratory study had been successful in uncovering the significant research in the EDC field. The

SCI list of the most highly influential scientists in the category was comprised of individual researchers and therefore the tally for each author was based on an author's total publications not publications on which they are the first author. The numbers shown above are not the same in both columns since the results reported in this dissertation uses a "times cited" value based on the document as the unit of analysis, therefore the scientist only as first author. Regardless, with the exception of Colborn et al. (1993) all of the authors that appear on the SCI list were also found by the keyword searches conducted for this study and thus were included in the dataset examined.<sup>16</sup> As shown in Table III, half of SCI's 20 most-cited scientists in "environment/ecology" were engaged in research related to endocrine disruption or closely related topics during the ten-year period between 1992 and 2002. Moreover, the overlap of highly influential scientists identified by the SCI metrics with this study's highly-cited authors underscored the impact that the emergence of the EDC hypothesis and the concomitant growth in publications was having on science in general.

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<sup>16</sup> The Colborn et al. (1993) paper was a review article and therefore not included in the SCI tally.

**Table XIII. Highly Influential Scientists Compared by Two Measures**

<b>SCI 1992-2002*</b>	<b>SCI 1992-2002* Ave Times Cited / Paper</b>	<b>Study Dataset 1980-2004 Ave Times Cited / Paper</b>
Ana Soto	154.5	118.33
Louis J. Guillette	68.5	53.24
John P. Sumpter	65.03	100.44
Jerry M. Melillo	43.51	43.5
Walter J. Weber, Jr.	32.09	0
Gerald T. Ankley	23.36	43.5
Derek C. G. Muir	18	12.67
Shinsuke Tanabe	17.67	13.5
Kevin C. Jones	13.99	15
John P. Giesy	13.85	37.84

\* Rankings of EDC Scientists among the SCI 20 Most-Cited Scientists in Environment/Ecology List, 1992-2002 (from SCI <http://www.in-cites.com/scientists/env-eco.html>).

### 5.2.3 Document Type

While only a few studies have examined the impact of document type or genre (e.g., review article or research paper) on citation behaviors, those that have saw a disproportionate number of review articles among highly cited papers (Aksnes, 2003) and it was expected that this would also be the case for this exploration of the EDC literature. Because review articles synthesize the existing literature on a topic, they are frequently used as surrogates for an entire body of work published previously on a topic and thus are used far more often than may be appropriate. In certain areas of study there are reviews that become synonymous with the historical framework of an entire field (i.e., Colborn et al., 1993). As previously discussed ample evidence was uncovered in this exploratory study to support this hypothesis.

This study confirmed what has been shown elsewhere that review articles tend to be more highly influential than research articles as measured by their subsequent citation (Aksnes, 2003). While research articles represented 81% of the documents in the entire dataset (1980-2004) and 83% of all citations, they averaged 17% citations per paper—

only half the citations received by review articles. Review articles represented 7% of the documents, 16% of all citations, but more than 37% citations per paper (average citation rate).

The top ten review articles ranked by citation counts ranged from 149 to 1163 times cited. Five were published in EHP (1163, 584, 358, 328, and 163 times cited), three in *Critical Reviews in Toxicology* (299, 233, and 162 times cited), and one each in the *Journal of Steroid Biochemistry and Molecular Biology* (305 times cited) and *Annual Review of Public Health* (149 times cited). By far, the most popular, and significant review article was that by Colborn et al. (1993).

### **5.3 Influence of Non-Bibliographic Attributes**

#### **5.3.1 Study Type**

A comparison of study topics by publication count, citation count, and average times cited (Chapter IV, Figures 2, 3, 4, 5, and 6) revealed that the high citation counts seen for review articles was only a part of the story. After each highly cited document was read and assigned a study topic, a graph was prepared which captured study topic, publications, year of publication, and average times cited. In comparing study topic graphs it became clear that when the data were divided by study type and not merely review articles versus research articles, that study topic had a profound impact on the citation count of an article (see Tables III through VII, Chapter IV).

A distillation of the entire body of highly cited EDC research by study type further supported the claim that EDC science is not a distinct field of science per se, rather one which has been socially constructed. Based upon the results of this study it

certainly appeared that while the average citation counts of the review articles underwent a large decline after 1996, those of the more specific topics did not.

### **5.3.2 Investigative Model**

It had been expected that studies concerned with effects on humans would be among the most highly cited and influential. Therefore, it was surprising to see that studies with direct relevance to humans were not more influential as determined by the number of citations and relative ranking in this list. Even when the citation counts of all the mammalian studies (rat, mouse, in vitro and in vivo, panther, and human epidemiologic) were combined they still did not compare in influence to the review articles.

The hypothesis that documents with direct relevance to human environmental health concerns would be more highly cited than other studies was not specifically validated by the results of this study. While research articles directly pertaining to humans were not among the most influential papers in the dataset, examination of historiographs for individual time periods did reveal that the most highly cited papers were review papers that synthesized the findings of others (from a variety of study types and investigative models) in a manner that made them directly relevant to human health. Even when such studies were highly presumptive in nature, they appeared to take on an importance that went beyond the sum of their parts. For example, the most highly cited studies were those that directly linked exogenous chemicals to decline in human sperm quality or male-specific development defects and testicular or human breast cancer incidence and mortality. Moreover, studies reporting the presence of presumed EDCs in media to which humans might be exposed were highly cited. These reports include

finding EDCs in dental sealants, wastewater treatment plant effluent, and the lining of cans.

This confirms what others have previously suggested, that thus far EDC science has been focused on fetal or neonatal exposures (Colborn, 1994; Krimsky, 2000; NRC, 1999). The most powerful, direct and causative, evidence that is available on the matter comes from studies on the pharmaceutical product diethylstilbestrol (DES) a synthetic estrogen. However, there appear to be other direct and causative data that go unnoticed in the EDC dataset, presumably because the causative agents are “natural” chemicals and not industrial. Studies with these chemicals did not appear to garner much interest despite their positive findings, and the significance of the chemical subject matter to the human and animal food supply.

### **5.3.3 Support or Negation of the EDC Hypothesis**

Understanding the relationship between study outcome (i.e., results) and citation frequency is complicated by the apparent bias that exists in the publication process toward papers reporting positive outcomes. Studies with positive outcomes are more likely to be published than studies with negative results (Callahan et al., 2002; Leimu & Koricheva, 2005). Interestingly, Leimu and Koricheva (2005) demonstrated that this bias against the publication of disconfirming studies tends to change over time and as time progresses, there is a greater chance that studies more critical of new and popular hypotheses will be published. I believe that the results reported here show the limited appeal of “negative” findings, or findings that do not support emerging trends.

The results of this exploration into the EDC literature revealed that when a study was supportive of the EDC hypothesis but involved “natural” estrogen sources and not

industrial it was largely ignored. This was shown in Chapter IV, Figure 5 where three studies found disturbing levels of estrogenicity from the dietary use of soy products, but none gained traction in the subsequent literature.

The visual representations highlighted several characteristics of the dataset that may have been otherwise overlooked. In particular it became apparent that the publications with little or no influence on EDC science may have some shared characteristics. For example the results from Faber and Hughes (1993) which reported that genistein (isoflavonoid found in soy) mimicked the effects of estrogen when administered to rats was not cited in the dataset.

Similarly, a study by Welshons et al. (1987) published in *Breast Cancer Research & Treatment* evaluated the estrogenic and antiestrogenic activity of three plant-derived metabolites found in the urine of women, especially those consuming a vegetarian diet which had been thought to be protective against the proliferation of breast cancer cells. Unexpectedly the researchers found that these compounds acted as weak estrogens and could promote and stimulate the growth of estrogen sensitive breast cancer cells.

Because the literature suggested that there is bias towards the *publication* of studies that confirm existing hypotheses, it was expected that this phenomena would be apparent in citation behavior as well and that articles supporting the EDC hypothesis would have higher publication and citation counts. In what may be the only study of its kind, Leimu and Koricheva (2005) found that the number of citations a paper received was influenced by whether its findings supported or disputed commonly accepted (popular) hypotheses. They suggested that citing behavior functioned as an instrument of social identification and persuasion as well as a linkage to background information. Even



those studies which fit the hypothesis, but do not fit into the idea of only industrial chemicals as culprits do not get the same degree of attention as do other studies.

#### **5.4 Representations of the Science**

An additional objective of this study was to explore the attributes of the EDC literature as they emerged and evolved over time by using visual representations (historiographs). This was accomplished by depicting the direct (citing/cited) relationships between documents within the dataset. The value of these historiographs was the perspective provided by arraying the data in a display that revealed relationships that were not immediately apparent through other means. In particular, it enhanced the ability to view areas of research linked by citation which may indicate common research streams. These visual representations of the citation relationships of the EDC literature are found in Chapter IV, Figures 8 through 14.

The visual explorations clearly depicted that a small number of papers were highly influential and furthermore the source for streams of research that remained fairly consistent over time. Therefore, while some of the initial review articles such as that by Colborn et al. (1993) were very highly cited, and were cited across categories of research (see Figures 2 through 6 in Chapter IV), they did not *specifically* drive new research. Whereas, other highly cited works were *directly* linked to the generation of new research. The importance of Colborn et al. (1993) within the dataset was immediately visible both by its representative node and by the number of links which pointed to it. The impact of this paper in various study topic areas was also visible in Figures 2-5 in Chapter IV.

As described in Chapter IV, a close reading of the papers represented by large nodes revealed five research streams that elicited high citations. The first related to

finding suspect estrogenic compounds that have made their way into wastewater treatment plant effluent to fish habitat and thus potentially to drinking water sources. The second related to the effects in fish from exposure to wastewater treatment plant effluent. The third concerned finding estrogenic compounds in sources, which pose a risk to humans (e.g., cans and dental sealants). The fourth research stream concerned adverse impacts on male reproduction. The fifth research stream concerned the association between breast cancer and endocrine disrupting chemicals.

## **CHAPTER VI**

### **CONCLUSION**

The emergence, growth, and development of the literature of the science of endocrine disrupting chemicals (EDCs) have been explored through citation analyses and historiographic representations. As hypothesized in Chapter II this development was not random. Rather, it would appear that there has been a systematic bias in this literature. This bias was observable in the citation counts between groups of papers with different attributes.

It appears that the initial drive to promote EDC as both a term and an issue came from a single review article (Colborn et al., 1993) and a well-coordinated effort by a group of concerned scientists eager to attract the attention of both the scientific community and the media to what appeared to be a troubling and yet unexplained cluster of problems (Krimsky, 2000). Searches of the Science Citation Index (SCI) databases revealed that the defining terms of the endocrine disruption issue (endocrine disrupt, endocrine disrupting, endocrine disruption, and endocrine disrupting chemical) were nowhere in the literature until 1993. This supports the idea that this term's introduction into the lexicon set off a cascade of social and political events that led globally to new ways of thinking about and regulating toxic chemicals. The introduction of the EDC term

into the political and social lexicon gave the EDC issue a life of its own within those realms, but may ultimately have had little or not relation to what happened in the science.

This study demonstrated that “endocrine disruption” is not, was not, and will likely never be a distinct scientific issue. It is rather multiple issues linked together because they associate potential environmental chemicals to hormonally mediated biological outcomes; however, most biochemical processes are regulated in some way or another by hormones. As previously discussed, the term itself is fraught with bias as it is not only imprecise and imprecise, but presupposes hazard.

This study explored the EDC literature for how various bibliographic and non-bibliographic attributes may have influenced it. Perhaps most significantly, this study revealed, quantified, and visually demonstrated that there were only a handful of publications that garnered substantial influence. These highly cited papers had attributes which made them sufficiently compelling and visible to attract attention and without these attributes they might have been ignored. These few papers appear to have given the EDC issue its “name” in much the same manner as brand identity might be constructed for a new product. Examining the entire literature in retrospect, it was impressive to observe the authority commanded by this rather small body of work. Particularly compelling was the impact of Colborn et al. (1993) which swept a complex group of biochemical aberrations, dozens of critical adverse outcomes, and untold numbers of possible causes, under a single umbrella term.

What is not known is whether the interest given the EDC issue was only the result of a little bit of science having had a persuasive advocate and good marketing campaign. The results here would support critics who have asserted that negative data have been

ignored. The literature would support the reluctance of editors to publish negative studies at the outset of a new issue.

Another area of interest is the recognition that there has been either a reluctance or failure by non-scientists to recognize that this is not a single issue but multiple issues that have become linked by virtue of a common name. The deconstruction of the literature reported here clearly demonstrates that the EDC literature is multidisciplinary and includes a range of journals, topics, and methods. However, it also clearly shows that the most highly cited studies were those that were generally the most likely to be alarming.

As the literature suggested that there was bias towards the *publication* of studies that confirm existing hypotheses, it was expected articles that supported the EDC hypothesis would be more prevalent in the dataset and more highly cited. If there was much scientific debate about the EDC hypothesis it certainly could not be discerned from the highly cited literature in the dataset examined. In the 276 highly cited papers none presented an outright challenge to the idea that there were chemicals in the environment capable of disrupting the endocrine system of wildlife and humans.

Major shifts in thinking appear to result from the confluence of several focusing events such as the publication of an important work, the announcement of a major finding, or a political event. In that way, the development of the climate change issue has several similarities to the EDC issue. It is multidisciplinary, the science will likely never be “certain” enough, the management required for protective policies appears daunting, and the worst case scenarios horrific. While measurements of atmospheric CO<sub>2</sub> have been continuously available since early in the 20th century, the topic did not gain

political traction until the later 1980s and is still viewed by many as uncertain science into the 21st century.

The rise in prominence of the science of climate change in the late 1980s was politically focused by several factors. These include the confluence of the extraordinarily hot summer of 1988, the ability to measure CO<sub>2</sub> in bubbles trapped in ice, the development of powerful computer models that made possible the generation of general circulation models, increased acceptance of the idea that human activity could profoundly impact the environment, increasingly global perspectives to modeling climate change, general notion that extreme weather patterns were increasing, and the publication of data which were alarming to the scientific community. There was, in addition, a shift occurring in the thinking among scientists, regulators, industry, and interest groups that it was smarter, safer, and more economical to prevent serious environmental problems from occurring rather to respond after the fact (Chambers & Brain, 2001).

Chambers and Brain (2001) examined the citation history of climate change science and found sparse use of catch-all terms such “climate change” or “global warming” in titles, abstracts, or keywords prior to 1987. Instead, they found more precise words that communicated specifics about techniques, geologic time periods, or geographic location. However, beginning in 1987 the use of the terms “greenhouse gases” began to increase. In 1988, the terms “global warming,” and “climate change” begin to increase, quadrupling from their use in 1986. The use of “greenhouse gas” increased ten-fold between 1989 and 1991 which not coincidentally was the year in which the Intergovernmental Panel on Climate Change (IPCC) report was released.

The scientists working on the effects of various hormonally active agents worked largely independent of one another until the early 1990s and the event that focused the attention of scientists, regulators, and the public was constructed by a group of concerned scientists who created interdisciplinary working groups and artfully handled the media. As described in Chapters II and IV, Theo Colborn is largely credited for energizing the scientific community around the issue of endocrine disruption. She embarked upon her professional career as a wildlife biologist with the World Wildlife Fund (WWF) as a new PhD (although well into her fifties). Colborn worked on a Great Lakes project in which she collated data from across disciplines and began seeing what she felt were troubling trends that had either been previously overlooked or ignored. She hypothesized that the common link between the dysfunctional reproductive behaviors, tumors, and developmental defects were exposures to endocrine altering environmental chemicals.

Colborn organized workshops that brought together scientists to share their research. These workshops involved those who would typically not have collaborated because they were from different, although related, fields. Together, they looked for common threads. Colborn was responsible for the many such conferences including those at which the groundwork for the precautionary principle was constructed. While Colborn's own research was not been highly cited, her 1993 review article was the most highly cited article in this study. She is quite possibly the most important element in bringing the issue of EDCs to light. She looked across disciplines, communicated with scientists in other fields, oversaw the writing of position statements, and brought attention to the EDC issue.

Colborn wrote a book for a general audience entitled *Our Stolen Future* (Colborn et al., 1996) in which Vice President Albert Gore wrote the foreword for the first edition. In this foreword, Vice President Gore wrote that Colborn had created something akin to a sequel to Carson's (1962) *Silent Spring*. Like Carson's classic work, Colborn painted a disturbing picture of how the impacts of ubiquitous and persistent synthetic chemicals might wreak widespread havoc in living systems, including humans. Most disturbing was the implication that these suspect chemicals disrupt hormonal systems including those that regulate reproduction and development, and that their effects might be seen not only in directly exposed species, but in their offspring as well.

The most impressive, although indirect, achievement of Colborn and the EDC alarm was the enactment of an ambitious program of chemical testing in the U.S. (and the legislative equivalent of the precautionary principle in the European Union that became law in June 2007). The EDC hypothesis led many in Washington to ask questions about the state of our knowledge of the effects of chemicals in general upon health and the environment. Regulators were shocked to learn that because the manufacturers of chemicals were not legally accountable for demonstrating the safety of their products before they enter into commerce, there were scant data available on the 70,000-plus chemicals that were in commerce. Of the 70,000 listed on the Toxics Substances and Control Act (TSCA) inventory, about 3,000 (non-polymeric) are produced in volumes greater than one million pounds per year (High Production Volume or HPV chemicals).<sup>17</sup> In 1998, the U.S. Environmental Protection Agency (EPA) determined that there was a full set of basic toxicological data on only 7% of the 3,000 HPV chemicals and fully 43%

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<sup>17</sup> In the interest of time and cost, polymers were generally excluded from this 3,000 count because it was agreed that they were less likely to be toxic because of their large molecular weight



of these 3,000 chemicals had not been characterized at even the most basic level (i.e., the determination of a lethal dose).

In attempting to remedy this lack of information a consortium of government and industry representatives agreed that six tests were needed to achieve a basic understanding of a chemical's potential impact on human health and the environment: Collectively known as Screening Information Data Sets (SIDS) these efforts (mandated in 1998) are just now getting underway.

Colborn's lobbying on behalf of the EDC issue precipitated the questions that drove the HPV testing program. The nature of the issues raised and the possible consequences of the chemicals of concern were understandable (low sperm count, breast cancer, transgender behavior) and frightening. They were also the impetus for raising awareness of the precautionary principle.

That a relative newcomer should have been the spark for the EDC hypothesis movement fits well with the thinking of scientists who have studied the social structures of scientific fields. Mutschke and Haase (2001) conducted sociocognitive analyses of science specifically looking at innovativeness and position within scientific networks and found that scientists at the periphery were more likely to be involved in transferring new ideas from one field to another. More established researchers that appeared to play a role in building consensus.

Several social scientists have taken an interest in the development of the EDC controversy. After studying the scientific origins of what he terms the "environmental endocrine hypothesis," Krimsky wrote that EDC science represented a significant paradigm shift in the history of toxicology and environmental sciences. Krimsky was

struck by the lack of clarity of the topic as an “epistemic entity” he believed was central to both research and the debate about EDCs in particular. His examination of the scientific literature revealed what he considered to be scant attention toward advancing a “theoretical framework” in which to ground either the existing or future research. He asked specifically

is there a falsifiable theory, a model, a loosely framed generalization, cluster of several independently testable hypotheses, an explanatory framework that guides hypothesis generation but is not itself testable, or the rudiments of a mechanistic explanation for studying” EDCs and their effects? (Krimsky, 2001, p. 132)

Krimsky’s discomfort with the lack of clarity was a concrete example of the disconnect between the scientists who “do” science and the way social scientists have studied it using frameworks that do not quite fit. When the EDC literature is studied from the perspective of its science, it becomes clear that a theory of endocrine disruption will not emerge, because no one is studying endocrine disruption per se. The reality is that although there has been much investigation concerning hormonally active agents, there are very few generalizable principles or consensual interpretations. True, this makes it difficult to determine whether any given study supports, rejects, or is neutral to a general theory. But this lack of theory does not seem to concern the scientists who perhaps more readily appreciate that the EDC issue is a political construct not a scientific construct.

When Krimsky presented his concern about the lack of theory in pursuing the science of endocrine disruption at an EDC conference in 2000, he was met with resounding criticism by the scientists in attendance who argued that the issues illuminated by the endocrine disrupting chemical controversy are not novel. They argued rather, that they are those that are typically subsumed under other disciplines such as toxicology, endocrinology, and other specialized areas in the organization of the scientific enterprise

(Hessler, 2000). Critics of the idea that there should be some encompassing theory of endocrine disruption also argued that because there is not a single outcome that is being investigated, it is unlikely that a single predictive model will ever be developed. Moreover, if a single predictive model were to be developed it would likely address a single chemical species. Some of the scientists who took issue with Krimsky's focus on endocrine disruption argued that what had occurred was not indicative of shifting paradigms, but was a return to less specialized (more integrative) approaches to the study of biological systems (i.e., basic biology as opposed to toxicology or genetics) the progress in which was actually being thwarted by the increased political saliency of the issue. The lack of a theoretical framework, a system which would facilitate linking an observation in nature to a generalizable principle (such as the biochemical expression of a particular gene) does not appear to be an issue for the scientists.

The lack of a clearly articulated framework did not appear to hinder the panel convened to review and assess EDC science for the National Research Council (NRC). They reported that "much of the division among panel members appears to stem from the different views of how we come to know what we know. How we understand the natural world is the province of epistemology. Committee members seemed to differ on some basic epistemological issues, which led to different interpretations and conclusions on the issues of [EDCs] in the environment" (NRC, 1999). The earlier panels convened to assess the state of the science were also not thwarted by lack of agreement on a clear framework from which to proceed. In fact, the earlier panels experienced far less controversy than the NRC panel. The more data that the panel had to review, and the more scientifically

specialized their membership, the more difficult their task became and the more nuanced they made their conclusion (NRC, 1999).

Government agencies agreed early on that further research was needed to confirm the reported findings and to determine the severity of potential trends. They also agreed that causal links to specific chemicals needed to be established where adverse impacts had already been seen. It was also agreed that methods were needed for detecting chemicals that were potentially able to disrupt hormone function. Systems were needed to prioritize or rank the risk of chemicals that were known or suspected to be hormonally active. Finally, actions were needed to limit the release of agents that were suspected or known to disrupt endocrine function into the environment.

In retrospect, the evolution of EDC science parallels the swift response of government agencies to what they perceived as evidence that EDCs posed a threat to human and wildlife populations. Studies in each of these areas of inquiry can be found in the dataset. Each of the agreed upon actions led to the release of research funds which in and of itself might have been enough impetus for a researcher to take up the EDC term. Future studies might examine how many research programs changed their terminology after 1993.

At the conclusion of any study there are always many unanswered questions. Some of these questions were obvious from the undertaking and others became apparent along the way. This study did not look at chemical of concern as an attribute, and so the question arose as the dataset was examined as to whether there was a systematic bias in the literature against certain types of chemicals. For example, adverse impacts associated with phytoestrogens were never discussed as a cause for concern despite what is known

about their growing dietary prevalence. Adverse outcomes were ignored if the molecule was of plant origin (regardless if it is genetically modified or processed) and was not ignored if it was an industrial chemical.

Other methodological questions arose as well. This study would have been richer had I examined the non-bibliographic attributes of the less highly cited articles. Although it is likely that I have not looked at all the literature of EDC science there is no question that I have looked at all the literature that has been influential. The most nagging unanswered questions will come from the future examination of the papers that were never cited and asking “why not.”

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## **APPENDIX**

## APPENDIX A

### ADDENDUM TO CHAPTER IV

#### 4.5.1. The Period from 1980-1995

Keyword searches revealed only thirty-five publications for the 15-year period between 1980 and 1995 therefore the decision was made to group all of these years together. Although as discussed, “endocrine disrupting chemical” as a term did not appear in the literature prior to 1993, the chemicals of concern to scientists and the issue in general were nonetheless under investigation and were being described in a variety of terms prior to that. Table XIV shows the publication counts for each year between 1980 and 1995 for there were hits from the keyword searches. These early years of the EDC literature were dominated by the review article written by Colborn et al. (1993) published in *Environmental Health Perspectives*.

**Table XIV. Publication Count and Citation Scores Listed by Year for 1980-1995**

Publication Year	Publication Count	GCS*
1987	1	76
1992	1	6
1993	3	1573
1994	4	325
1995	26	2224

\*GCS: *Global Citation Score*

Table XV ranks the document types by number of publications and citation scores for the period from 1980-1995. Research articles predominate in the number of papers published however, the three review articles receive nearly half of all the global citations, and twice the number of local citations for the time period in question. Table XVI further demonstrates the impact of the Colborn et al. (1993) review.

**Table XV. Publication Counts & Citation Scores by Document Type for 1980-1995**

Document Type	Publications	GCS*
Article	29	2498
Editorial Material	3	148
Review	3	1558

\*GCS: *Global Citation Score*

\*\*GCS: *Global Citation Score*

**Table XVI. First Authors Ranked by Citation Scores (1980-1995)**

1st Authors Ranked by Global Citation Score	GCS*
COLBORN T, 1993, ENVIRON HEALTH PERSPECT, V101, P378	1176
JOBLING S, 1995, ENVIRON HEALTH PERSPECT, V103, P582	506
BROTONS JA, 1995, ENVIRON HEALTH PERSPECT, V103, P608	362
DAVIS DL, 1993, ENVIRON HEALTH PERSPECT, V101, P372	328
KELCE WR, 1994, TOXICOL APPL PHARMACOL, V126, P276	200
GUILLETTE LJ, 1995, ENVIRON HEALTH PERSPECT, V103, P157	144
FACEMIRE CF, 1995, ENVIRON HEALTH PERSPECT, V103, P79	132
GOLDEY ES, 1995, TOXICOL APPL PHARMACOL, V135, P77	127
COLBORN T, 1995, ENVIRON HEALTH PERSPECT, V103, P135	119
NEWBOLD R, 1995, ENVIRON HEALTH PERSPECT, V103, P83	107

\*\*GCS: *Global Citation Score*

Table XVII lists the countries from which the published papers were received during the period from 1980-1995 and again, the United States dominated the work in this field. Also, because there were so few contributions to the literature during this time period, the Colborn paper influenced the institutional rankings as well (Table XVIII). Colborn's work was performed when she was working for the World Wildlife Fund and as such the WWF is first on the list. Table XIX demonstrates the impact of Colborn's work on the ranking of the journal *Environmental Health Perspectives* (EHP).

**Table XVII. Countries Ranked by Publication and Citation Counts (1980-1995)**

Countries Ranked by Publication Counts			Countries Ranked by Citation Counts		
Country	Number	Percent	Country	GCS*	Percent
USA	25	65.79%	USA	3,136	71.42%
CANADA	3	7.89%	CANADA	506	11.52%
UNKNOWN	3	7.89%	UNKNOWN	432	9.84%
DENMARK	2	5.26%	DENMARK	156	3.55%
SPAIN	2	5.26%	SPAIN	88	2.00%
CHILE	1	2.63%	CHILE	67	1.53%
FINLAND	1	2.63%	FINLAN	6	0.14%
UK	1	2.63%	UK	0	0.00%

**Table XVIII. Institutions Ranked by Publication & Citation Counts (1980-1995)**

Institutions Ranked by Publication Counts			
Institution	Institution Type	Publication Count	Percent
WORLD WILDLIFE FUND	Env.Advocacy	4	5.9%
UNKNOWN	Unknown	3	4.4%
US EPA	Government	3	4.4%
N CAROLINA STATE UNIV	Academic	2	2.9%
TUFTS UNIV	Academic	2	2.9%
UNIV COPENHAGEN	Academic	2	2.9%
UNIV FLORIDA	Academic	2	2.9%
UNIV GRANADA	Academic	2	2.9%
UNIV WISCONSIN	Academic	2	2.9%
AMER HLTH FDN	Non-Profit/Ind. Funded	1	1.5%
CAL ENV PROTECT AGCY	Government	1	1.5%
CORNELL UNIV	Academic	1	1.5%
CUNY	Academic	1	1.5%
DUKE UNIV	Academic	1	1.5%
ENVIRONM CANADA	Government	1	1.5%

Institutions Ranked by Citation Counts			
Institution	Institution Type	Citation Count (GCS)	Percent
WORLD WILDLIFE FUND	Env.Advocacy	1337	15.8%
TUFTS UNIV	Academic	1246	14.7%
UNIV MISSOURI	Academic	1176	13.9%
IMPERIAL CANC RES FUND	Government	506	6.0%
UNIV GRANADA	Academic	432	5.1%
US EPA	Government	391	4.6%
CORNELL UNIV	Academic	328	3.9%
CUNY	Academic	328	3.9%
MED UNIV S CAROLINA	Academic	328	3.9%
UNIV CALIF IRVINE	Academic	328	3.9%
UNIV CALIF SAN FRANCISCO	Academic	328	3.9%
UNIV FLORIDA	Academic	276	3.3%
JOHNS HOPKINS UNIV	Academic	200	2.4%
UNIV N CAROLINA	Academic	200	2.4%
UNIV COPENHAGEN	Academic	156	1.8%

**Table XIX. Journals Ranked by Publication Counts & Citation Scores (1980-1995)**

Journal	PubCount	GCS**	GCS %
ENVIRON HLTH PERSPECTIVES	18	3310	78.73%
TOX & APPLIED PHARM	2	327	7.78%
CLINICAL CHEMISTRY	2	158	3.76%
BREAST CANCER RES & TREATMENT	1	76	1.81%
ENVIRON TOX & CHEM	1	69	1.64%
REPRODUCTIVE TOXICOLOGY	1	69	1.64%
ARCH OF INSECT BIOCHEM & PHYS	1	64	1.52%
COMP BIOCHEM & PHYS C-PHARM TOX & ENDOCR	1	54	1.28%
JOURNAL OF ANIMAL SCIENCE	1	40	0.95%
J OF THE AM COLL OF TOX	1	22	0.52%

\*\* GCS: *Global Citation Score*

#### 4.5.2 The Period from 1995-1998

Table XX depicts the near doubling of EDC science publications that was occurring during the period between 1995 and 1998. The document types being published (Table XXI) are not unlike those seen previously. It was not surprising to see that review articles were being cited at a greater frequency than research articles. The top authors are listed in Table XXII, the top institutions in Table XXIII. In Table XXIV we see for the first time the globalization of research into EDC science and in Table XXV the inclusion of journal Environmental Toxicology and Chemistry into the list of journals.

**Table XX. Publication Counts & Citation Scores Listed by Year for 1995-1998**

Publication Year	Publications	GCS**
1995	32	2,573
1996	50	2,762
1997	118	3,998
1998	215	6,636

\*\* GCS: *Global Citation Score*

**Table XXI. Document Type Ranked by Publication and Citation Score (1995-1998)**

Document Type	Publications	% Pub	GCS**	% GCS
Article	254	60.9	12358	77.15%
Review	33	7.9	3108	19.40%
Editorial Material	40	9.6	518	3.23%
Letter	8	1.9	20	0.12%
News Item	54	12.9	12	0.07%
Meeting Abstract	26	6.2	3	0.02%
Reprint	2	0.5	0	0.00%
Totals	417	99.9	16019	100.00%

**Table XXII. First Authors Ranked by Citation Scores (1995-1998)**

Top Twenty 1st Authors Ranked by Global Citation Score	GCS**
Toppari J, 1996, ENVIRON HEALTH PERSPECT, V104, P741	584
Jobling S, 1995, ENVIRON HEALTH PERSPECT, V103, P582	506
Olea N, 1996, ENVIRON HEALTH PERSPECT, V104, P298	386
Nagel SC, 1997, ENVIRON HEALTH PERSPECT, V105, P70	378
Brotons JA, 1995, ENVIRON HEALTH PERSPECT, V103, P608	362
Kavlock RJ, 1996, ENVIRON HEALTH PERSPECT, V104, P715	358
Sharpe RM, 1995, ENVIRON HEALTH PERSPECT, V103, P1136	261
Shelby MD, 1996, ENVIRON HEALTH PERSPECT, V104, P1296	257
Folmar LC, 1996, ENVIRON HEALTH PERSPECT, V104, P1096	253
Steinmetz R, 1997, ENDOCRINOLOGY, V138, P1780	248

\*GCS: Global Citation Score= # of times the document is cited in all SCI databases

**Table XXIII. Institutions Ranked by Publication and Citation Counts (1995-1998)**

Highly Ranked Institutions by Publication Counts			
Institution	Institution Type	Pub Count	Percent
Brunel Univ	Academic	11	4.9%
Univ Florida	Academic	13	5.8%
US EPA	Government	24	10.6%
Tulane Univ	Academic	6	2.7%
NIEHS	Government	12	5.3%
Univ Granada	Academic	10	4.4%
Univ Missouri	Academic	11	4.9%
Tufts Univ	Academic	5	2.2%
Univ Copenhagen	Academic	4	1.8%
World Wildlife Fund	Interest Group	8	3.5%
Med Res Ctr	Academic	5	2.2%
Procter & Gamble Co	Industry	4	1.8%
Univ Mississippi	Academic	4	1.8%
Michigan State Univ	Academic	7	3.1%

(continued on next page)

**Table XXIII. (continued)**

<b>Highly Ranked Institutions by Citation Counts</b>			
<b>Institution</b>	<b>Institution Type</b>	<b>GCS*</b>	<b>Percent</b>
Brunel Univ	Academic	2357	11.8%
Univ Florida	Academic	1670	8.4%
US EPA	Government	1491	7.5%
Tulane Univ	Academic	1119	5.6%
NIEHS	Government	1031	5.2%
Univ Granada	Academic	1011	5.1%
Univ Missouri	Academic	1000	5.0%
Tufts Univ	Academic	834	4.2%
Univ Copenhagen	Academic	808	4.0%
World Wildlife Fund	Interest Group	701	3.5%
Med Res Ctr	Academic	689	3.4%
Procter & Gamble Co	Industry	629	3.1%
Univ Mississippi	Academic	546	2.7%
Michigan State Univ	Academic	510	2.6%
Indiana Univ	Academic	501	2.5%

**Table XXIV. Countries Ranked by Publications and Citation Counts (1995-1998)**

<b>Countries Ranked by Publication Counts</b>			<b>Countries Ranked by Citation Counts</b>		
<b>Country</b>	<b>Number</b>	<b>%</b>	<b>Country</b>	<b>GCS*</b>	<b>%</b>
USA	203	42.7%	USA	10207	47.6%
Unknown	93	19.6%	UK	4043	18.8%
UK	43	9.1%	Spain	1097	5.1%
Germany	23	4.8%	Canada	972	4.5%
Canada	21	4.4%	France	931	4.3%
Spain	15	3.2%	Denmark	905	4.2%
France	10	2.1%	Finland	817	3.8%
Italy	10	2.1%	Germany	530	2.5%
Netherlands	9	1.9%	Sweden	417	1.9%
Japan	8	1.7%	Netherlands	386	1.8%

**Table XXV. Journals Ranked by Publications and Citation Counts (1995-1998)**

Journal	Pubs	Pubs %
ENVIRONMENTAL HEALTH PERSPECTIVES	69	16.5%
CHEMICAL WEEK	23	5.5%
ENVIRONMENTAL SCIENCE & TECHNOLOGY	19	4.6%
ENVIRONMENTAL TOXICOLOGY & CHEMISTRY	19	4.6%
ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY	17	4.1%
TOXICOLOGY & INDUSTRIAL HEALTH	16	3.8%
CHEMICAL & ENGINEERING NEWS	14	3.4%
EUROPEAN CHEMICAL NEWS	13	3.1%
REGULATORY TOXICOLOGY & PHARMACOLOGY	9	2.2%
TRAC-TRENDS IN ANALYTICAL CHEMISTRY	9	2.2%

Journal	GCS	GCS %
ENVIRONMENTAL HEALTH PERSPECTIVES	6219	38.8%
ENVIRONMENTAL TOXICOLOGY & CHEMISTRY	1274	8.0%
ENVIRONMENTAL SCIENCE & TECHNOLOGY	1012	6.3%
TOXICOLOGY AND INDUSTRIAL HEALTH	712	4.4%
CRITICAL REVIEWS IN TOXICOLOGY	632	3.9%
ENDOCRINOLOGY	492	3.1%
JOURNAL OF STEROID BIOCHEMISTRY & MOLECULAR BIOLOGY	385	2.4%
JOURNAL OF ENDOCRINOLOGY	383	2.4%
REGULATORY TOXICOLOGY & PHARMACOLOGY	274	1.7%
TOXICOLOGY & APPLIED PHARMACOLOGY	227	1.4%

*GCS: Global Citation Score*

*Publication n = 417; Total Citations = 16,019*

#### 4.5.3 The Period from 1998-2000

Between the years 1998 and 2000 there appeared to be a leveling off of the number of documents published yearly as identified by the keyword searches conducted. As shown in Tables XXVI, and XXVII and total of 814 papers were located, of which 630 were research articles and 67 were reviews. The Ankley et al. (1998) paper was the most highly cited within the dataset and the Jobling et al. (1998) paper was the most cited globally (Table XXVIII).

**Table XXVI. Publication Counts & Citation Scores Listed by Year for 1998-2000**

Publication Year	Publications	GCS**
1998	250	7422
1999	251	6490
2000	313	6597

\*\*GCS: Global Citation Score



**Table XXVII. Document Type Ranked by Publication and Citation Score (1998-2000)**

Document Type	Publications	GCS**
Article	630	18171
Review	67	2903
News Item	55	41
Meeting Abstract	47	3
Editorial Material	32	142
Letter	9	17
Reprint	1	0

\*\*GCS: *Global Citation Score*

**Table XXVIII. First Authors Ranked by Citation Scores (1998-2000)**

Top Twenty 1st Authors Ranked by Global Citation Score	GCS**
Jobling S, 1998, ENVIRON SCI TECHNOL, V32, P2498	400
Routledge EJ, 1998, ENVIRON SCI TECHNOL, V32, P1559	335
Gray LE, 1999, TOXICOL IND HEALTH, V15, P94	309
Sonnenschein C, 1998, J STEROID BIOCHEM MOL BIOL, V65, P143	305
Tyler CR, 1998, CRIT REV TOXICOL, V28, P319	299
Vom Saal FS, 1998, TOXICOL IND HEALTH, V14, P239	262
Belfroid AC, 1999, SCI TOTAL ENVIR, V225, P101	211
Larsson DGJ, 1999, AQUAT TOXICOL, V45, P91	211
Sohoni P, 1998, J ENDOCRINOL, V158, P327	208
Matthiessen P, 1998, ENVIRON TOXICOL CHEM, V17, P37	194

\*\*GCS: *Global Citation Score=the number of times the document is cited in all SCI databases*

Once again, the United States contributed the most publications to the dataset with approximately 40% of the publications, but at this point we began seeing a growing influence of Japanese contributions as well as those from the United Kingdom. The U.S. government continued to be the top institution for the number of publications of EDC science (Table XXIX); however, most citations were received by articles from Brunel University. The comparison of publication and citation counts from around the world is found in Table XXX). The journal with the greatest contribution to the dataset continues to be EHP, with Environmental Toxicology and Environmental Health in second place (Table XXXI).

**Table XXIX. Institutions Ranked by Publication and Citation Counts (1998-2000)**

<b>Highly Ranked Institutions by Publication Counts</b>			
<b>Institution</b>	<b>Institution Type</b>	<b>Pubs</b>	<b>Pub %</b>
Unknown	Unknown	83	5.8%
US EPA	Government	48	3.3%
Univ Texas	Academic	23	1.6%
Univ Missouri	Academic	22	1.5%
Brunel Univ	Academic	20	1.4%
Michigan State Univ	Academic	17	1.2%
Univ Florida	Academic	16	1.1%
NIEHS	Government	16	1.1%
Texas A&M Univ	Academic	15	1.0%
Natl Inst Hlth Sci	Government	12	0.8%
Natl Ctr Toxicol Res	Government	11	0.8%
US FDA	Government	11	0.8%
Univ Calif Davis	Academic	10	0.7%
Univ Tokyo	Academic	10	0.7%
Univ Guelph	Academic	9	0.6%

<b>Highly Ranked Institutions by Citation Counts</b>			
<b>Institution</b>	<b>Institution Type</b>	<b>GCS*</b>	<b>GCS %</b>
Brunel Univ	Academic	2149	4.5%
US EPA	Government	1794	3.8%
Michigan State Univ	Academic	850	1.8%
Univ Texas	Academic	841	1.8%
Univ Missouri	Academic	835	1.8%
Univ Florida	Academic	688	1.5%
Ctr Env Fisheries & Aquaculture Science	Government	660	1.4%
Univ Western Ontario	Academic	613	1.3%
Univ Illinois	Academic	613	1.3%
Tufts Univ	Academic	591	1.2%
Texas A&M Univ	Academic	505	1.1%
Tulane Univ	Academic	473	1.0%
Univ Calif Davis	Academic	426	0.9%

**Table XXX. Countries Ranked by Publications and Citation Counts (1998-2000)**

<b>Countries Ranked by Publication Counts</b>			<b>Countries Ranked by Citation Counts</b>		
<b>Country</b>	<b>Number</b>	<b>%</b>	<b>Country</b>	<b>GCS*</b>	<b>GCS %</b>
USA	334	34.6%	USA	9907	36.2%
Japan	116	12.0%	UK	4324	15.8%
UK	105	10.9%	Canada	1775	6.5%
Unknown	83	8.6%	Germany	1744	6.4%
Germany	61	6.3%	Japan	1611	5.9%
Canada	44	4.6%	Netherlands	1413	5.2%
France	30	3.1%	Denmark	1029	3.8%
Italy	26	2.7%	Sweden	1009	3.7%
Netherlands	23	2.4%	Spain	993	3.6%
Spain	22	2.3%	France	784	2.9%

**Table XXXI. Journals Ranked by Publications & Citation Counts (1998-2000)**

Journal	Pubs	Pubs %
ENVIRONMENTAL HEALTH PERSPECTIVES	78	9.3%
ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY	39	4.6%
ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY	27	3.2%
SCIENCE OF THE TOTAL ENVIRONMENT	26	3.1%
TOXICOLOGICAL SCIENCES	26	3.1%
TOXICOLOGY AND INDUSTRIAL HEALTH	23	2.7%
CHEMOSPHERE	21	2.5%
ENVIRONMENTAL SCIENCE & TECHNOLOGY	20	2.4%
CHEMICAL WEEK	18	2.1%
MARINE ENVIRONMENTAL RESEARCH	18	2.1%

Journal	GCS	GCS %
ENVIRONMENTAL HEALTH PERSPECTIVES	3247	15.3%
ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY	1701	8.0%
TOXICOLOGY AND INDUSTRIAL HEALTH	1197	5.6%
ENVIRONMENTAL SCIENCE & TECHNOLOGY	1175	5.5%
SCIENCE OF THE TOTAL ENVIRONMENT	1048	4.9%
AQUATIC TOXICOLOGY	800	3.8%
TOXICOLOGICAL SCIENCES	788	3.7%
CRITICAL REVIEWS IN TOXICOLOGY	665	3.1%
JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY	556	2.6%
CHEMOSPHERE	521	2.4%

*GCS: Global Citation Score*

*Publication n = 841*

*Total Citations = 21277*

#### 4.5.4 The Period from 2000-2004

The publication and citation scores for the period 2000-2004 are shown below in XXXII. The meteoric rise seen at the end of the 1990s was no longer occurring, yet there was nonetheless a small steady increase in the number of documents being published each year. The corresponding GCSs are too few to draw inferences from but the published documents are still clearly having some influence. Again, vast majority of published documents are either articles or reviews, and reviews for this time period are about 10% of all the documents published. The reviews are however cited with greater frequency than are research articles (Table XXXIII). The list of the most highly cited authors in shown in Table XXXIV.

**Table XXXII. Publication Counts & Citation Scores Listed by Year for 2000-2004**

Publication Year	Publications	GCS**
2001	477	8078
2002	559	7167
2003	617	835
2004	198	1492

\*\*  
GCS: Global Citation Score

**Table XXXIII. Document Type Ranked by Publication and Citation Score (2000-2004)**

Document Type	Publications	GCS**
Article	1461	22708
Review	131	3149
Meeting Abstract	72	6
Editorial Material	37	77
News Item	31	36
Letter	12	8
Correction	3	0

\*\*  
GCS: Global Citation Score

**Table XXXIV. First Authors Ranked by Citation Scores (2000-2004)**

First Author, Pub Year, Source	GCS**
Hayes TB, 2002, PROC NAT ACAD SCI USA, V99, P5476	202
Devlin RH, 2002, AQUACULTURE, V208, P191	163
McLachlan JA, 2001, ENDOCRINE REV, V22, P319	144
Parks LG, 2000, TOXICOL SCI, V58, P339	132
Kuch HM, 2001, ENVIRON SCI TECHNOL, V35, P3201	125
Metcalfe CD, 2001, ENVIRON TOXICOL CHEM, V20, P297	124
Lange R, 2001, ENVIRON TOXICOL CHEM, V20, P1216	113
Andersen HR, 2002, TOXICOL APPL PHARMACOL, V179, P1	104
Fang H, 2001, CHEM RES TOXICOL, V14, P280	103
Silva E, 2002, ENVIRON SCI TECHNOL, V36, P1751	102

There are two important observations for this time period. First, is the rising influence of the EDC research program being conduct in Japan (Tables XXXV and XXXVI). The second, and more pertinent to this study, is to note how the number of different publication contributing to the literature has broadened. The journals contributing the most publications to the dataset are EHP, Environmental Toxicology

and Chemistry, Toxicological Sciences, Pure and Applied Chemistry, Aquatic Toxicology, Journal of Chromatography A, and Environmental Science and Technology (Table XXXVII). This is also likely reflected in the topics as well.

**Table XXXV. Institutions Ranked by Publication and Citation Counts (2000-2004)**

<b><u>Highly Ranked Institutions by Publication Counts</u></b>			
<b>Institution</b>	<b>Institution Type</b>	<b>Pubs</b>	<b>Percent</b>
US EPA	Government	73	13.1%
Univ Tokyo	Academic	40	7.2%
NIEHS	Government	36	6.5%
Univ Florida	Academic	32	5.7%
Natl Inst Hlth Sci	Government	29	5.2%
CSIC	Government	28	5.0%
Environm Canada	Government	28	5.0%
Brunel Univ	Academic	24	4.3%
Hokkaido Univ	Academic	24	4.3%
Michigan State Univ	Academic	23	4.1%
US FDA	Government	22	3.9%
Univ Texas	Academic	19	3.4%
Univ Missouri	Academic	19	3.4%
Univ Calif Davis	Academic	19	3.4%
Natl Inst Environm Studies	Government	18	3.2%
Japan Sci & Technol Corp	Industry	16	2.9%
<b><u>Highly Ranked Institutions by Citation Counts</u></b>			
<b>Institution</b>	<b>Institution Type</b>	<b>GCS*</b>	<b>Percent</b>
US EPA	Government	1845	19.0%
Brunel Univ	Academic	822	8.5%
CSIC	Government	725	7.5%
Univ Tokyo	Academic	558	5.7%
NIEHS	Government	528	5.4%
Univ Florida	Academic	493	5.1%
Natl Ctr Toxicol Res	Government	421	4.3%
Michigan State Univ	Academic	415	4.3%
Environm Canada	Government	366	3.8%
Stockholm Univ	Academic	327	3.4%
Tulane Univ	Academic	322	3.3%
Univ Texas	Academic	319	3.3%
Hokkaido Univ	Academic	303	3.1%

**Table XXXVI. Countries Ranked by Publications and Citation Counts (2000-2004)**

<b>Countries Ranked by Publication Counts</b>		<b>Countries Ranked by Citation Counts</b>	
<b>Country</b>	<b>Number</b>	<b>Country</b>	<b>GCS*</b>
USA	571	USA	9819
Japan	381	Japan	4065
UK	169	UK	3319
Germany	154	Germany	2996
Canada	96	Canada	1662
Spain	61	Spain	1390
France	54	Denmark	1164
Italy	54	Netherlands	1136
Denmark	49	Italy	797
Netherlands	45	Sweden	780

**Table XXXVII. Journals Ranked by Publications & Citation Counts (2000-2004)**

<b>Journal</b>	<b>Pubs</b>	<b>% Pubs</b>
ENVIRON HEALTH PERSP	133	5.9%
ENVIRON TOX & CHEM	110	4.9%
TOXICOL SCIENCES	72	3.2%
PURE & APP CHEM	53	2.3%
AQUATIC TOXICOLOGY	48	2.1%
J CHROMATOGRAPHY A	47	2.1%
ENV SCI & TECHN	45	2.0%
REPRO TOX	44	1.9%
TOXICOLOGY	43	1.9%
CHEMOSPHERE	42	1.9%

<b>Journal</b>	<b>GCS</b>	<b>GCS %</b>
ENVIRON HEALTH PERSP	2317	8.9%
ENVIRON TOX & CHEM	2093	8.1%
TOXICOL SCIENCES	1353	5.2%
ENV SCI & TECHN	982	3.8%
J CHROMATOGRAPHY A	789	3.0%
CHEMOSPHERE	665	2.6%
AQUATIC TOXICOLOGY	647	2.5%
TOXI & APPLIED PHARM	539	2.1%
TOXICOLOGY & INDUSTRIAL HEALTH	528	2.0%
REPRO TOX	474	1.8%