MORE THAN FILLING IN THE BLANKS: KNOWLEDGE MANAGEMENT AND THE PHARMACEUTICAL PROTOCOL

THESIS

Presented to the Graduate Council
of Texas State University-San Marcos
in Partial Fulfillment
of the Requirements

for the Degree

Master of ARTS

by

Linda Sue Coker, B.A.

San Marcos, Texas
December 2005

This thesis is dedicated, with much love, to my mother, B. Ellen,

and to Grandma Jo and Grandma Flossie.

ACKNOWLEDGEMENTS

I would like to begin by thanking my entire family and circle of friends, for encouraging me to complete my goals. Special thanks go to my husband, Lenny, and to my sons, Sondy and Trevor, for their continued support. Extra appreciation goes to my father, Ed Anderson, and my step-mother Joyce, for their ongoing inspiration. Many thanks go to my brother, Larry, and his wife Debbie, to my sister, Jo Anne, and her husband Sam, and to my brother, Alan, for listening to me and helping me whenever they could. Special thanks also go to Jody and Beverly for their patience. Very special thanks go to my friends and co-workers for their support and encouragement.

I am especially thankful to the members of my thesis committee. My deep appreciation goes to Dr. Rebecca Jackson, whose assurance buoyed me as I needed it, and to Dr. Miriam Williams, with gratitude and admiration. To my graduate advisor, Dr. Libby Allison, I am forever grateful for her tenacity, patience, and faith, and from whom I learned to understand completely the phrase, "Don't worry about it."

This manuscript was submitted on October 25, 2005.

TABLE OF CONTENTS

LISTING OF TABLE

Page

LIST OF FIGURES

Page

ABSTRACT

MORE THAN FILLING IN THE BLANKS:

KNOWLEDGE MANAGEMENT AND

THE PHARMACEUTICAL PROTOCOL

by

Linda Sue Coker, B.A.

Texas State University-San Marcos

December, 2005

SUPERVISING PROFESSOR: LIBBY ALLISON

The scope of documenting processes and data in the pharmaceutical industry is extensive, but documents called "protocols" help guide information for scientists, reviewers of documents in regulatory agencies, and business people. My thesis explores how pharmaceutical protocols, as technical documents, help "manage knowledge" to further scientific studies and manufacture a product that is both safe and effective for

public use. "Knowledge management" is an abstract idea that has become an essential part of and should become an explicit approach and strategy of contemporary managers. Technical writers, too, should have this approach and strategy. Knowledge management blends perspectives of technology, organizations, and people into discussions about the conversion of tacit (implied) knowledge to explicit (expressed) knowledge, and the types of technology that can control explicit knowledge for competitive gain. Groups, such as managers, subject matter experts (SMEs) and technical writers, who are educated about knowledge management and can understand and practice knowledge management theories, can ensure that pharmaceutical protocols for needed drugs are written as accurately, effectively, and efficiently as possible. Pharmaceutical protocols are far more than documents with blanks that need to be filled in; they help convey some of the information that is needed to get a drug approved by regulatory agencies such as the Food and Drug Administration (FDA.)

The pharmaceutical industry uses protocols extensively, but little research is available on how these protocols manage information. An inquiry into the history of the pharmaceutical protocol and the rhetorical situation of the protocol helps demonstrate the relationship between the data in the protocol and manufacturing, regulatory, and business interests. For confidentiality purposes, I created a composite company called "LC Pharmaceuticals," and used the pseudonyms of "Benjamin Johnson" and "David Williams" for names of two experienced scientists I interviewed to describe activities of gathering data and describing procedures performed by technical writers and SMEs. The pharmaceutical manufacturing protocol is used as a model for discussion.

Several knowledge management theories relate to pharmaceutical protocols. The first is that of "mental models," also known as schema or patterns, which are organizational principles (beliefs) that include "error treatment" (how writers treat each other's errors) and the presence of a "sharing culture" (how they share information.) Creating a successful organizational structure helps produce successful subsequent documents that help technical writers and SMEs collect specific information for the dossier. The second theory of knowledge management is the "seed" document model, a structure initially designed for the preparation of a filing or "dossier" for submission to a regulatory agency, but which can also be used on a smaller-scale framework such as a pharmaceutical protocol. Other theories include discussions about tacit or implied knowledge and explicit or fully expressed knowledge, and conversion of tacit knowledge to explicit knowledge. Another theory is the development of documents as "artifacts" and how the management of tacit knowledge also can be seen as the tacit management of managing knowledge, suggesting that the content of the tasks should include the description of the various tasks and the identification of who owns or is responsible for performing the tasks. A final theory addresses the writing of documents for regulatory requirements. Controlling and managing knowledge in documents created during the drug development process is critical, because the documents communicate information that is scrutinized by government regulatory agencies such as the FDA.

A limited number of examples of protocols are available because of the confidential nature of pharmaceutical research and manufacturing processes. For this reason, studying the conversion of tacit knowledge to explicit knowledge can be cumbersome since examples are rare. Therefore, the composite LC Pharmaceuticals and

my communication with Johnson and Williams further guided my explorations of knowledge management and the pharmaceutical protocol.

The impact of knowledge management theory on the pharmaceutical protocol is affected by the impact of technological innovations, such as "eXtensible Markup Language" (XML) web-based applications, on pharmaceutical protocols. Application of principles of usability research, combined with knowledge management theories, focuses on the user to create a "friendly" interface that helps ensure that the output of the technical writer is executed accurately and efficiently.

Research for this thesis used qualitative methodology to answer several questions. The first question reviews the history and rhetorical situation of the protocol in the pharmaceutical industry, in addition to what happens when the protocol addresses issues other than scientific issues, such as regulatory requirements. The second question asks why the form of the protocol is so important to its users. Another question examines the purpose of the protocol as a requirement other than the documentation of science, addressing the business issues as well. A final question addresses the need for the protocol in the pharmaceutical industry. The qualitative, rather than quantitative, methodology of using a literature survey, creating an ethnographic study with LC Pharmaceuticals as a composite company, and conducting an interview with skilled scientists created the approach needed to use knowledge management theories for analysis of pharmaceutical protocols.

Further inquiry into the relationship of the protocol and knowledge management theory presents several more topics of research. For example, analysis is needed on the relationship of knowledge management theory and the pharmaceutical protocol on an

international and/or global perspective. Additional investigation is needed on regulatory issues and knowledge management theories in pharmaceutical protocols. Also, examination is needed on the political nature of a pharmaceutical protocol and knowledge management theory. Finally, another topic of research is the effect of knowledge management theory on project management in the pharmaceutical industry.

CHAPTER I

INTRODUCTION

The overall scope of documenting processes and data in the pharmaceutical industry is extensive, but specific documents called "protocols" help guide information for a wide variety of audiences such as scientists, reviewers of documents in regulatory agencies, and business people. My thesis explores how the pharmaceutical protocol, as a technical document that contains a detailed plan or record of a scientific or experimental procedure or research ("Protocol" OED, def. 3; Merriam-Webster, def. 3b; Encarta, def. 7), helps "manage knowledge"–"the organization of intellectual resources and information systems within a business environment" (Encarta) – to further scientific studies and manufacture a product that is both safe and effective for public use. Though "knowledge management" is an abstract idea, the management of knowledge has become an essential part of and should become an explicit approach and strategy of contemporary managers (Sanchez 1) and I contend that technical writers should also have this approach and strategy. The broad topic of knowledge management blends perspectives of technology, organizations, and people into discussions about the conversion of tacit or implied knowledge to explicit or expressed knowledge and the types of technology that can control the explicit knowledge "for a competitive gain (e.g., intranets, groupware, and

knowledge repositories)" (Coakes, Willis, and Clarke 1). This thesis examines theories of knowledge management that include tacit and explicit knowledge, concepts of mental models or schema, visualizing documents as guides and artifacts, and addressing regulatory requirements within a framework to help understand how pharmaceutical protocols help manage knowledge.

In the pharmaceutical industry, protocols are technical documents written by technical writers that communicate procedures found in non-clinical and clinical trials, laboratory methods, and manufacturing of product, in addition to the validation of manufacturing, packaging and cleaning processes. Pharmaceutical protocols are far more than documents with blanks that need to be filled in; they help convey some of the information (such as final formulation ingredients, chemistry test methods, and chemistry test results) that is needed to get a drug approved by regulatory agencies like the Food and Drug Administration (FDA). Protocols also describe the scope of the project in terms of tasks, limits of the tasks, and sometimes the amount of money charged for the tasks. In this sense, the pharmaceutical protocol presents information or "knowledge" in a format that manages scientific data for submission to the appropriate regulatory agency. This formatting of the protocol provides a "schema," or mental pattern, that helps the technical writer convert the Subject Matter Expert's (SME's) tacit knowledge into explicit knowledge for users of the protocol in pharmaceutical companies.

In pharmaceutical companies, several distinct groups such as managers, SMEs, (e.g., chemists and engineers), and technical writers can understand and practice knowledge management theories while working with technological tools and innovations. These groups can ensure that pharmaceutical protocols for needed drugs are written as

accurately, effectively, and efficiently as possible. Protocols and reports generated from protocols are a type of "disciplined writing" (Hagge 418 – 19) that are key components of pharmaceutical dossiers, which are vast collections of manufacturing records, laboratory reports, miscellaneous pertinent data, and documents pertaining to the study of the safety and efficacy of a drug ("Dossier," def. 1). For technical writers, managers, and SMEs, this process of protocol creation and development can be cumbersome. However, by managing the knowledge written in a pharmaceutical protocol, technical writers can anticipate that a drug will receive a more rapid review and quicker acceptance by government regulatory agencies such as the FDA in the United States and its counterparts on the global level. I therefore argue that with more education about knowledge management, the managers, SMEs, and technical writers in the pharmaceutical industry can create documentation more effectively and efficiently.

The Protocol in the Pharmaceutical Industry

Although the pharmaceutical industry uses protocols extensively, there has been little research on how these protocols manage information such as scientific data, regulatory guidance, and business issues. An inquiry into the history of the pharmaceutical protocol and the rhetorical situation of the protocol's audience, purpose, and context will help demonstrate the relationship between the data in the protocol and manufacturing, regulatory, and business interests. One way to explore the pharmaceutical protocol is to look at the development and evolution of a specific kind of protocol in the pharmaceutical industry. I will examine the pharmaceutical manufacturing protocol. (See Appendix A for a sample model of a pharmaceutical manufacturing protocol.) Much

information in the pharmaceutical industry is sensitive and confidential in nature. Therefore, for this thesis, I have created a composite company called "LC Pharmaceuticals" and will use the pseudonyms of "Benjamin Johnson" and "David Williams" for names of two experienced scientists I interviewed to support the description of the activities of data-gathering and writing tasks performed by technical writers and SMEs associated with the writing of a protocol for a product called "Marvel Gel 1%" or simply, Marvel Gel. SMEs at LC Pharmaceuticals are people who are involved in the manufacturing process and include scientists, "compounders" and packagers of product, and recordkeepers. Scientists are involved in research and developmental stages of Marvel Gel as well as in production activities. (Some of the production activities include testing product either in the bulk stage or after the bulk product is packaged.) Compounders follow specific instructions to combine carefully measured ingredients in the proper mixing vessel for the predetermined mixing time and speed. Packagers ensure the product is processed into the appropriate containers, such as tubes or bottles. Recordkeepers ensure that the categorization and assembly of the documents generated throughout the manufacturing process are accurate and correspond to the requirements set forth by the protocol. Protocols, like most scientific documents, are organized logically, and instructional texts outline ways to create and format scientific documents and protocols, but they only provide general statements, not specific details for any one kind of document or for any specific company. Protocols can also address business issues (Bonk; Friedman, Furberg, and DeMets; Hamilton; O'Malley; Velanovich; Vickers).

Knowledge Management Theory

Many topics of knowledge management theory support the process of creation, review, and distribution of pharmaceutical protocols (Coakes, Willis, and Clark). However, my thesis focuses on a literature review of knowledge management theories:

- "mental models," also known as schema;
- "seed" documents;
- the conversion of "tacit" knowledge to "explicit" knowledge;
- the development of documents as "artifacts"; and
- writing for regulatory requirements.

These theories help describe how technical writers, scientists, and other SMEs currently gather data and turn tacit knowledge into explicit knowledge for documents so that procedures can be established that will benefit the process of bringing a drug product to market.

Mental Models

Fernanda Menezes Ferrari and José Carlos de Toledo present a model for analyzing knowledge management on an organizational level, using the term "mental model" to describe four structural elements of knowledge management: principles, contents, processes, and infrastructure (Ferrari and de Toledo 117). Principles (beliefs) include "error treatment" (how writers treat each other's errors) and the presence of a "sharing culture" (how they share information). These types of principles address knowledge management in an organizational sense (Ferrari and de Toledo 117-29). Mental models can also considered as "schema" (patterns), creating a successful

organizational structure and subsequent documents. A focus on the principles of error treatment and cooperation demonstrates the value of a culture that nurtures the sharing of information needed for guidance in creating documents such as protocols. Sharing information and learning from errors is essential in creating a systematic process for developing documents that help technical writers and SMEs collect specific information for the dossier.

Seed Documents

Stephen A. Bernhardt and George F. McCulley explore how a "seed" document can help provide "a systematic document development process" that will help drug development teams, which are cross-functional in nature, overcome the challenges of gathering data and communicate scientific knowledge in an organized fashion. They demonstrate how a seed document (Bernhardt and McCulley 22-34) can be a structure for the preparation of a filing or "dossier" for submission to a regulatory agency such as the FDA. The pharmaceutical dossier shapes the knowledge resources for the pharmaceutical company and provides the reasons for why the drug should be approved. Though protocols and their related documents are but one part of the dossier, they are a critical part. A seed document also could be a smaller-scale framework that can help guide the requirements for a shorter document such as a pharmaceutical protocol. Protocols themselves are applications of knowledge management because they form seed documents and help convert tacit knowledge to explicit knowledge. (See Appendix C for a view of Bernhardt and McCulley's "seed" document.)

Tacit Knowledge and Explicit Knowledge

Knowledge management theory also includes a discussion about tacit knowledge, which is knowledge in an organization that is implied, understood or inferred, and explicit knowledge, or knowledge that is not implied and is fully expressed. Richard Herschel, Hamid Nemati, and David Steiger explain how tacit and explicit knowledge can interact productively when the technical writer uses the SOAP (Subjective Objective Assessment Plan) knowledge exchange protocol in a clinical setting. Ricky Laupase discusses rules of guidance for the transfer of tacit knowledge to explicit knowledge. For instance, Scientist A knows how to test the quantity of a chemical in a formula, and the technical writer converts this knowledge to written language that becomes codified in the protocol.

Artifacts

Kristian Kreiner considers how the management of tacit knowledge can also be seen as the "'tacit management' of managing knowledge" (113), suggesting that the content of the tasks should include the description of the various tasks and the identification of who has the ownership of or responsibility for performing the tasks (112). As the technical writer outlines the tasks in the form of a protocol, the protocol becomes an artifact, or tool, that helps convert the tacit knowledge to explicit knowledge. One task of technical writers is to help convert an SME's tacit knowledge about the product to explicit knowledge in the pharmaceutical protocol. Identifying the ownership of the tasks in a document (such as a protocol) adds legitimacy and control to knowledge as an asset to a company (112 – 13).

Writing for Regulatory Requirements

Controlling and managing knowledge in documents created during the drug development process is critical because the documents communicate information that is scrutinized by government regulatory agencies such as the FDA. In Medical Writing in Drug Development: A Practical Guide for Pharmaceutical Research, Robert J. Bonk presents an overview of the drug development process with a focus on the regulatory documents needed for government agency approval and the types of documents needed for marketing and communication. Bonk maintains that most pharmaceutical writing lies in the regulatory documents which are the "building blocks of knowledge (59)." Using Bonk's work, I will attempt to show how regulatory requirements influence the pharmaceutical protocol and become part of the storehouse of knowledge within the industry.

From Template to Signature

The activities and tasks that technical writers write about and SMEs perform are common throughout the pharmaceutical industry. However, a limited number of actual examples of protocols are available because of the confidential nature of pharmaceutical research and manufacturing processes. Studying the conversion of tacit knowledge to explicit knowledge can be cumbersome in this circumstance because examples for the examination of the schema, or sharing of information for protocol development and research, are rare. Therefore, the composite LC Pharmaceuticals and my communication with the two scientists, Benjamin Johnson and David Williams, help guide my explorations of template organization; characteristics of a consistent, readable, and well-

formatted document; gathering of information; protocol review processes; and finalizing the protocol. Screenshots of the model protocol show short sections to illustrate text, formatting and overall protocol design, in addition to an examination of the development and evolution of the document itself. This exploration helps the reader more fully understand the concept of what the pharmaceutical protocol is, what a protocol looks like, and how it helps manage knowledge.

The Future of the Pharmaceutical Protocol

One of the outcomes of the impact of knowledge management theory on the pharmaceutical protocol should be the impact of technological innovations such as web-based applications on pharmaceutical protocols. The print and web formats are dissimilar in some ways, yet they can communicate the same information to the reader. By applying principles of usability research with knowledge management theories, managers and technical writers can focus on the user to create a "friendly" interface that helps ensure that the output of the technical writer is accurate and executed efficiently when meeting deadlines. "E'X'tensible Markup Language" (XML) software applications are one way to help streamline the protocol process to help bring drugs to market more quickly and more cost-effectively.

Methodology for Research Study

For my examination of the relationship between theories of knowledge management and pharmaceutical protocols, my research for this thesis used a qualitative

methodology to answer my questions about the relationship of the scientific information in the protocol to the manufacturing, regulatory, and business communities:

- What is the history and rhetorical situation of the protocol in the pharmaceutical industry? What happens when the protocol attends to other than scientific issues, such as regulatory requirements?
- Why is the form of the protocol so important to its users?
- Should one of the purposes of the protocol be a requirement other than the documentation of science, addressing the business issues as well?
- Why is the protocol necessary to the pharmaceutical industry?

The qualitative, rather than quantitative, methodology of using a literature survey, creating an ethnographic, or cultural, study with LC Pharmaceuticals as a composite company, and conducting an interview with skilled scientists helped me understand the overall framework of the approach I needed in order to use knowledge management theories for my analysis of pharmaceutical protocols. My interview with Benjamin Johnson and David Williams provided valuable background information for the study of the pharmaceutical protocol because of their wide experience in the pharmaceutical industry and their personal familiarity with and influences on the development of protocols at a company such as LC Pharmaceuticals. Developing LC Pharmaceuticals into an ethnographic study using common processes and documents found in typical pharmaceutical companies provided me with a method to keep an academic distance from an actual company while respecting the confidential nature of information in the pharmaceutical industry. The technique of using LC Pharmaceuticals as a general

workplace allows an open discussion of the knowledge management theories presented in this thesis and how they apply to the pharmaceutical protocol.

A survey of numerous writings available on pharmaceutical protocols and theories of knowledge management presents a wide variety of qualitative approaches to knowledge management and its relationship to protocols. Focusing on knowledge management theories found in an organizational and cultural structure rather than the types of theories relating to an information technology structure allows a clearer perspective on the analysis needed to support the arguments stated in this thesis. Interaction of people such as technical writers and SMEs within an organization like LC Pharmaceuticals will affect the management of knowledge and its representation in the protocol. Information on pharmaceutical protocols primarily centers on discussions of clinical trials, with little data from actual examples of how to construct a protocol. As described in Chapter II of this thesis, books and journal articles describe the form of the protocol in general rather than specific terms; therefore, presenting an abbreviated sample of a pharmaceutical protocol in the appendix helps the reader visualize the protocol. Exploring the literature and using a composite company to help describe activities about knowledge management and pharmaceutical protocols, and conducting an interview with individuals who are experts in their positions provided the information needed for the analysis completed for this thesis.

CHAPTER II

THE PROTOCOL IN THE PHARMACEUTICAL INDUSTRY

Although protocols are widespread throughout the industry, there has been little research on how these protocols communicate information such as scientific data, regulatory guidance, and business issues. This chapter explores how the protocol in the pharmaceutical industry, as a technical document, interfaces with the drug industry and helps manage knowledge to enhance scientific studies in order to manufacture a product that is safe and effective for public use. In particular, I will look at the evolution and development of a specific kind of protocol in the pharmaceutical industry, the manufacturing protocol.

In the pharmaceutical industry, the manufacturing protocol, as the name suggests, guides the manufacturing process of a drug. The manufacturing protocol is a systematic study of the manufacturing process used for a drug or drug product. The general structure of a study protocol contains the necessary information that a scientist expects to see in the document, such as the methodology for a test on the active ingredient of a product. The information for the study is a narrative form with a general design and, in the case of a manufacturing protocol, will describe the "operating features" (Meinert and Tonascia 304) of the manufacturing process. Operating features of a pharmaceutical manufacturing

protocol would include the information such as ordering the chemical components and packaging materials, the provision for making the product, and a matrix for samples topull off the line for testing by the chemistry department. This type of protocol lacks "specific details needed for day-to-day execution" (Meinert and Tonascia 304) of the manufacturing process. These details usually are noted in manuals of operation (Meinert and Tonascia 304). This information includes a header with the company's name and logo, the type of activity described by the protocol, document coding for tracking purposes, a date (such as a publication date or an effective date), a table of contents, the objectives of the protocol, study design, and organization (Friedman, Furberg, and DeMets 10-11). Many types of protocols use this basic structure, including the manufacturing protocol. (See Appendix A for a view of an abbreviated sample pharmaceutical manufacturing protocol.)

History and Rhetorical Situation of Purpose and Context

During my interview with Benjamin Johnson and David Williams at LC Pharmaceuticals about protocols, they discussed the general history and the rhetorical situation of the purpose, context, and audience at LC Pharmaceuticals. The purpose and context blend throughout the history of the manufacturing protocol. Johnson explained that the pharmaceutical industry has used protocols for many years to outline the work performed by the users of the protocol, such as batch sampling and chemistry testing. "The purpose of a protocol," he said, "is to set forth a scope of work that needs to be done prospectively so that the party that needs the work done and the party doing the work are on the same 'wavelength' so that they all know what needs to be done." "Initially,"

Johnson said, "LC Pharmaceuticals successfully implemented assay validation protocols[1] to help build business for the company." Then the company designed a general structure for the batch-producing protocols, which eventually integrated all aspects of batch production into one protocol as it is in the current outline format. Johnson further explained that the outline format at LC Pharmaceuticals includes an introduction to the protocol, a description of the research and development phase, chemical needs, packaging needs, testing, and the like. David Williams added that protocols not only tell people what tasks need to be done, but they also set limits to the task so that the client and LC Pharmaceuticals understand the scope of the project and the amount of money that would be spent on production. As time went on and the company gained experience with multiple projects, other sections were added to the protocol, such as reporting and documentation requirements. However, the general workflow described by the protocol remained the same. (For excerpts from my interview with Johnson and Williams, see Appendix B.)

Rhetorical Situation of Audience

Regarding the audience of the protocol, Williams noted that the manufacturing protocol addresses both internal and external clients, thus enabling the company to use resources more efficiently by requiring fewer meetings with key personnel involved in the manufacturing process. Johnson added that the value of a meeting is that the occasional interface between the client and the SMEs allows open discussion and consensus to be reached regarding the details of the project. Then, when the technical writers receive the information, they would ensure that the manufacturing protocol would

contain the outline of the parts of the project required for the manufacturing process. The internal audience of the protocol includes individuals critical to the project, such as research and development personnel, testers, and recordkeepers. In addition to having a client as an external customer, government agencies, and even global committees also are considered an "external customer" of the protocol. Following regulatory guidance is important because the data collected from the protocol must follow the appropriate FDA guidelines and regulations for the drug industry. Some drugs and drug products are in a separate class of drugs called "Scheduled" drugs, which are regulated by other government entities such as the Drug Enforcement Agency (DEA). Therefore, the protocol needs to address the manufacturing and documentation requirements for these agencies as well. The International Conference of Harmonization (ICH) also influences the protocol because it addresses issues such as the number of samples required, their testing, and the storage conditions for the samples. For example, ICH guidelines suggest that storing samples in specialized chambers at 25°C in 60% relative humidity (RH) for thirty-six months, 30°C in 65% RH for twelve months, and 40°C in 75% RH for six months usually will provide a "typical" environment for long term evaluation of a product. Testing "Marvel Gel 1%" at LC Pharmaceuticals at specific test points (e.g., month 12 at 25°C/60% RH) will give valuable information regarding the stability of the product. ICH guidelines are used in the manufacturing protocol at LC Pharmaceuticals because the resulting data can be used for the approval of the drug product in Western Europe and Japan, as well as the United States.

Protocol Form

The form of the protocol is important to its users because it must convey information accurately and succinctly. The display of information in a protocol is plain and straightforward, sharing its form with other types of scientific writing. Many authors of instructional articles that explain the "how-to" of writing a science article show a familiar sequence of sections. Cindy Hamilton offers the "established pattern" (2744) commonly seen in scientific articles written and submitted for publication (2479 – 83):

1. Title and Abstract
2. Introduction
3. Materials and Methods
4. Results
5. Discussion and Conclusion
6. References

Kevin O'Malley demonstrates a clear method of writing a scientific paper, taking the project from the protocol to the actual publication of the article based on the study that the protocol describes. Briefly stated, he cites the need for a title page, list of authors, an introduction, methods, results, discussion, acknowledgements, references, abstract, and conclusion (30-31). The next page shows a checklist for the publication of a scientific paper, as reproduced from O'Malley's article.

Checklist *

1. An abstract of up to 150 words. This should adequately summarise the contents of the paper.
2. Running heads and keywords if necessary[.]
3. The address of the place of work of each author at the time the work was done, together with his or her appointment and qualifications if the journal demands them.
4. Adequate reference to or description of methods.
5. All values given in full with the appropriate units.
6. All members correct and tally with those given in tables and illustrations.
7. References should include:
   (a) the surname and initials of all authors (or of only the first three if there are more than six);
   (b) the title of the articles or chapters;
   (c) the final page numbers of each article;
   (d) the editors of books;
   (e) the publisher of each book;
   (f) the place of publication of books;
   (g) the year of publication of books.
8. Are all references cited in the text listed at the end? Are all references listed at the end mentioned at least once in the text?
9. Signatures of all authors. Have they all contributed substantially?
10. Permission for copyright material or patent photographs.
11. Statement on duplication.
12. Declaration of interest.
13. Spell out all abbreviations at least once in the manuscript.

* Based on a presentation given by Dr[.] S[.] Lock, Editor, The British Medical Journal and reproduced by permission. (32)

M.D. Vickers' publication uses the simple table below to outline the various sections of a protocol for a clinical trial:

Table 1. Sections of a protocol.

Title page
Summary
Introduction*
Objectives
Selection criteria
Personnel
Trial design*
Treatment plan
Observations and assessments*
Handling adverse events*
Statistical design*
Documentation
Consent*
Post-trial medication and follow-up
Financial arrangements

* Likely to be essential in every trial. (49)

The forms for the three protocol outlines are similar. The established pattern described by Hamilton, the checklist noted by O'Malley, and the list of sections presented by Vickers demonstrate the general structure for the information in a clinical trial protocol that is also seen in the manufacturing protocol.

As in scientific articles, some of the information in a protocol is presented in tabular or graphic form. Results of large quantities of data are best handled in tables or graphs, although too many figures can create a cluttered look. Data presented in a table should not be duplicated in a graph because of space limitations in most journals (Hamilton 2481). However, graphs are an effective way to communicate information either in a science article (O'Malley 31) or in a protocol. Clear presentation of data helps

the reader make inferences that lead to better decisions, conclusions, and actions when necessary (Tufte 53).

Knowledge management theory even impacts the form and display of information in the protocol. Specifically, the outline form and logical flow of information in the protocol uses Bernhardt and McCulley's seed document model to capture and categorize the activities required to manufacture and package a pharmaceutical product. The categories in the protocol outline and graphic display create a visual schema or pattern that is predictable to the SMEs and users of the protocol. Technical writers use the contributions of data from the SMEs during the processes of sharing information as the writers finalize the knowledge in protocol form. For example, at LC Pharmaceuticals a list of ingredients in a protocol can result from the client sharing a formula with the SMEs and technical writers. The SMEs – here, chemists – verify the ingredients and the quantity of each ingredient in the formula and give the confirmed formula to the technical writer. Then the writer puts the list of ingredients in tabular form in the appropriate section of the protocol where, for instance, the purchasing department can use the list to order the ingredients, and where the ingredient list is used for verification of data in other documents included in the dossier. Thus, the technical writer uses the form of the protocol to manage knowledge by categorizing and sharing information needed by the protocol's users.

Protocol Use in the Pharmaceutical Industry

Protocols benefit the pharmaceutical industry because they assist the users by communicating results from clinical trial studies and descriptions of manufacturing

processes of product to regulatory agencies such as the FDA (Friedman, Furberg, and DeMets 10). Since the form of the pharmaceutical protocol is similar to other forms of scientific and medical writing, scientists and manufacturers who use them usually feel comfortable with the creation and execution process of the protocol. The logical arrangement of the sections of information allows the data to be collected in an organized manner using specific criteria. Vic Velanovich takes the form of the scientific article and applies it to the medical article, stating that the logic developed in the medical article is critical to its validity as a scientific proof. He notes that the

> medical research article is the primary instrument of reporting theories, hypotheses, and evidence for this purpose. Toward this end, the function of the medical research article is threefold: the presentation of a new hypothesis, which in some ways changes the present theory and in that sense competes with the established hypothesis; the presentation of data related to the new hypothesis, and the presentation of an argument to discriminate between competing hypotheses - or supplying a value for some natural constant (e.g., survival rate) whose existence is guaranteed but whose value is left unspecified by the hypothesis/theory. (259-60)

He concludes that faults in the logic of the argument depend on "the truth of the premises (or rather, the level of probability) (264)" and how well the conclusions follow from the premises. Similarly, a manufacturing protocol uses a standard form of introduction and structured sections. The logical ordering of sections provides a format that can help prevent possible errors because the methodology presented in the protocol is discussed

with multiple personnel experienced at their jobs before the tasks are set forth in the protocol.

Addressing Business Issues

Business issues between LC Pharmaceuticals and the client usually are addressed in financial agreements outside the pharmaceutical protocols. However, because the protocol is a flexible document that reflects various aspects of a project, financial arrangements can be included in the protocol as necessary (Vickers 49). Budgeted items such as services, materials, and costs can be a segregated section of the protocol, just as the introduction and results are separate sections (Meinert and Tonascia 217 – 31). Even if a protocol does not describe business issues or financial arrangements, the expectation would be to keep costs of the development of a drug within a reasonable budget. Thus, the protocol can serve many purposes within the pharmaceutical industry.

CHAPTER III

KNOWLEDGE MANAGEMENT THEORY

Knowledge management is a broad subject that includes technology and organizational theory (Coakes). Knowledge management theories, such as "mental models" or schema, using a "seed" document," tacit and explicit knowledge, the conversion of tacit knowledge to explicit knowledge, documents as artifacts, and the influence of regulatory requirements describe the creation, review, and distribution of the pharmaceutical manufacturing protocol. These theories are important because they convincingly describe how technical writers and SMEs should gather scientific data that help bring a product to market. Knowledge management theories also help the reader understand the rhetorical situation of a pharmaceutical protocol and the value of the outline form of the protocol. A literature review on the influence of these theories of knowledge management on the pharmaceutical industry will provide the background for this chapter. Although a library exploration and an online search of literature will show limited information solely about pharmaceutical manufacturing protocols, the theories used for other types of protocols, such as clinical trial protocols, can apply to the manufacturing protocol as well. LC Pharmaceuticals, along with Benjamin Johnson and David Williams, will provide a framework for discussion of the pharmaceutical manufacturing protocol.

Knowledge management theories should systematically and methodically, rather than reactively, influence the creation, review, and distribution of the pharmaceutical manufacturing protocol. According to Ferrari and de Toledo, "organizations need to look for more structured approaches to knowledge management, in a way to make its members aware of the importance of organizing resources in order to obtain the value of knowledge" (117). The pharmaceutical protocol at LC Pharmaceuticals, originally created by scientists such as Johnson and Williams, provides the kind of structure for documents that LC Pharmaceuticals needs to produce a high quality finished product for its clients. The template for writing the protocol, which combines technology with formatted instructions, helps guide the technical writer in gathering information for the project. In addition, the protocol template provides a logical sequence and orderly arrangement of tasks for the formulators, compounders, packagers, testers, and recordkeepers, who use the protocol to guide their work. The protocol template is a guiding document, similar to the seed document that Bernhardt and McCulley describe, in that it helps the technical writer accurately state the requirements for the project which could include such things as the ingredients used in a formula, types of packaging, and testing criteria. The technical writers set up the template using a generalized style guide previously agreed upon by the technical writers. Technical writers interface with the management staff, constantly providing input to the contents of the protocol template to ensure accuracy of the information in the final protocol (Bonk; Herschel et al.; Kreiner; Laupase).

"Mental Models" or Schema

Ferrari and de Toledo propose a model that uses four elements that work together to create a successful organizational structure of knowledge management: principles, contents, processes, and infrastructure. The first element of "principles" contains the beliefs (not the practices) of the organization. One of the beliefs is the "mental model" that includes error treatment and a sharing culture in an open climate. These mental models can show how the technical writers need to balance the technical and regulatory requirements suggested by the template with the requirements of the project and the client. For example, the SMEs would need to share information with the technical writer early in the management of a project with a product classified as a "scheduled"[2] drug by the Drug Enforcement Agency (DEA). The technical writer would need to ensure the information is stated properly in the protocol in the event of an inspection by the DEA of the documents generated by protocol.

As Ferrari and de Toledo note, the open climate fosters the "liberty and . . . good use of the organization member's creativity, whether limiting or reinforcing the knowledge creation" (118). Ferrari and de Toledo refer to Leonard-Barton on the manner in which the mental model of error treatment is related to the knowledge creation as "attempt and error." If the error made by, for instance, a technical writer, is treated as "something abhorrent," then the "creation form may be penalized" (118). Thus, the best atmosphere for a technical writer to become creative and effective is an atmosphere in which the pharmaceutical protocol is treated as a way of sharing information to work out problems rather than as a treatise that must be perfect immediately and forever. Sharing knowledge is important to the technical writers, who should participate in a "sharing

culture." Cooperation among the writers with the SMEs is encouraged (qtd. in Beijerse 1999) and demonstrates how the idea of "Who exchanges the knowledge has the power" replaces "Who holds the knowledge has the power" (118). The protocol becomes a way of sharing knowledge and providing guidance to all, even those who perform the more rudimentary tasks in the manufacturing process. These mental models represent an important discipline of knowledge management that relates the protocol template to the development of the project (118). This management of knowledge leads to efficiency in assembling knowledge from individuals throughout the company and in sharing it with those who will benefit.

The "Seed" Document

Assembling and sharing large amounts of knowledge with others in an organization can become difficult to manage. In "Knowledge Management and Pharmaceutical Development Teams: Using Writing to Guide Science," Bernhardt and McCulley describe one particular problem in pharmaceutical companies:

> Within a cross-functional development team, data, information, and strategic knowledge are widely dispersed across individuals from different functions within the organization. A major challenge (to pharmaceutical companies) is finding ways for teams to work together to consolidate what they know and to present it consistently across a set of documents. (22)

They suggest a "seed" document that "enables teams of drug developers to use writing as a constructive activity throughout the drug development process" and go on to describe how the seed document helps "capture all the issues associated with a project" (24). A

seed document can help categorize the information from a sharing culture and, therefore, help manage its knowledge. Using the notion of "seed document," the protocol template also can be a seed document that gathers data and information together as a single source of information to describe a manufacturing process. Each section of the protocol contains information about a project from the inception of the project in the research and development phase to the publication of data and analysis in the completed documentation.

Just as Bernhardt and McCulley's seed document is a structured document that gathers information to sort out the issues of product development, the manufacturing protocol acts as a seed document to gather the information needed to state the process development of a product. Bernhardt and McCulley's seed document is issue-focused so that teams can concentrate their energies on the most difficult development challenges; whereas, the protocol template at LC Pharmaceuticals is process-focused so that the technical writer, the SMEs, and the client can concentrate on the process used to manufacture the product successfully. The seed document described by Bernhardt and McCulley contains columns or sections that represent areas of exploration for the client to identify, such as issues, responses, rationales, and support. This type of seed document differs from the protocol as a seed document in that the protocol does not interpret or articulate science as data patterns become clearer. Nor does (or should) the protocol explore conflicts in how the members define the key issues and how to address those issues, as does the seed document created by Bernhardt and McCulley (24). Many of the ideas found in either type of seed document use tacit and/or explicit knowledge to convey

knowledge to members of the team. Thus, Bernhardt and McCulley's seed document could be used as a basis for a protocol.

Tacit and Explicit Knowledge

Tacit and explicit knowledge theories describe two types of knowledge found in the pharmaceutical protocol. These two theories are important to this thesis because they explain the types of knowledge that SMEs and technical writers exchange with each other. In "Tacit to Explicit Knowledge Conversion: Knowledge Exchange Protocols," Herschel, Nemati, and Steiger portray tacit knowledge and explicit knowledge as interactions that should work together; however, "usually one is managed at the expense of the other (Earl and Scott, 1998; Hansen et al., 1999)" (107). These authors go on to state, "while emphasizing one strategy over another may alleviate several operational knowledge management issues, it can also compromise knowledge creation activities. Indeed, to ignore the interaction of explicit and tacit knowledge is to potentially inhibit innovation *vis-a`-vis* the generation of new capabilities, products, and services (Choo, 1998; Nonaka and Takeuchi, 1995)" (107).

Herschel, et al., suggest, "structuring mechanisms might be useful in improving the tacit to explicit knowledge conversion process" (107) and recommend "examining the potential for knowledge exchange protocols to make this activity more productive" (107). They describe a "knowledge exchange protocol (as) a process that structures information exchange in such a way that the provider of the information and/or the recipient of the information can systematically present/recall information in a focused manner" (107). These authors describe the "SOAP" (Subjective, Objective, Assessment, Plan) protocol as

an example of a knowledge exchange protocol that relates the tacit knowledge of a clinician to the SOAP protocol, which "allows clinicians to accumulate knowledge about their patients over time." By structuring the documentation of the patient-clinician dialogue and the clinician's thinking and actions, tacit knowledge becomes external or explicit and can be shared with another clinician. Herschel, et al., describe how the SOAP protocol "provides a consistent framework" (107) for the following:

- structuring clinician-patient narratives;
- understanding the clinician's thinking about perceived problems and issues;
- learning about techniques and tests employed by the clinician in the knowledge creation process; and
- sharing the clinician's reasons for actions taken to address patient issues.

In other words, the SOAP process provides a consistent mechanism for documenting:

- what the physician understands about the patient's situation (sense making activities);
- how the physician closes gaps in his/her understanding about the patient's situation (knowledge creation); and
- what actions the physician takes relative to treatments (decision making). (107-8)

In the same way that these authors describe the SOAP protocol in the medical community as an example of a knowledge exchange protocol, the pharmaceutical

protocol also should be considered a type of knowledge exchange protocol. Using the bullets above in the description of the framework and mechanism of the SOAP protocol and replacing SME/client terms for the clinician/patient terms, the pharmaceutical protocol also provides a consistent framework for:

- structuring the narrative between the SMEs and the client;
- understanding the SMEs' thinking about the process;
- describing the learning about techniques and tests employed by the SMEs in the knowledge creation process; and
- sharing the SMEs' and the client's reasons for actions taken to address production issues.

In a manner similar to the SOAP process, the pharmaceutical protocol provides a consistent mechanism for documenting:

- what the SMEs understand about the client's situation (sense-making activities);
- how the SMEs close gaps in their understanding about the client's situation (knowledge creation); and
- what actions the SMEs and the client take relative to the manufacturing process (decision making).

The table on the following page adapts Table 1 of the article to outline the SOAP process and compare the activities of the knowledge exchange protocol to the pharmaceutical protocol:

"SOAP"	Herschel, Nemati, Steiger Knowledge exchange protocol	Pharmaceutical protocol
Subjective (a brief narrative of the patient's expressed complaints)	Structuring clinician-patient narratives	Structuring the narrative between the SMEs and the client
Objective (a description of the specific activities used to better learn the true nature of the patient's situation)	Understanding the clinician's thinking about perceived problems and issues	Understanding the SMEs' thinking about the process
Assessment (a description of the specific activities used to better learn the true nature of the patient's situation)	Learning about techniques and tests employed by the clinician in the knowledge creation process	Describing the learning about techniques and tests employed by the SMEs in the knowledge creation process
Plan (a prescribed course of action for the patient to alleviate the problem(s)	Sharing the clinician's reasons for actions taken to address patient issues	Sharing the SMEs' and the client's reasons for actions taken to address production issues
Understanding the situation	What the physician understands about the patient's situation (sense making activities)	What the SMEs understand about the client's project (sense-making activities)
Closing the gap	How the physician closes gaps in his/her understanding about the patient's situation (knowledge creation)	How the SMEs close gaps in their understanding about the client's project (knowledge creation)
Taking action	What actions the physician takes relative to treatments (decision making)	What actions the SMEs and the client take relative to the manufacturing process (decision making)

Table 3 – a Outline of SOAP process comparing the knowledge exchange protocol to the pharmaceutical protocol

In the context of the pharmaceutical protocol, the tacit knowledge shared between the SMEs and the client results from experience in the industry, becoming explicit knowledge upon discussion and documentation. The structured narrative in the protocol displays an outline format used to present each section of the protocol. Each general section represents a department with responsibilities to perform the tasks presented in the protocol. Then, within each general section are subsections describing the various departments with more focused and detailed tasks. For example, the general section of Chemistry could have subsections describing the testing of raw material components, preliminary testing of bulk (unpackaged) product, testing of packaged product, and testing of the stability of the packaged product after it has remained in storage conditions controlled for temperature and humidity for a specific length of time. The outline structure expresses the thought processes regarding the tasks of the project so that both the SMEs and the client understand and agree to accomplish the specific tasks. In exchanging knowledge about the tasks for the protocol, usually both the SMEs and the client have a tacit understanding of the overall scope of the tasks required for the project. However, occasionally, the SMEs and client may misunderstand specific topics of the project. When this happens, knowledge sharing between the SMEs and the client can help clarify the topics. Then, the SMEs share the information with the technical writer, who documents the topics in the protocol. Thus, the manufacturing protocol provides the framework that converts the tacit knowledge shared between the SMEs and the client into explicit knowledge in the visible documentation of the protocol and its related tasks.

Illustration of the route of the protocol at LC Pharmaceuticals starts with the sharing of fundamental information needed for the manufacturing of a product. The

SMEs share with the technical writer the information, such as ingredients, size of the batch, and type of package. The technical writer then writes the information into the framework of the protocol and returns the protocol to the SMEs for review. Then the technical writer incorporates the review comments from the SMEs into the protocol and submits a final copy for approval. Eventually, the developer of the dossier for the product includes the protocol and the documents generated from the activities outlined by the protocol for submission to the FDA.

Guidelines for Converting Tacit Knowledge to Explicit Knowledge

In the creation of a pharmaceutical manufacturing protocol, the transfer of tacit knowledge to explicit knowledge needs to be guided to help improve the transfer process between the SMEs of LC Pharmaceuticals and the client. Conducting research at three management consulting firms in Australia, Ricky Laupase conducted "semi-structured" interviews, collecting data based on five propositions:

1. Formal meetings encourage consultants to share tacit knowledge with others through a socialization process.
2. In externalizing tacit knowledge, metaphors, narratives, and analogies are important, as they assist individuals to articulate tacit knowledge.
3. Hybrid organizational structure can support knowledge conversion processes.
4. Reward systems, as part of a supportive organizational culture, will encourage knowledge conversion activities.

5. Information technologies will not support, facilitate, and enable knowledge conversion processes (217).

Laupase then proposes six guidelines based on the outcome of his research. These guidelines are beneficial when consultants use them to convert "'valuable' tacit knowledge to organisational explicit knowledge" (223):

- Handle meetings informally, rather than formally, since an "informal atmosphere relaxes the tension of formal relationships" and creates an open forum for people to ask questions needed to understand the project.
- Use metaphor, analogy, and narrative to express tacit knowledge. Learning to express tacit knowledge may require training and mentoring.
- Associate the expression of tacit knowledge with a reward system exchanged for time and energy spent on the process.
- Use "loose" and/or "network" organizational structures. When a project comes in, a "loose" organizational structure can become a hierarchical structure and when the project is complete, the structure can become loose again. Share knowledge equally with colleagues in the "network" structure.
- Encourage tacit-to-explicit knowledge conversion by including a reward system in an annual or semi-annual review.
- Use technology to express and store tacit knowledge, such as email (e.g., Microsoft Outlook®) and groupware applications (e.g., Microsoft Access®, Lotus Notes®). Provide a usable method of knowledge expression and keep a database of instructions for future review (223).

These guidelines, created by Laupase to help consultants, also help manage the knowledge that technical writers use to write a manufacturing protocol. Consultants and technical writers can employ many aspects of the above guidelines in similar ways. For example, developing a product such as Marvel Gel at LC Pharmaceuticals involves formal and informal meetings, expression of tacit knowledge, and sharing of explicit knowledge within a flexible organizational structure that uses technology to help communicate knowledge.

Like consultants, technical writers use informal meetings to share information and ask questions about projects and ways to execute the projects. Technical writers and consultants both can draw on metaphor, analogy, and narrative as they express tacit knowledge, such as describing the smell of an ingredient as "similar to menthol" or the shade of blue of a tube as "sky blue." Because of their writing skills, technical writers may be more skillful than consultants at expressing tacit knowledge in a document. Consultants and technical writers both can use "loose" and "network" organizational structures at their workplaces. A project that is introduced to a consultant or a technical writer can be subjected to several layers of organization throughout its stages of approval and development, experiencing an accountability or "tightening" while working within the hierarchy. When the project is complete, there is less accountability and the hierarchy loosens. In the case of a manufacturing protocol at LC Pharmaceuticals, the project manager introduces the project to the SMEs and the technical writer, who then interface with all the departments or hierarchy of the company that will help bring the project to completion or "handed-off" to the commercial production department. This hierarchy includes the finance department, the research and development department, the testing

departments and the ordering and recordkeeping departments. All of these departments are involved in the approval and development of the product as it moves through the first stages of the manufacturing process. When the product is ready for commercial production, the project is transferred to another department that handles day-to-day commercial production activities. At the point of hand-off, the SMEs and the technical writer can relax and network with each other, sharing knowledge about the successes of the project and what processes and communications needed improvement. Since technology is an asset for both consultants and technical writers, "high tech" methods, materials, and devices such as computer hardware and software applications, along with low tech uses of items such as binders with printed materials, provide the means to organize and store information for future review by consultants and technical writers, and for instruction to people unfamiliar with the project. Eventually, as Laupase notes, consultants, as well as SMEs, and technical writers appreciate rewards for efforts spent on a project and a job well done, and should receive these rewards when promised or on a regular basis with a review system (223). Laupase observes, too, that the need for these guidelines shows an organization can value both tacit and explicit knowledge, yet not be adept at converting tacit knowledge into explicit knowledge (223). This type of knowledge transfer is one of the tasks of technical writing, especially considering the influence of regulatory requirements on the manufacturing protocol. Explicit knowledge expressed in a protocol can mean the difference between approval from or denial by a regulatory agency. The main goal is to get the product to market, and the writer's task is vital to that goal.

The Protocol as an Artifact

The manufacturing protocol at LC Pharmaceuticals attempts to manage knowledge by transferring knowledge from a tacit phase to an explicit phase. In "Tacit Knowledge Management: The Role of Artifacts," Kristian Kreiner notes how the management of tacit knowledge also can be seen as the tacit management of knowledge (112). In other words, the tacit, or unexpressed, knowledge becomes explicit as the technical writer interprets tacit knowledge and codifies the knowledge in the protocol document. The outline form of the protocol with its directive and (usually) brief text is easily readable and quickly understood by both the users of the protocol and the client. According to Kreiner, content of the tasks include the description of the various tasks that need to be completed and the identification of who has the ownership of or responsibility for performing the tasks (112). Not only do the different sections of the protocol describe the various departments of LC Pharmaceuticals, but they also describe the ownership of the tasks. An important aspect of the content of the text in the protocol is the tacit knowledge outside the visible description of the tasks in the protocol – the tasks needed and how the writer describes the tasks in the protocol. If the protocol inadvertently omits a required task, then the dossier will be incomplete because of the missing data failing to become explicit knowledge. This would be an example of the tacit management of knowledge.

Most SMEs would agree that tacit knowledge in the context of a pharmaceutical project should convert to explicit knowledge in order to document the processes, specifications, and test results for the client, who will likely include the documents in the dossier required by the FDA before a product can be marketed. However, if restrictive

language is included in the protocol, then the protocol ends up binding contributors to the project, such as the chemists who formulate the product, the technicians who weigh the raw materials, and the chemists who test the compounded product. The finished product (for example, packaged bulk product such as Marvel Gel filled into a tube) is an "artifact," because the artifact results from input to a document created by the technical writer using input from the SMEs and the client, in this case to describe the manufacturing process used for a product. Using Kreiner's model, the term "artifact" can also apply to the manufacturing protocol document itself, which is written by the technical writer with input from the SMEs and the client, describing the process used to manufacture a product. Tacit knowledge about a project gives value to the resulting product; therefore, transforming the tacit knowledge of the SMEs to explicit knowledge usable by the company to manufacture the product is an important goal of the company's management (122), and is an example of tacit knowledge management. One of the technical writer's tasks is to convert tacit knowledge about the product to explicit knowledge in the manufacturing protocol. Kreiner suggests that the document (such as a protocol) can identify the ownership of the tasks, which adds legitimacy and control to knowledge as an asset to a company (112 – 13).

Writing to Include Regulatory Requirements

The type of writing style that a technical writer directs toward regulatory requirements reflects the conversion of tacit knowledge to explicit knowledge and tacit knowledge management. Scientific writing, such as medical writing, can demand considerable skill in knowledge management by the technical writer, requiring significant

input from scientists and/or healthcare workers, and utilizing a specific kind of writing that must communicate details clearly and succinctly. For instance, Bonk demonstrates how medical writing, especially in the pharmaceutical industry, includes writing documents for submission to regulatory agencies. Although he addresses the clinical trial type of protocol, some of the principles compare to the pharmaceutical manufacturing protocol. For example, Bonk states that the clinical trial protocol "provides the basis, in terms of objectives and methods, for a clinical trial" (11). Similarly, the manufacturing protocol at LC Pharmaceuticals provides the basis for the process used in manufacturing a product. Bonk describes how the clinical trial protocol contains the major points of

- Clearly defined objectives
- Criteria for inclusion and exclusion
- Drug dose and regimen
- Clinical versus pharmacological end points
- Definitions of success and failure
- Statistical design and analysis (11 – 12)

This essential information in a clinical trial protocol, which will vary from trial to trial, permits the investigator of a clinical trial to study the drug's reaction in humans scientifically yet safely (12)[3]. Similarly, the manufacturing protocol begins with objectives and goes on to outline the manufacturing methods, with a section for each department. Both types of protocols arrange methodology to demonstrate the science used for the project. Just as the clinical trial protocol shows the methodology of evaluating a drug's reactions in humans, the manufacturing protocol shows the methodology used in manufacturing the product that uses the drug. For the manufacturing

protocol, the technical writer gathers the data from the SMEs and transfers the data as knowledge into the format used for the protocol. Neither type of protocol addresses all of the regulatory requirements, but the data resulting from each type of protocol will become part of the body of documentation used for submission to the FDA. Some of the regulatory requirements for documentation from the manufacturing protocol could be copies of batch records, test methods, and test results from the manufacturing process. These documents (but not necessarily the protocol itself) are part of one of the sections of a regulatory submission, for example, Section 3 of the New Drug Application (NDA) (42-44). These documents are highly confidential and should be handled with discretion. The protection of one's intellectual property is of utmost importance in today's world market.

Bonk uses the example of a medical writer to outline the responsibilities that the writer has toward the documents needed for a drug submission. For the manufacturing protocol, the technical writer is responsible for the visible portion of the protocol, and therefore can be a prominent player on the project team. To help keep the project on schedule, the technical writer must effectively interact with all project members and contributors. Most importantly, the technical writer must maintain a high level of quality in the distributed documents, because a "timely, but unusable document does not contribute to an effective regulatory submission" (46). Therefore, the writer must have rhetorical skills that can produce a document that is consistent, readable, and formatted well. As the person who delineates the tasks needed from the initiation of the project to the completion of the process, the technical writer becomes a key player in the process of guiding a product to market. All tasks depend on the writer's ability to describe and

explain the specific tasks for others to follow. Outlining tasks in a protocol starts with a pattern that guides tacit and explicit knowledge from project inception to the final copy.

CHAPTER IV

FROM TEMPLATE TO SIGNATURE

Understanding knowledge management theories and the role of the protocol in communicating scientific information in the pharmaceutical industry helps demonstrate how drug products advance from the early stages of research and development to production on a commercial level. Throughout the drug development process, several types of protocols are used to describe the development of drugs for human and animal use. Pharmaceutical protocols for pre-clinical trials, clinical trials, and manufacturing are some of the types of protocols that outline the tasks needed to develop the data required for submission to regulatory agencies such as the FDA in the United States, the Medicines Control Agency (MCA) in the United Kingdom, the Ministry of Health, Labor and Welfare (MHLW) in Japan, and other global agencies. In this chapter, I demonstrate the application of knowledge management theory and models to the pharmaceutical protocol. A pharmaceutical manufacturing protocol describes the tasks needed to manufacture and package the bulk product used for pre-clinical and clinical trials, and for stability studies. A major concern for pharmaceutical companies regarding protocols is the issue of confidentiality. Sensitivity issues arise regarding confidentiality concerns– legal issues, intellectual property, regulatory issues, and development concerns such as formulation development, assay development, manufacturing, and packaging processes

(Bernhardt and McCulley). For this reason, I will reference documents and processes based on a case study of a manufacturing protocol template using the composite company LC Pharmaceuticals and the two experienced scientists, Benjamin Johnson and David Williams, to discuss the pharmaceutical manufacturing protocol. For this case study, LC Pharmaceuticals manufactures prescription drugs using manufacturing protocols to help guide the manufacture and packaging of product.

Creating the Template

Technical writers manage knowledge from the start of the protocol process as soon as the SMEs notify the writers of the project and the writers start to gather information needed to complete the protocol from the SMEs. Creating a pharmaceutical protocol involves interaction of tacit knowledge and explicit knowledge by the technical writer and SMEs. Education in both the arts and sciences is helpful to understand the basic concepts of the manufacturing project and to carry out the actual writing of the protocol. A technical writer can learn a great deal of information about certain chemical processes and concepts by writing protocols. Effective writing about chemical processes requires that a technical writer have analytical and organizational abilities to be able to explain the requirements of the project as well as interpersonal skills to interface cooperatively with the people who have information needed for the protocol. Gathering information internally from the Project Manager (PM) and SMEs is sometimes tedious. The PM is concerned with meeting the client's financial goals and clinical trial deadlines, while the SME is concerned with the technical requirements of the project. One of the roles of the technical writer is to gather the data and communicate the information in a

straightforward, clear manner so that both the external client and the internal personnel understand the tasks required by the project. Eventually, technical writers gain their own set of experience and knowledge about the documents and their content, resulting in the sharing of tacit knowledge and explicit knowledge (Selamat and Chourdrie). One example of this process is illustrated at LC Pharmaceuticals when the exchange of information between the SMEs and the writer begins to use abbreviated language and acronyms such as "'stab' samples" for "stability samples" and "ETOH" for ethyl alcohol.

The pharmaceutical manufacturing protocol is the best way to communicate manufacturing and packaging information because it is designed to break the information into easily readable segments using precise language to explain the required tasks. Johnson and Williams explain that technical writers at LC Pharmaceuticals use protocol templates based on Microsoft® Word® documents combined with Microsoft® Excel® spreadsheets to create artifacts that help guide the user of the protocol through the manufacturing process. In my interview, the two scientists shared how the template serves as a "thought trigger," reminding the technical writer of the regulatory guidelines required by the FDA and the Standard Operating Procedures (SOPs) required by LC Pharmaceuticals. Technical writers at LC Pharmaceuticals eventually developed several protocol templates ranging in length from one to twenty pages. Each Word® template contains small Word® tables and an Excel® workbook, which has tables of information linked into the Word® document. Complex formulas in the spreadsheet calculate the hours for work required to complete a task, such as performing a chemistry test on the Active Pharmaceutical Ingredient (API) of a product or determining the work required to package a batch of product into bottles. The spreadsheets also note information such as

the product formula, packaging requirements, testing information, and reporting requirements. The template describes the numerous procedures for compounding and packaging samples for process development, clinical supplies, and stability testing. Even though the templates vary in size, many graphic features remain the same to help create the document, or artifact, that identifies LC Pharmaceuticals, the client, and the project.

The technical writer should employ theories of knowledge management when using various tools to display and compile information. The seed document model and visualizing the protocol as an artifact are especially helpful in understanding the importance of exhibiting the protocol and computing the levels of effort and costs associated with the activities in the protocol. Although many types of publishing and word-processing software are available, Word® and Excel® are useful tools in assembling and calculating the information needed in a pharmaceutical manufacturing protocol. The basic template in its generic form has many areas where the technical writer will write the tasks and name the components specific to a project. The name of the client and the product are displayed on the title page as well as in the header or footer for consistent identification of the project. Figures 4 – a and 4 – b on the next page demonstrate how headers and footers carry over information common to the entire protocol so that the pages can be tracked easily by all users.

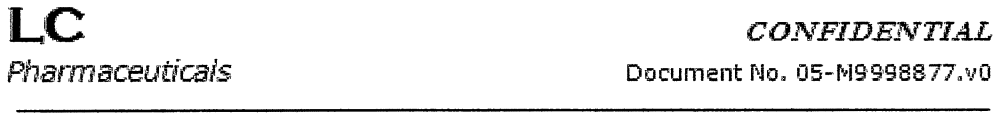

Fig. 4 – a Example of a header of a pharmaceutical manufacturing protocol

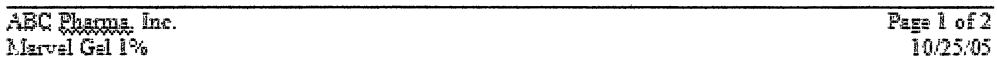

Fig. 4 – b Example of a footer of a pharmaceutical manufacturing protocol

The header, as shown above in Figure 4 – a, contains identifiers for LC Pharmaceuticals such as the company logo/name, the protocol tracking number, and draft status as needed. Similarly, the footer, as shown above in Figure 4 – b, contains the client's name, the product name, number of pages, and date. Figure 4 – c on the next page shows an Excel® table that clearly displays detailed cost information and an invoicing schedule.

Service	Section	Cost	Invoice Schedule	
			On Signing	On Completion of Bulk Mfg
Research & Development	2	$10,000		
Chemistry Testing	4	5,000		
Services Total		$15,000	7,500	7,500
Fees				
Chemical Components	3	160		
Fees Total		$160	160	0
Grand Total		**$15,160**	**$7,660**	**$7,500**

Fig. 4 – c Example of an Excel® table in a pharmaceutical manufacturing protocol.

The technical writer helps manage knowledge by ensuring that the users of the information in the protocol can accurately track the project and its costs as described in the protocol.

Organizing the Template

The manufacturing protocol template is organized into sections, using a "schema" or pattern to manage the knowledge, with respect to the various departments using the information. The table of contents shown on the next page in Fig. 4 – d provides a pattern for all departments at LC Pharmaceuticals that are involved in producing a product for a client's clinical trials and stability studies as well.

Contents

Fig. 4 – d Example of a table of contents of a pharmaceutical manufacturing protocol

The above schema, or table of contents, includes sections for research and development, chemical components, chemistry testing and a business addendum. It can also include sections such as operations (manufacturing processes), microbiology testing, and preparation and gathering of documentation for FDA submission. Although each section is distinct, the sequence of the sections is an example of the "seed" document concept developed by Bernhardt and McCulley. The knowledge management model of seed documents ensures an accurate flow of information to documents needed for New Drug Applications (NDAs) submitted to the FDA. The technical writers use the pharmaceutical manufacturing protocol at LC Pharmaceuticals as a seed or guiding document that helps the users of the document understand the upcoming tasks.

Formatting the Template

The technical writer should use knowledge management theories such as the seed document, the protocol as an artifact, and tacit and explicit knowledge when formatting a pharmaceutical protocol. Formatting a template to a usable protocol requires the technical writer to evaluate the text in the Word® template and the spreadsheets in the linked Excel® workbook – an example of converting tacit knowledge to explicit knowledge. Although visual considerations of a protocol could vary widely, LC Pharmaceuticals, similar to other pharmaceutical companies, has formatting conventions that help project a professional image. Consideration of the rhetorical situation relating to "levels of design" (Kostelnick and Roberts) aids both the technical writer and the user of the pharmaceutical manufacturing protocol. Intra-level and inter-level design of textual components use consistent formatting styles for font type and size, numbering, bullets, boldface, and spacing (Fig. 4 – e below), which also apply to extra-level design of the Excel® tables. Colored text in the template could indicate that the technical writer can change the information as it pertains to a client or product, and then reset the color to black. For instance, "Name" could change to "ABC Pharma, Inc." (See Fig. 4 – f on the next page.)

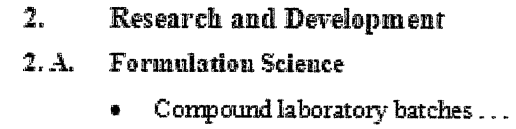

Fig. 4 – e Example of text formatting in a pharmaceutical manufacturing protocol

1. Introduction

This protocol outlines the activities whereby LC Pharmaceuticals will manufacture for ABC Pharma, Inc., one (1) 600-kg batch of Marvel Gel 1% and package into 30-g tubes for process development, supplies for a Phase III clinical trial, and stability studies. LC Pharmaceuticals will perform chemistry testing on the product.

Fig. 4 – f Example of text formatting that could be colored in a pharmaceutical manufacturing protocol.

Similarly, "hidden" text can describe optional activities, such as a microbiology test requirement, and *italicized* text for instructions on the placement of a specific "lot" code to identify the batch. The formatting conventions help with the readability of the document and make it easier for the technical writer to edit the template accurately and efficiently.

Gathering Information for the Protocol

Gathering information and sharing knowledge needed to complete the protocol requires input from several sources, including online databases and the interactions of technical writers and SMEs. Information for the protocol can be forwarded from the SMEs to the technical writer in a number of ways. One widely used method is by an electronic mail discussion, with or without attachments of data. Another electronic way is for the SME to put the information in a folder in a shared drive for access by key personnel who need the information for the project[4]. A third way is for the SME to present the information by hard copy to the technical writer either in person or through the mail system. Receiving hard copy information is becoming cumbersome because

access to the knowledge in the documents is more difficult. Navigation of online documents using key words or phrases is becoming a more efficient and accurate survey of information compared to a review of printed documents (Laupase).

Reviewing the Protocol

After the technical writer applies information provided by the client and SMEs at LC Pharmaceuticals, the protocol template converts to the "draft" status. As a result of knowledge management, the draft of pharmaceutical manufacturing protocol is a meaningful step toward understanding the scope of the project. O'Malley maintains that a "well written protocol is an absolute essential for a rigorous scientific investigation" (30). The protocol often calls for many drafts before it is completed and routed for final signatures. After the technical writer gathers information from project discussions and documents, then the writer converts the tacit knowledge into explicit knowledge as either text data or spreadsheet data. Then the technical writer updates the information and electronically copies the draft to a folder in a shared electronic drive for review by LC Pharmaceuticals staff. A representative from each department reviews the protocol to ensure that the technical writer has captured the requirements of the project and that the technical requirements of the project are within FDA guidelines and SOPs of LC Pharmaceuticals. A "maturation" of the protocol is desirable to allow time for thoughtful review (Meinert and Tonascia 269-70). Checking and reviewing processes could overlook critical points if performed under the constraint of an unrealistic deadline (Meinert and Tonascia 270), resulting in an inaccurate protocol that would need revision.

Gathering Reviewers' Comments

After the review period has expired, the technical writer should further manage knowledge with a thorough, methodical examination of comments from the department representatives and then updates the draft of the protocol. To examine the comments, the technical writer electronically accesses the review folders and reads the reviewers' comments. Reviewers of protocols can insert comments regarding the accuracy of the text of the protocol or about the data in the tables. Comments also include a confirmation of the amount of work required to complete a task, such as the efforts needed for chemistry testing or to gather the data for the documents to include in the dossier for submission to the FDA. Depending on the type of comments submitted by the reviewer, updating the original draft of the protocol can be as simple as, for example, manually inserting text in the Word® document to describe special considerations needed for a particular manufacturing process. The comments also may be more complex, such as addressing changes in the linked Excel® tables to update chemistry testing data. Sometimes, the SMEs may not complete their review of the protocol because they do not have access to critical information about testing requirements, or the scope of the project may require the manufacture of another batch. These instances compromise the efficiency of the technical writer and the document (which may result in a missed deadline.) The technical writer then updates the original draft of the protocol with the reviewers' comments, checks that the format conforms to the style used by LC Pharmaceuticals (Meinert and Tonascia 269), and electronically routes the pharmaceutical manufacturing protocol for signature by the appropriate approving authorities.

Finalizing the Protocol

Knowledge management of the project is finalized with signature completion on the pharmaceutical manufacturing protocol, signifying that the client and LC Pharmaceuticals agree with the technical content (and financial considerations, if included) of the protocol (Meinert and Tonascia 270). Then the technical writer electronically distributes the protocol to the internal departments at LC Pharmaceuticals and to the client, and notifies the financial department. As the project moves forward, the client and various departments at LC Pharmaceuticals may reconsider certain aspects of the project, requiring revision of the protocol. For instance, the client may realize that a chemistry specification may need to change or problems may occur with a packaging component. These types of issues with specifications, packaging, and the like, could require a revision to the protocol and a change to the timeline and costs of the project. Then the technical writer could step in to revise the protocol to address the changes and ensure that the packaged product will meet the client's requirements for data to submit to the FDA.

CHAPTER V

THE FUTURE OF THE PHARMACEUTICAL PROTOCOL

Drug research in the global pharmaceutical industry is competitive, expensive, and essential. Technical writers, SMEs, and managers play an instrumental role in the pharmaceutical industry because they can apply knowledge management theories, models, and strategies to help make sure pharmaceutical protocols of all varieties will be accurate and efficient documents. Within a knowledge management approach to documentation, pharmaceutical protocols should continue to interface with technology, including web-based applications, which will likely change the current style of writing used for print-based protocols and other similar types of scientific writing. However, rhetorical principles (Kostelnick and Roberts 5) found in print compare to the same elements found on the web. The need to appropriately address audience, explain purpose, and place information into the proper context is fundamental to communicating information regardless of the medium. Even style guides used to determine punctuation, capitalization consistency, and notate documentation and the like must meet these rhetorical principles. Numerous style guides are available to instruct on the "how-to" of science writing designed for the print medium (Bonk; Hamilton; Huth; O'Malley; Strunk and White). The web today, however, uses style and layout similar to newspaper style

and layout in the design of easy-to-read screen documents (Bricklin). Usability of web sites is critical to efficiency and is as important as web site readability (Barnum 2-3). Web applications, such as "eXtensible Markup Language" (XML), can help manage the large volume of information acquired by drug research in the pharmaceutical industry. Web interface is becoming more important to writing about drug research and the manner in which the regulatory agency conducts the approval process of drug submissions. Technical writers, with expertise in the science, medical or pharmaceutical industries, also should use knowledge management theories and strategies for documentation accuracy and efficiency in the applicable medium of communication.

Knowledge Management in Print versus Web

Since the pharmaceutical industry uses protocols to outline projects to bring products to market, the dissemination of knowledge in the protocols can be cumbersome. Kostelnick and Roberts describe the rhetorical situation of audience, purpose, and context as fundamental to the document because "it depends on the context in which your readers use your document" (5). Both print and web can deliver the same information, but in dissimilar formats. Complexity in typography and grammar can affect the efficiency of reading and comprehension of the material in printed versus web form (Laporte, et al. 1479). Kostelnick and Roberts note that in text linear components, such as letters, words and numbers, are "physically small," yet these components have a "significant . . . rhetorical effect" (119). Components in sentences, too, have a rhetorical effect. An analysis of the overall content of the print-based science document will show a longer, more complex sentence structure (Gopen and Swan 552). Generally, the web-based

version of text will reveal shorter sentences with a more efficient sentence structure (Nielsen, Schemenaur, and Fox). Since print displays information using a different medium from the web, the variation in presentations may affect conversion of an SME's tacit knowledge to explicit knowledge because eye-viewing patterns of print differ from eye-viewing patterns of web pages. Eye-tracking research shows that differences in eye-viewing patterns from print to web or vice versa could cause the SME to overlook critical information or misread information (Poynter Institute). The dissimilar conversions also could influence the general style of writing in science. Posting information on the web may eventually alter the expression and style of science writing and the protocol from the current tendency of complex sentence structure to a simpler sentence structure (Bricklin).

Knowledge Management and Usability

Knowledge management models and results of usability studies and research can work together in creating a practical and more efficient web interface for the design of web-based pharmaceutical protocols. Carol Barnum notes that usability in web interface, with its focus on the user, can facilitate the learning of the application and efficiency of its users (Barnum 6), which could reduce errors and increase efficiency when applied to tasks in the workplace. Pharmaceutical protocols must be accurately written and meet specific deadlines for completion. As possible users of a web interface, technical writers should be aware of the potential for mistakes in writing protocols (Musen et al. 291-96) for the web. As shown in Chapter III, the mental model of knowledge management explained by Ferrari and de Toledo stresses that the manner in which supervisors and co-workers treat errors in the workplace should be supportive and encouraging, especially

when writers explore the usability of web-based protocols. Therefore, the need for cooperation among the technical writers to resolve issues of using different technologies while working toward deadlines is critical. Writers should work together to devise ways of reducing inaccuracies by openly observing the errors and sharing ideas on how to prevent them from happening again, especially while under the pressure of time limits. Managing knowledge in web interface usability needs an openly supportive team of technical writers who can help assure that errors are minimized and deadlines are met.

In addition to error reduction and efficiency, usability is affected by the different methods that learners and users of information "store information in either short-term memory for immediate use or long-term memory for later or continual use" (Barnum 104). Barnum notes that people remember five to nine numbers, based on a "rule of 7, plus or minus 2, which holds that people can retain seven pieces of information in short-term memory, plus or minus two pieces" (qtd. in Miller). For long-term memory, learners and users develop "schema" or patterns of action and behavior (104) that enable new information to either follow a familiar pattern or modify an existing one. Adult learners use schema as part of a minimalist approach to learning, which includes "active involvement in learning right away" (111). Bernhardt and McCulley's "seed" document provides a schema to help manage knowledge as the companies prepare documents included in the dossier for submission to the FDA. Similarly, technical writers use tables of contents to establish a pattern that helps manage the information in pharmaceutical protocols. The seed document and protocols provide the schema that helps convert tacit knowledge of the SMEs to explicit knowledge found in pharmaceutical companies. Since protocols use a table of contents, the layout of sections in a protocol is predictable.

Writers can appreciate the practical application of web-based applications for protocols because using a web-authoring tool for managing the volume of content may be a more efficient means of gathering the data used to write protocols (113) than gathering data by segments. Eventually, people will benefit because this type of knowledge can be transferred globally by using through technology.

Knowledge Management and XML Applications

Further globalization of the pharmaceutical industry will require an efficient management of knowledge used in the process of bringing drugs to market (Bernhardt and McCulley). Technical, web-based applications help ease printed data into a usable web format. Software applications used for calculations, databases, desktop publishing, and word processing are distinctive in their purposes and are widely used in the pharmaceutical industry. As demonstrated in Chapter IV of this thesis, Microsoft Word® is an example of a word processing application that can be used for writing a pharmaceutical protocol. Another system of application is "eXtensible Markup Language" or "XML," which is a system of making notations or "markups" in the application so that the user is able to create a specific programming language for displaying documents in an enterprise environment (Adobe Systems XML and PDF 2, 6). For instance, an XML markup can generate an HTML, PDF, and Word copy of the same file, enabling the user to have just one master document to update (Adobe Systems XML and PDF 1). As long as the "displays of data are truthful and revealing," management of web-based information is desirable (Tufte 53).

XML enhances the interchange of information between organizations by facilitating the access and transfer of the information. Document type definitions (DTDs) "specify the elements that will be allowed in the databases and the relationships among these elements" (Applen 301-13). DTDs facilitate knowledge management because they describe the allowable information structure of an XML document. DTDs contain no actual empirical data or information that might be needed; they "contain only metadata–that is, data about data" (308). J.D. Applen gives an example of XML technology and virtual documents whereby an epidemiologist researches a rare disease using XML to research several databases. Searching for "phrases, combinations of phrases or unique patterns of verbal usage" (309) allows the epidemiologist to have access to key passages in case studies. The epidemiologist could put these passages in a database or email them to other scientists working on the same problem. Thus, an XML application can manage knowledge and share it with others to further their research study (309), as long as the simplicity of storing and transferring information does not result in a cumbersome, ineffective system (310).

XML applications are a means to manage the volume of information that is needed for drug research and submission for approval by the appropriate regulatory agency (Adobe Systems FDA). XML data and schema help government agencies (such as the FDA) to integrate and process data into internal and external systems using Web services (Adobe Systems Government).

The following page shows a screenshot (Fig. 5 – a) of a simple "Google" search on the Internet for "xml application in the pharmaceutical industry," yielding many sites with information helpful in planning the future protocol.

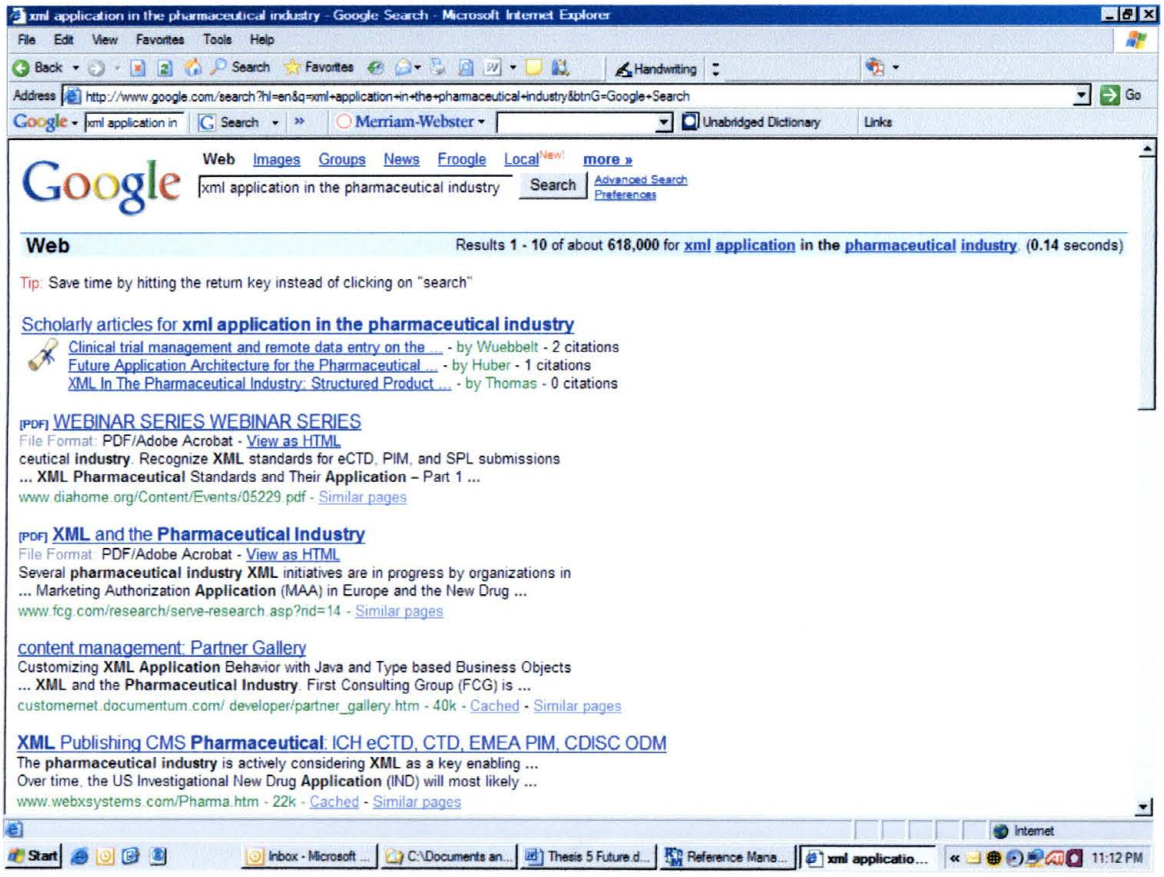

Fig. 5 – a Google search for "xml application in the pharmaceutical industry" (Oct. 18, 2005)

Example of a Web-Based Protocol

Examples of web-based, pharmaceutical protocols are quite limited because of the confidential nature of the data and processes in the pharmaceutical industry. However, the website for BIO.COM® (www.bio.com), with its focus on life sciences, also addresses biotechnology and pharmaceutical industries and displays information useful to the discussion of knowledge management and the pharmaceutical protocol.

Figures 5 – b, 5 – c, and 5 – d show a sequence of screenshots showing the path to the laboratory method protocol describing the "Neutralization and Equilibration of Phenol."[5]

Fig 5 – b Home page of BIO.COM® (www.bio.com) using the link http://www.bio.com/index.jhtml;jsessionid=WTDE45EHFDOK3R3FQLMSFEWHUWBNQIV0 (Oct. 18, 2005)

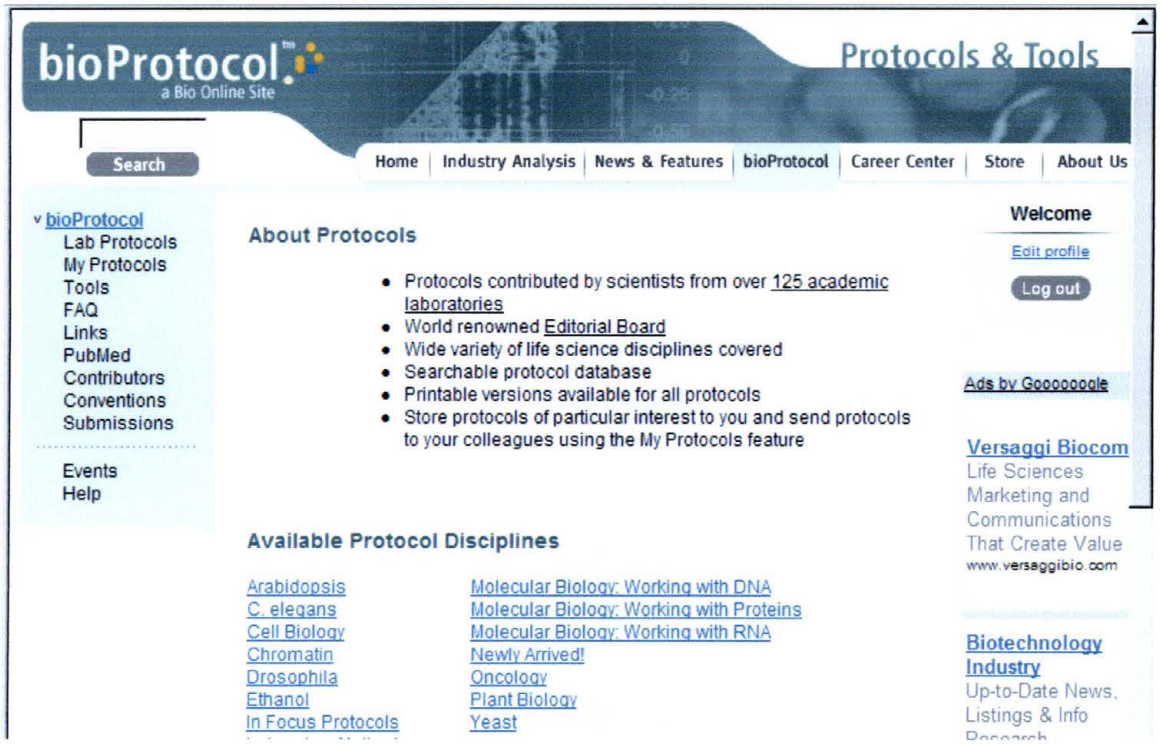

Fig. 5 – c "bioProtocol" tab using the link http://www.bio.com/protocolstools/index.jhtml;jsessionid=WTDE45EHFDOK3R3FQLMSFEWHUWBNQIV0 (Oct. 18, 2005)

Fig. 5 – d Lab Protocol "Neutralization and Equilibration of Phenol" using the link http://www.bio.com/protocolstools/protocol.jhtml?id=p560 (Oct. 18, 2005)

Figure 5 – d shows a snapshot of a portion of the first page of the web-based protocol. Even though this protocol is written in hypertext markup language (HTML), one can determine from the data on the image that XML could be used to note information such as the title, contributor, and steps in the procedure. Tabs can replace the traditional table of contents, noting the sections of the protocol using the model of the seed document. The display of information is arranged well and uses visually pleasing

screen text design of notable links with sans serif font and a contrasting color scheme of font, banner, and background that is easy to read (Kostelnick and Roberts 107, 143, 425-28). A calculation function may be limited, although an alternate method of calculation found in spreadsheets could be used. The BIO.COM® website uses knowledge management principles found in the seed document concept, tacit and explicit knowledge, and the mental model of sharing, which aid in navigation of the site and help share information easily with the reader.

Web-interface of knowledge management theory and protocols affect the use of information in the context of a printed document compared to the screen display of a web application, usability of web applications, and the use of XML to help categorize and manage volumes of information needed for a pharmaceutical protocol. Since the protocol should convey information as clearly and as efficiently as possible, the use of web-based tools should become more important in managing the knowledge required in the protocol.

CHAPTER VI

CONCLUSION

This thesis demonstrates that even though the scope of documenting processes and data in the pharmaceutical industry is extensive, the pharmaceutical protocol manages knowledge to provide information to a wide variety of audiences such as scientists, reviewers of documents in regulatory agencies and business people. As technical documents, pharmaceutical protocols communicate procedures found in non-clinical and clinical trials, laboratory methods, manufacturing of product, and validation of manufacturing, packaging, and cleaning processes. The pharmaceutical protocol presents knowledge in a format that manages scientific data for submission to the appropriate regulatory agency, such as the FDA or another global agency. Managers in pharmaceutical companies should learn and practice knowledge management theories such as error treatment and cooperation, and use models such as seed documents and artifacts. Interfacing knowledge management theory with technological tools, software, and innovations can ensure that technical writers communicate pharmaceutical protocols for needed drugs as accurately and efficiently as possible with the result of a more rapid review and acceptance by the FDA, expand scientific studies, and manufacture a product that is safe and effective for public use.

Limited information is available on how pharmaceutical protocols convey information such as scientific data, regulatory guidance, and business issues, even though the pharmaceutical industry extensively uses protocols. Studying the history and the rhetorical situation of the pharmaceutical protocol can show the relationship between the data in the protocol and manufacturing, regulatory, and business interests. Most instructional texts use general statements to describe the logically organized format for writing scientific documents and protocols. Therefore, using LC Pharmaceuticals as a representative model of a pharmaceutical company, the protocol, and interviewing experienced scientists helps support the discussion of activities of data gathering and writing tasks performed by technical writers and SMEs associated with the writing of a protocol.

Even though knowledge management theory is a broad topic, specific theories of knowledge management, such as mental models, using seed documents, conversion of tacit knowledge to explicit knowledge, development of documents as artifacts, and writing to address regulatory requirements, support the process of creation, review, and distribution of pharmaceutical protocols. These theories of knowledge management help describe how technical writers, SMEs, and managers present and manage data in the pharmaceutical protocol in order to expedite the process of bringing a drug product to market. Mental model principles of error treatment and cooperation explain how a culture that shares knowledge is a culture that values its ability to share knowledge for guidance in creating documents such as protocols. Bernhardt and McCulley's concept of a seed document helps provide the structure for a systematic process of document development that assists in bringing together and organizing cross-functional drug development teams

which gather scientific data for documents used in large dossiers submitted to regulatory agencies such as the FDA. The seed document model of knowledge management also can apply as a "schema," or pattern, to a smaller document such as a pharmaceutical protocol. Additional theories of knowledge management theory include the SOAP knowledge exchange protocol to describe the interaction of tacit knowledge and explicit knowledge, the rules of guidance for transfer of tacit knowledge to explicit knowledge, and artifacts that outline tasks that help tacit and explicit knowledge manage each other. Regulatory requirements can create "building blocks" of information, which can influence the way a technical writer develops the pharmaceutical protocol. Technical writers should use each of these knowledge management theories to convert tacit knowledge about the product into explicit knowledge in the pharmaceutical protocol.

The activities and tasks that pharmaceutical technical writers and SMEs perform are typical throughout the pharmaceutical industry; however, studying the protocol to understand the conversion of tacit knowledge to explicit knowledge can be difficult. Because of the confidential nature of research and manufacturing activities of the pharmaceutical industry, access to examples of schema or mental models of sharing information can be problematic. Restricted access to documents hampers the study of how technical writers manage knowledge in this industry.

As the pharmaceutical protocol continues to interface with technology and web-based applications, theories of knowledge management and technology should help the technical writer make the pharmaceutical protocol more accurate and efficient as the writer prepares the documents required for the drug approval process. Although print and

web pharmaceutical protocols display identical information in different ways, each type of document should be carefully yet efficiently prepared.

Several questions of interest for further study of knowledge management theory and pharmaceutical protocols follow from the research performed for this thesis. More inquiry into the relationship of the protocol and knowledge management theory presents, among others, the following questions:

- What is the relationship of knowledge management theory and the pharmaceutical protocol in an international and/or global perspective?
- How can regulatory issues and knowledge management theories in a pharmaceutical protocol be explored more deeply?
- What is the political nature of a pharmaceutical protocol and knowledge management theory?
- What is the effect of knowledge management theory on project management in the pharmaceutical industry?

The researchers of these questions can use various methodologies to implement their studies. Qualitative methodology options of a literature review, an ethnographic study, and the interview process used in this could also be used to research the above questions. Other methodologies include empirical study of the interactions between subject matter experts and technical writers, other types of ethnographic studies, and quantitative analyses of survey results. Ongoing study of knowledge management theory and pharmaceutical protocols (and general pharmaceutical writing) should continue to add to the current base of knowledge about knowledge management theory and pharmaceutical protocols. This type of knowledge would help expedite a much-needed

drug from research to market to maintain overall health from an individual level to a global level.

Technical writers can employ knowledge management theories described in this thesis when using web applications, thus enhancing the usability, readability, and access to the information in the protocol. The technical writer who becomes skillful in the use of these theoretical tools will be the technical writer who is of value to the profession. Those who are the most proficient will be the most valuable. The future of pharmaceutical writing will benefit from the strides made in the study of the transfer of knowledge through technology, and the technical writer who becomes skilled in the management of knowledge through technology will be the most valuable of all. Since pharmaceutical research is global, competitive, costly, and necessary, the managers who apply knowledge management theories and models, and use knowledge management strategies can help make sure that all types of pharmaceutical protocols will be efficiently and accurately produced documents for future submission to regulatory agencies such as the FDA.

NOTES

[1] "Assay validation" protocols prove that a chemistry test method (assay) will work in the laboratory that is performing the test. These protocols "define the assay, its proposed use . . . and prospectively assigns acceptable values for the (a)ssay (p)arameters" ("Assay Validation").

[2] A "scheduled" drug is defined as a drug on a governmental list of drugs that are subject to the same legal controls and restrictions – usually used with a Roman numeral from I to V indicating decreasing potential for abuse or addiction ("Schedule").

[3] A pre-clinical trial protocol would describe the tasks for analyzing the effect of a drug on animals (Meinert and Tonascia 3).

[4] Various types of software are available to help with the electronic management of document. Knowledge management theory and document management systems are subjects beyond the scope of this thesis, but are indeed topics of further research.

[5] Phenol is a corrosive poisonous crystalline acidic compound (C_6H_5OH) present in coal tar and wood tar. This compound is used in the manufacture of resins and plastics, dyes, and pharmaceuticals (as aspirin) and as a topical anesthetic in dilute solution ("Phenol," def.1).

APPENDIX A

A SAMPLE PHARMACEUTICAL MANUFACTURING PROTOCOL

The format and content of the three-page sample protocol in Appendix A is generic information from general instructional texts referenced in the resources cited in the thesis. It is intended to exemplify the theories presented and applications made throughout the thesis. It is not intended to display format or content of a protocol from any particular actual company.

LC
Pharmaceuticals

CONFIDENTIAL
Document No. 05-M9998877.v0

ABC Pharma, Inc.
Marvel Gel 1%

TTB Compliance: Permit pending
IND

A manufacturing protocol for a 600-kg active batch of Marvel Gel 1% packaged into 30-g tubes to conduct a Phase III clinical trial and stability studies to investigate the effects of the product on subjects presenting with dermatitis.

Contents

LC Pharmaceuticals

Benjamin Johnson — Date
Manager of Chemistry
Research and Development

David Williams — Date
Manager of Production
Operations

Name — Date
Project Manager

Client

(Sign above and print name below) — Date

(Print)

(Title)

(Additional signature, if required.) — *Date*

(Print)

(Title)

PO # _____

1. Introduction

This protocol outlines the activities whereby LC Pharmaceuticals will manufacture for ABC Pharma, Inc., one (1) 600-kg batch of Marvel Gel 1% and package into 30-g tubes for process development, supplies for a Phase III clinical trial, and stability studies. LC Pharmaceuticals will perform chemistry testing on the product.

2. Research and Development

2. A. Formulation Science

- Compound laboratory batches . . .

3. Chemical Components

Chemical Components			
Component	**Part #**	**Quantity**	**UOM**
Purified Water USP	123	2.00	L
Ethanol USP	456	27.00	kg
Methylparaben NF	789	17.00	kg
Triethanolamine NF	1011	15.00	kg
Carbomer USP	1213	17.00	kg
Propylparaben NF	1415	16.00	kg
Sodium Dermatol	TBD	6.00	kg

4. Chemistry

4. A Stability Testing. Store samples horizontally.

Product Specification		
Method #	**Test**	**Acceptance Criteria**
05-1234	Description	Pass
05-5678	Viscosity	TBD
05-9101	Active Assay (L = xx% w/w)	% L

(HIDDEN TEXT) ICH Guidelines for Stability Testing: 25 ℃ – 3/6/9/12/18/24/36
30 ℃ – 6/9/12
40 ℃ – 3/6

LC
Pharmaceuticals

CONFIDENTIAL
Document No. 05-M9998877.v0

BUSINESS ADDENDUM

A – 1. Schedule of Services and Fees

Service	Section	Cost	Invoice Schedule	
			On Signing	On Completion of Bulk Mfg
Research & Development	2	$10,000		
Chemistry Testing	4	5,000		
Services Total		$15,000	7,500	7,500
Fees				
Chemical Components	3	160		
Fees Total		$160	160	0
Grand Total		**$15,160**	**$7,660**	**$7,500**

APPENDIX B

INTERVIEW QUESTIONS WITH EXCERPTS:

BENJAMIN JOHNSON AND DAVID WILLIAMS

March 4, 2005

1. For background and context, please state your name, age and level of education.

.....

2. What is your job title and job description? Describe briefly your job history prior to this job.

.....

3. What is the chronology of the "protocol" at LC Pharmaceuticals? How did the format come about?

Johnson: Protocols in general have been used for many, many years in the pharmaceutical industry to set about a scope of work that needs to be done prospectively so that the party that needs the work done and the party doing the work are on the same wavelength, and they all know what needs to be done. Depending on what kind of protocol it is, there may be acceptance criteria involved or maybe just a "record the outcome" type of protocol. Or it may be a protocol that drives the production in a batch or any number of things. But in terms of the organizations that I grew up in, we began using protocols to help

build our business, and I think that may be where you're trying to go with this, and I'll look at it from that perspective.

In the mid '70s we began using protocols to help some prospective clients of LC Pharmaceuticals to do assay validations. Those were the first protocols that I'm aware of that we successfully implemented. We made some good money at it, so we started building a structure for protocols for batch production, and then integrated all aspects of batch production into one protocol in [an] outline format. So that's from a historical standpoint I recall.

Johnson: Well, I don't know what you (David) remember. But I, well, to me it was just like, this just makes sense! These are the work pieces that we need. Why not just make it into an outline?

.....

Johnson: Like penalties and things for not meeting certain timelines.

Williams: Yes, not meeting timelines. And so it's a little bit different than what we ended up with. But with the move to go with a little more detail than what I remember some of the older protocols having.

4. Define the audience for the protocol.

Williams: So what you're saying was that the protocol was developed not just as a document to external but to the internal client.

Johnson: Yes, to keep our sanity so that each group would know what their "marching orders" would be so the client wouldn't be upset.

LC: Gosh, I'll bet those were some intense meetings!

5. Explain the purpose of the protocol.

LC: So then, the purpose of the protocol would be to summarize, I guess, a lot of the information and put it in a format that people can understand as "marching orders."

Johnson: Some of it. You know, you can read these things and see that part of it has the work described right there within – and we think of these big, batch-producing protocols. But all the work is described right there. Often it will direct you to another protocol that is anticipated. Then it will tell you, "I know a protocol can be generated to address this other issue like assay validation, cleaning validation or some study that needs to be done."

Williams: I see it that it tells people what needs to be done and it also I think lays out limits. Particularly that introductory protocol very often brings on the project in terms of what we're going to do and what we're not going to do. Maybe we're going to send things somewhere else to have it done. But it does define limits so it isn't an open-ended project. Then it also discusses from a client perspective, "What is it going to cost you? When does LC Pharmaceuticals expect to be compensated for whatever work is being done?" And also, the client also has an expectation of, "I don't owe until certain things happen." So, I think the way it's currently structured it's a blend of both a description of what's going to happen and it's also a business document.

6. How would the protocol be used in a context other than pharmaceutical manufacturing?

Johnson: What do you mean by "other than pharmaceutical manufacturing?" There are protocols that address research work, is that what you mean by the "other than?"

LC: Yes, like clinicals or . . .

Johnson: Or in-vitro work or clinical work that is done either here . . . or somewhere else.

LC: OK. In other words, like pharmaceutical manufacturing would be your basic batch-producing . . .

Johnson: Yes, or assay validations or development of assays depending on the other things, too, like research. Those are more "fuzzy" protocols because you have to give freedom to the people that are doing the work to think. You can't confine them within the protocol to just think one certain way. You've got to give them freedom so they can "blossom out" their ideas.

LC: Where does that "blossoming" get reported? In their notes? In reports?

Johnson: Yes, in their notes and in reports and in development reports.

Williams: Some of that would be if the client came in and said, "I have this active ingredient that I believe will work for a dermatological condition." You guys create a vehicle and a process and make something that's physically and chemically stable. So, when they would do that your initial protocol would have to be pretty open because "you don't know what you don't know" yet. Your client

just comes in, but you're still sort of stuck with saying, "Well, we think this is going to cost about 'X'." We have to have something because the client also doesn't have an infinite checkbook. Most of them don't, anyway!

7. Tell me about the "authority" of a protocol. Is the authority in the description of the scope of the project? Product specifications? Testing schedules? etc.

.....

8. Describe the influences toward development of the protocol other than specific projects, e.g., ICH guidelines, FDA guidance, and regulatory agencies such as the DEA, TTB, etc.

Williams: What I've seen happen as, even when I came on board, the protocols were much thinner, so to speak, than they are today. But rules have changed in the last 10 years and, for example, when I came on board we were just beginning to talk about "cleaning validations." Until that time we never talked about them; we didn't do them. And so the protocols began to address the requirements to do this and also to develop test methods to do it and then follow-on protocols to do the cleaning validations. The protocols were also talking about "process validations," because at that time 10 years ago that was the – no, 12 years ago – that was the important thing. But that was coming out of the FDA. They wanted you to prove the process is reproducible. The next thing they came out with was: prove that your equipment is clean. The next validation they came out with was prove your packaging process does indeed put the number of units - grams, milliliters , whatever you've claimed, in your bottle. But when I started, that wasn't an issue. You know, your label may have said "4 ounces," but you didn't have to prove or

have a process that you could validate that said with some degree of reliability every time you did this process that things were packaged properly. They had the right amount in them. You didn't have to do that.

LC: So the protocol has started to reflect the FDA guidance as well. Not only our growth as a company.

Williams: And then the ICH, the International Conference on Harmonization. They began to come out with international standards for testing the product's storage conditions, test points and the like. This information then was incorporated into the protocol. For example, when I started we would normally test products at 40°C/75% relative humidity for 3 months. And that was all the further out we would go. Then the client would use that data to support shelf life when they made the submission to the FDA. ICH basically came out and said, "You should go to 6 months." They didn't say you "had to." They said you "should." It has now become a standard. So now you see almost invariably for any drug product the 6 month rather than 3 month 40°C temperature.

9. How has technology influenced protocol development?

Williams: You have a question here: How has technology influenced protocol development? Now, when you talk about that are you talking about technology of things that have to be done? Or the process of generating the protocol?

LC: My first take was the computer technology such as what the Tech Writer uses.

Williams: Well, again, 12 years ago when I started, protocols were typewritten. There were no computers, no word processors. Everything was typewritten. All

tables, everything was just . . . typewritten. I don't know any other way to describe it: typewritten. In time we brought on Word and then protocols were typed in Word format, and all tables in Word were just Word tables. Then we went to simple tables that were done in Excel that were linked. We still had to manually enter the hours into the protocol Excel table but then ultimately the Excel tables summated them on a separate table and said, "This is the cost." Then we moved further and began to develop Excel tables that could address the major things that were happening because we sat down with people and said, "Tell us what the average level of effort is to do a particular test." And we looked at all the common tests that were done in Chemistry, Microbiology, how much time it takes on average for Line Inspection to do what it does or to compound a batch or whatever, and we loaded all these into tables. So then, it reached a point that someone said, "We're going to make 4 batches." You plugged in 4 batches and the system then calculated how much it was going to cost to do that - how many hours/level of effort it was going to take to do that. The same thing with packaging: if you said/told the system, "This is our split and these are the number of packages" it would begin to calculate for you the level of effort in packaging, the level of effort in line inspection. That's how it got to where it went. I don't know where it's going from here. I'm sure it will be streamlined.

10. Have protocols always included cost information? If not, when did cost information begin to be included? Why would cost information not be a separate document such as a purchase order or a simple invoice?

.....

11. Do other companies use a document similar to the LC Pharmaceuticals protocol? What do their protocols look like?

.....

12. What do you see as the future of the protocol? A business document? Should it include more (or less) technical information?

Williams: It's hard for me to say because you have some people who believe it's a business document and some people believe that it's a technical document. What it really comes down to is how you're going to do business. That's what I see as the future of the protocol. Until you decide how you want to convey information internally and externally to the client and to the people inside the company to do the project, you can't really, in my mind, improve/streamline/ make less complex or any other euphemism you want, change a protocol until you define what it's purpose is and how you're going to address the things that the protocol addresses now.

13. Who can I contact outside of LC Pharmaceuticals for feedback on the protocol?

.....

WORKS CITED

Adobe Systems, Inc. "Food and Drug Administration: Drug Approvals are More Efficient when New Drug Applications are Submitted as Searchable PDF Files." 2002: 1-4. Adobe Systems, Inc. San Jose, CA. <http://www.adobe.com/epaper/spotlights/fda/pdfs/fda.pdf> 22 Oct. 2005.

---"Electronic Forms Solutions using XML and PDF: A Technology Primer for the Adobe XML Architecture." 2003: 1-16. Adobe Systems Inc. San Jose, CA. <http://www.adobe.com/enterprise/pdfs/xml_whitepaper.pdf> 22 Oct. 2005.

---"Adobe Government Forms: Serving People First." 2004: 1-4. Adobe Systems, Inc. San Jose, CA. <http://www.adobe.com/government/pdfs/95003217_gov_forms_sol_ue.pdf> 22 Oct. 2005.

Applen, J. D. "Technical Communication, Knowledge Management, and XML." Technical Communication 49.3 (2002): 301-13.

"Assay Validation." <http://www.cbrlabs.com> October 2, 2005.

Barnum, Carol M. Usability Testing and Research. Boston: Longman, 2002.

Bernhardt, Stephen A. and George A. McCulley. "Knowledge Management and Pharmaceutical Development Teams: Using Writing to Guide Science." Technical Communication 47.1 (2000): 22-34.

Jensen, Lee, ed. "BIO.COM®" 2005. <http://www.bio.com> 20 Oct. 2005.

Bonk, Robert J. Medical Writing in Drug Development: A Practical Guide for Pharmaceutical Research. Binghamton, NY: The Pharmaceutical Products Press, 1998.

Bricklin, Dan. "How to write for the INTRAnet: A web-site that discusses how to create good business documents in the linked, on-screen environment of Intranets and the Internet." 1998. <http://www.gooddocuments.com/homepage/homepage.htm> 12 Oct. 2005.

Coakes, Elaine, ed. Knowledge Management: Current Issues and Challenges. Hershey, PA: IRM Press, 2003.

Coakes, Elayne, Dianne Willis, and Steve Clarke, eds. Knowledge Management in the Sociotechnical World: the Graffiti Continues. London, England: Springer, 2002.

"Dossier." Webster's Third New International Dictionary, Unabridged. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> 2 Oct. 2005.

Ferrari, Fernanda Menezes and José Carlos de Toledo. "Analyzing the Knowledge Management through the Product Development Process." Journal of Knowledge Management 8.1 (2004): 117-29.

Friedman, Lawrence M., Curt D. Furberg, and David L. DeMets. Fundamentals of Clinical Trials. 3rd ed. New York, NY: Springer-Verlag, 1998.

Gopen, George D. and Judith A. Swan. "The Science of Scientific Writing." American Scientist 78.6 (1990): 550-58.

Hagge, John. "The Value of Formal Conventions in Disciplinary Writing: An Axiological Analysis of Professional Style Manuals." Journal of Business and Technical Communication 8.4 (1994): 408-62.

Hamilton, Cindy W. "How to Write and Publish Scientific Papers: Scribing Information for Pharmacists." American Journal of Hospital Pharmacy 49 (1992): 2477-84.

Herschel, Richard T, Hamid Nemati, and David Steiger. "Tacit to Explicit Knowledge Conversion: Knowledge Exchange Protocols." Journal of Knowledge Management 5.1 (2001): 107-16.

Huth, Edward J. How to Write and Publish Papers in the Medical Sciences. 1st ed. Philadelphia, PA: ISI Press, 1982.

---Writing and Publishing in Medicine. 3rd ed. Baltimore, MD: Williams & Wilkins, 1999.

Johnson, Benjamin (pseudonym) and David Williams (pseudonym). Personal Interview. 4 Mar. 2005.

"Knowledge management." <http://encarta.msn.com/dictionary> 3 Oct. 2005.

Kostelnick, Charles and David D. Roberts. Designing Visual Language : Strategies for Professional Communicators. Boston: Longman, 1998.

Kreiner, Kristian. "Tacit Knowledge Management: The Role of Artifacts." Journal of Knowledge Management 6.2 (2002): 112-23.

LaPorte, Ronald E., et al. "Papyrus to PowerPoint (P 2 P): Metamorphosis of Scientific Communication." British Medical Journal 325 (2002): 1478-81.

Laupase, Ricky. "The Process of Converting Consultants' Tacit Knowledge to Organisational Explicit Knowledge: Case Studies in Management Consulting Firms." Knowledge Management: Current Issues and Challenges. Ed. Elayne Coakes. Hershey, PA, USA: Idea Group Publishing, 2003. 212-25.

Meinert, Curtis L. and Susan Tonascia. Clinical Trials: Design, Conduct, and Analysis. New York, NY: Oxford University Press, Inc., 1986.

Musen, M. A., et al. "Knowledge Engineering for a Clinical Trial Advice System: Uncovering Errors in Protocol Specification." Bulletin du Cancer 74.3 (1987): 291-96.

Nielsen, Jacob, P. J. Schemenaur, and Jonathon Fox. "Writing for the Web." <http://www.sun.com/980713/webwriting/> 22 Oct. 2005.

O'Malley, Kevin. "From Protocol to Publication: Preparation of a Scientific Paper." Irish Medical Journal 80.1 (1987): 30-32.

"Phenol." Webster's Third New International Dictionary, Unabridged. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> 3 Oct. 2005.

Poynter Institute. "Viewing Patterns for Home Pages." <http://www.poynterextra.org/eyetrack2004/viewing.htm> 2004. 25 Jul. 2005.

"Protocol.". Encarta Dictionary Online <http://encarta.msn.com/dictionary> 2005.

"Protocol." Webster's Third New International Dictionary, Unabridged. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> 6 Oct. 2005.

"Protocol.". Oxford English Dictionary Online 1989. <http://80-dictionary.oed.com> 20 Mar. 2005.

Sanchez, Ron, ed. Knowledge Management and Organizational Competence. Oxford, England: Oxford University Press, 2001.

"Schedule." Webster's Third New International Dictionary, Unabridged. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> 2 Aug. 2005.

Selamat, Mohamad Hisyam and Jyoti Choudrie. "The Diffusion of Tacit Knowledge and its Implications on Information Systems: the Role of Meta-abilities." Journal of Knowledge Management 8.2 (2004): 128-39.

Strunk, William and E. B. White. The Elements of Style. 3rd ed. Boston: Allyn and Bacon, 1995.

Tufte, Edward R. Visual Explanations: Images and Quantities, Evidence and Narrative. Cheshire, CN: Graphics Press, 1997.

Velanovich, Vic. "The Logic of the Medical Research Article." Theoretical Medicine 14.3 (1993): 257-65.

Vickers, M. D. "Organising Clinical Research: 2. Writing the Protocol." The British Journal of Clinical Practice 43.2 (1989): 49-51.

VITA

Linda Sue Coker was born in San Antonio, Texas, on April 3, 1954, the daughter of B. Ellen Garrison, R.Ph. and Edward L. Anderson, M.D. (Ms. Coker enjoys her mother's claim that in 1950 she was the third female pharmacist hired in San Antonio.) After graduating from Thomas Jefferson High School, San Antonio, Texas, in 1972, Ms. Coker entered the University of Texas at Austin. She then attended Grossmont Junior College in El Cajon, California, and eventually transferred to the University of California, San Diego, where she earned the degree of Bachelor of Arts, Linguistics, from the University of California, San Diego in March 1979. During the following years she was employed at Datapoint Corporation in San Antonio, and then at Xerox Corporation in Austin and San Antonio, Texas. She currently is employed as a Technical Writer at a pharmaceutical company in San Antonio. In September 2002, she entered the Graduate College of Texas State University-San Marcos.

Permanent Address: 552 Kerlick Lane

New Braunfels, Texas 78130-6616

This thesis was typed by Linda Sue Coker.