

MES in Pharmaceutical Industries

- Focus Packaging

Author: Fredrik Clausson

Supervisors: Associate professor Mats Johnsson, Department of Design Sciences, Institution of Packaging Logistics, Lund University.

Ph.D. Student Fredrik Nilsson Department of Design Sciences, Institution of Packaging Logistics, Lund University.

Manager Manufacturing Thomas Schwarz, Filling & Packaging H69 Aventis Behring GmbH

Dr. Christoph Kraus, IT Solutions, Aventis Behring GmbH.



Acknowledgements

I, Fredrik Clausson, performed this Master Thesis as the final work, before I received my degree in mechanical engineering. The work was done during autumn and winter 2002/2003, at the institution of Design Science at Lund and the Department of Packaging Logistics in Lund, Sweden. The work was mainly carried out at the pharmaceutical company, Aventis Behring GmbH in Marburg, Germany.

During the creation of this master thesis many different persons has been involved answering questions and giving support. Here by I want to thank all these persons and give a special thank to my supervisors, Thomas Schwarz and Dr. Christoph Kraus at Aventis Behring GmbH as well as Fredrik Nilsson and Associate professor Mats Johnsson at Lund University.

I also want to thank the Fleischmann family by whom I stayed during my time in Marburg, their support have enabled me to focus on this study.



Abstract

The purpose of this study was to identify advantages, disadvantages and aspects that have to be considered when implementing Manufacturing Execution Systems (MES).

MES is a rather new software system, which is linking the business systems in companies with the control systems on the factory floor. Today the communications between the different levels are mainly managed manually. Through MES the communication is made electronically in real time, which reduces the administrative work and the risk for mistakes.

This study is a qualitative case study. It is based on observations and interviews at Aventis Behring, a pharmaceutical company. Personnel in the Final Packaging Department as well as other linked departments were interviewed to identify the advantages, disadvantages and aspects MES can create. Also theories concerning MES and control were used as a base for the work.

Advantages identified with MES were improved regulatory compliance, improved planning, execution and control, safer material flow, improved component location information, knowledge generation, improved customer satisfaction, increased transparency, improved information flow, documentation problem reduction, improved retrieval of historical data, reduced lead-time, reduced cycle time, reduced past due orders, reduced stock levels and work in progress, increased quality, reduced administrative work, better support of company objectives and improved evaluation possibilities. Another advantage the software has is that it consists of several different functions, which enables to build a system that best suits the needs.

Disadvantages with the system are the difficulties to identify and to quantify the benefits and costs of the system. The organisation will also have a greater risk exposure and a break down in the system can have devastating consequences because no alternative systems can be used. A successful pilot project would give indications to proceed expanding the system into other organisations. But an unsuccessful project does not necessarily mean that the system should not be expanded. There are many factors that are specific in a pilot project and it might be the case that the system first becomes beneficial in a larger scale.

Aspects that has to be considered when implementing MES are for example how to save the generated knowledge, reduce the information overload, interface with other systems, saving the flexibility, react to changes in regulatory compliance and the financing of the system.

Pharmaceutical industries are specific for the product value and the high level of regulatory requirements. This makes it more beneficial to implement MES in this industry than others. It is therefore likely to think that similar industries will have the most benefit of MES, but the benefits is shown to be so considerable that the system would be profitable to implement within most sectors.





Contents

1	INTRODUCTION.....	5
1.1	BACKGROUND	5
1.2	DEFINITION OF THE PROBLEM	6
1.3	PURPOSE	7
1.4	FOCUS / LIMITATIONS	7
1.5	TARGET GROUP.....	7
1.6	DISPOSITION	8
1.7	COMPANY DESCRIPTION	9
1.7.1	<i>Aventis</i>	9
1.7.2	<i>Aventis Behring</i>	10
2	METHOD.....	13
2.1	METHOD INTRODUCTION	13
2.2	RESEARCH APPROACH	14
2.2.1	<i>Analytical approach</i>	14
2.2.2	<i>System approach</i>	15
2.2.3	<i>Actor approach</i>	15
2.2.4	<i>The method approach in this study</i>	16
2.3	QUANTITATIVE AND QUALITATIVE STUDIES.....	16
2.3.1	<i>Qualitative study</i>	17
2.3.2	<i>Quantitative study</i>	17
2.3.3	<i>This study</i>	17
2.4	VALIDITY AND RELIABILITY	18
2.4.1	<i>Validity</i>	18
2.4.2	<i>Reliability</i>	18
2.4.3	<i>The validity and reliability of this study</i>	19
2.5	DATA COLLECTION	19
2.5.1	<i>Observation</i>	19
2.5.2	<i>Interview</i>	20
2.5.3	<i>Information handling</i>	20
2.5.4	<i>My data collection</i>	21
2.5.5	<i>Frame of Reference</i>	22
2.5.6	<i>Regulatory Compliance</i>	22
2.6	ANALYSING TOOLS	22
2.6.1	<i>Aeneis</i>	22
2.6.2	<i>Net Present Value</i>	22
2.7	RESOURCE DISTRIBUTION	23
2.8	MODEL	24
3	FRAME OF REFERENCE	25
3.1	PLANNING, EXECUTION AND CONTROL.....	25
3.2	COMPUTER SYSTEMS	27
3.3	MANUFACTURING EXECUTION SYSTEM (MES).....	28
3.3.1	<i>History</i>	28
3.3.2	<i>What is MES</i>	28
3.3.3	<i>MES users</i>	30
3.3.4	<i>MES connected with other manufacturing systems</i>	30
3.3.5	<i>Functions</i>	31
3.3.6	<i>Benefits</i>	33
3.3.7	<i>Costs</i>	33
3.3.8	<i>Evaluation</i>	34



4	REGULATORY COMPLIANCE.....	35
4.1	FDA REGULATIONS	35
4.1.1	<i>Electronic Records</i>	35
4.2	GOOD MANUFACTURING PRACTICE	38
4.2.1	<i>Subpart G, Packaging and Labelling Control</i>	38
4.2.2	<i>Subpart J, Records and Reports</i>	39
5	EMPIRICAL RESULTS	41
5.1	DESCRIPTION OF FINAL PACKAGING DEPARTMENT	41
5.1.1	<i>Organisation</i>	41
5.1.2	<i>Production</i>	42
5.1.3	<i>Production facts</i>	42
5.1.4	<i>Description linked Systems</i>	43
5.2	WORKFLOW	44
5.2.1	<i>Fine planning</i>	44
5.2.2	<i>Print batch (order) records</i>	44
5.2.3	<i>Request Components</i>	44
5.2.4	<i>Deliver Components</i>	44
5.2.5	<i>Commissioning</i>	45
5.2.6	<i>Prepare order</i>	45
5.2.7	<i>Processing the order</i>	45
5.2.8	<i>Redeliver material</i>	45
5.2.9	<i>Calculate reconciliation and check documents</i>	45
5.2.10	<i>Release order</i>	45
5.3	MATERIAL FLOW	46
5.4	DOCUMENTS.....	47
5.4.1	<i>Document description</i>	47
5.4.2	<i>Document problems</i>	50
5.5	INFORMATION AND DOCUMENT FLOW	52
5.6	CASE ACTIVITIES.....	54
5.7	REGULATORY COMPLIANCE	54
6	ANALYSIS.....	55
6.1	MES FUNCTIONS.....	55
6.1.1	<i>Why these functions</i>	55
6.1.2	<i>Why not the other functions</i>	57
6.2	DESCRIPTION MES WORKFLOW	59
6.2.1	<i>Fine planning</i>	59
6.2.2	<i>Print batch records</i>	59
6.2.3	<i>Request Components</i>	59
6.2.4	<i>Deliver Components</i>	60
6.2.5	<i>Commissioning</i>	60
6.2.6	<i>Prepare order</i>	60
6.2.7	<i>Process order</i>	60
6.2.8	<i>Redeliver components</i>	61
6.2.9	<i>Calculate reconciliation</i>	61
6.2.10	<i>Check data</i>	61
6.2.11	<i>Release order</i>	61
6.3	MATERIAL FLOW	61
6.3.1	<i>Transportation</i>	61
6.4	MES CASE ACTIVITIES.....	62
6.5	INTERFACES.....	62
6.6	ORGANISATION AND PRODUCTION REQUIREMENTS	64
6.6.1	<i>Business Reengineering</i>	64
6.6.2	<i>Defined equipment and stock points</i>	64
6.6.3	<i>Personnel</i>	64
6.6.4	<i>Regulatory Compliance</i>	65
6.6.5	<i>Flexibility</i>	66
6.7	BENEFITS.....	66
6.7.1	<i>Increased Information transparency</i>	66
6.7.2	<i>Cycle time and lead-time reduction</i>	66



6.7.3	<i>Improved planning and scheduling</i>	67
6.7.4	<i>Increased regulatory compliance</i>	67
6.7.5	<i>Documentation problem reduction</i>	67
6.7.6	<i>Defect reduction</i>	69
6.7.7	<i>MES supports the company objectives</i>	69
6.7.8	<i>Benefit summary</i>	70
6.8	COSTS.....	70
6.9	NET PRESENT VALUE	72
7	CONCLUSIONS	75
7.1	ADVANTAGES AND DISADVANTAGES.....	75
7.1.1	<i>MES advantages</i>	75
7.1.2	<i>MES disadvantages</i>	76
7.2	MES ASPECTS.....	77
7.2.1	<i>How to save the generated and existing knowledge</i>	77
7.2.2	<i>Customer orientation</i>	77
7.2.3	<i>Flexibility versus control</i>	78
7.2.4	<i>Interfacing</i>	78
7.2.5	<i>Information improvement or information overload</i>	79
7.2.6	<i>Regulatory Compliance changes</i>	79
7.2.7	<i>Financing a pilot project</i>	79
7.3	MES IN A PLANNING, EXECUTION AND CONTROL CONTEXT.....	80
7.4	MES IN OTHER INDUSTRIES.....	81
7.5	FINAL SOLUTION.....	81
7.5.1	<i>Strategy</i>	82
7.6	FURTHER STUDIES.....	83
8	REFERENCES	85
8.1	PUBLISHED SOURCES.....	85
8.2	COMPANY INTERN SOURCES.....	86
8.3	VERBAL SOURCES.....	86
8.4	ELECTRONIC SOURCES.....	87
	APPENDIX I – FINAL PACKAGING DEPARTMENT (SECOND FLOOR)	89
	APPENDIX II - FINAL PACKAGING DEPARTMENT (FOURTH FLOOR)	90
	APPENDIX III – CURRENT CASE ACTIVITIES	91
	APPENDIX IV – MES CASE ACTIVITIES	94
	APPENDIX V – NET PRESENT VALUE CALCULATIONS	96

Dictionary

Active components	Teil Gefertigte (TG) -Ware
Arrival	Wareneingang
Carton label	Kastenzettel
Central Storage	Hochregallager
Final Packaging Department	Endfertigung
Folding	Falzen
Carton	Faltschachtel
Holding (zone)	Bereitstellungszone
Labelling	Etikettieren
Insert	Packungsbeilage
Medical devices	Medizinische Einmalartikel
Order	Auftrag
Printing	Drucken
Shipping Department	Versand
Packaging	Verpacken
Packaging material	Packmittel
Shipping	Versand
Spare active components	Überschüssige TG-Ware
Standard package	Normpaket
Supervisor	Teamleiter
Documents	
Accompanying list for exemplification and quality control	Begleitliste für Muster und Qualitätskontrolle
Accompanying list medical devices	Begleitliste Einmalartikel
Accompanying list Packaging Material	PM-Begleitliste
Accompanying list semi finished	TG-Begleitliste
Assignment closure Final Packaging	Auftragsabschluss Endfertigung
Checklist control devices	Checkliste Kontrolleinrichtungen
IPK test certificate	IPK Prüfprotokoll
Hand over ready goods to shipping	Übergabe Fertigware an Versand
Operation verification	Tätigkeitsnachweis
Line clearance	Arbeitsplatzfreigabe
Pallet card	Palettenschein
Bill of Material	Stückliste
Production accompanying list	Fertigungsbegleitliste
Transport order	Transportauftrag
Workstation protocol	Arbeitsplatzprotokoll

1 Introduction

This chapter introduces the subject MES in a large content to the reader as well as describes the problems that are treated in this master thesis. The final part presents the purpose and the focus of the study.

1.1 Background

“Competing in today's markets can be compared to a high stakes race such as the Tour de France, Indianapolis 500 or America's Cup. The team that completes the course in the least time wins.”

Peter Cross, 1997¹

In a business context, the winner is the one who gets the product to the customer in shortest time. In process industry of today it has become important with flexible and customer focused production.² The manufacturers are driven to deliver quality products tailored for specific needs of individual customers.³

Focus on the entire Value Chain from the first producer to the final customer has become a key success factor. The competition has transformed from battle between companies to a battle between Value Chains.⁴

To remain competitive in today's market, manufacturers must become adopted to managing automation, which is able to manage change. With the rate of change accelerating exponentially, managing change is as critical as getting quality products out the door on time. The technology implemented today can aid or hinder the ability to do so.⁵ In the past there has been a focus on resource planning and accounting activities, this is not enough anymore. Today the focus has to be more on the product, needing a system that handles the production and controlling at the manufacturing level.

In this environment it is vital that real-time information is transparent, and distributed throughout the entire value chain. This makes the material handling more accurate and the production more flexible and reliable.⁶

¹ Cross, Peter (1997) “MES and ADC: A Dynamic Duo for Execution Excellence”, Page 1.

² Kaplan Robert S., Cooper Robin (1997) *Cost & Effect; Using Integrated Cost Systems to Drive Profitability and Performance*, Page 1-3.

³ Hakansson, Bill (1997) “Execution-Driven Manufacturing Management for Competitive Advantage”, Page 1.

⁴ Kilger, Cristoph & Stadler, Hartmut (2000) *Supply Chain Management and Advanced Planning*.

⁵ Wingate, Frank (1997) “Breakthrough Automation Strategies”

⁶ Persson, Göran & Virum, Helge (1998) *Logistik för konkurrenskraft*, Page 31

“Every manufacturing company is a complex web of activities and information flows. Properly managed these activities and this information can help the company achieve its goals.”

Bill Hakansson, 1997⁷

In this context it is also important to find the tools that can support the transformation of the company to a flexible, efficient and customer oriented manufacturer. Aventis Behring GmbH has already identified that a Manufacturing Execution System (MES)⁸ might be one tool that can help the company to achieve its goals.

Aventis Behring is in the process of defining what tasks should be included in a possible MES. In this process it is important that all functions of the company are joined to find a MES and a vendor that in the best way suits the companies and national and international authorities needs. To do this Aventis Behring has started a project group called MES Strategy where not only personnel from different departments are included but also consultants that are familiar with MES and also with the current SAP system. The company is in the process to decide if the next step will be to test a MES pilot system in the Final Packaging Department. This department has been chosen because Aventis Behring believes that there significant benefits can be reached. It will then be decided if MES is a valuable tool to use when competing on the market and if so extending MES to other sections.

1.2 Definition of the problem

In pharmaceutical industries control of the production process is essential. If something is done incorrectly, it could lead to disastrous consequences for the patient as well as the company. Pharmaceutical industry has to do everything in its power to avoid this scenario. Therefore Good Manufacturing Practice (GMP) is used in most of the larger pharmaceutical companies world wide, to ensure a high level of security.⁹ FDA the US Food and Drug Association is also forcing restrictions on companies producing medical products for the US market. The restrictions make the production less flexible and the administrative work becomes massive.

The administration causes increase in the lead-time. The work becomes complicated with many possibilities for mistakes. This has also been seen in the Final Packaging Department where approx 20 percent of the production orders are returned from the Quality Assurance Department due to missing values or filled out incorrectly etc. The problem is causing irritation and additional work.¹⁰

The large administration and documentation is limiting the information transparency. In the Final Packaging Department it is difficult to get information about specific order data as well as where in the production process an order and its specific material is located.

In order for a company to remain flexible it is vital to have a planning system and process that can be changed easily. In the Final Packaging Department the resource planning systems are not automatically reacting to changes in the production. If a delay or breakdown occurs in the process, this is not automatically changed in the estimated plan. A change due to production disturbance or changes in the customer order causes extra work because a new resource plan

⁷ Hakansson, Bill (1997) “Execution-Driven Manufacturing Management for Competitive Advantage”, Page 1.

⁸ McClellan, Michael (1997) *Applying Manufacturing Execution Systems*, Page 22-23.

⁹ Lange, Lothar, et al (1992) *Good Clinical Practice I*, Page 49-56.

¹⁰ Personal Interview, Thomas Schwarz

has to be made more or less by hand. It also becomes difficult to estimate when an order is going to be finished.

The plan is as described above to implement MES first as a pilot project in the Final Packaging Department to decide if the lead time and time for administrative work can be significantly reduced. Aventis Behring also believes that MES could increase the information transparency and simplify the planning process.

For companies thinking of introducing MES it is difficult to know if it is a valuable investment, which set of system functions are profitable to include, what the requirements are on such a system, what benefits can be reached, what the costs are, and how long the payback period of a MES is. They also do not know what aspects that have to be considered when implementing MES.

1.3 Purpose

The purpose of this master thesis is to:

Identify advantages, disadvantages and aspects that have to be considered when implementing MES.

The purpose can be divided into various objectives as follows:

- Identify production requirements
- Identify organisation requirements
- Identify benefits achieved with MES
- Identify costs with MES
- Decide if MES can be seen as a profitable investment
- Identify MES aspects

In the last part of the method chapter a model is presented illustrating the different elements that are considered to fulfil the purpose of this study.

1.4 Focus / limitations

The work is carried out at the Final Packaging Department. Therefore the focus will be to identify what requirements this department has on a MES system, requirements from other departments within Aventis Behring will not be considered.

The work will also focus on the standard work- material- and information-flow in the Final Packaging Department. Therefore no consideration will be taken to the exceptions that might occur in these flows.

1.5 Target group

This master thesis is addressed to employees of Aventis Behring and personnel within the institution of Packaging Logistics at Lund University. It is assumed that the reader has some knowledge about logistics and Supply Chain Management. Basic theories in these subjects will therefore not be presented in this study.

1.6 Disposition

In figure 1.1 is the disposition of this master thesis illustrated

The *first chapter* is an introduction to the master thesis, giving an overall picture of the background and the problem. The purpose of the study is defined. This chapter builds the main structure of the work carried out.

The *second chapter* deals with the method that has been used to reach the purpose of the thesis. Here different method theories are described, as well as how they have been used.

Different theories concerning planning, control and execution are presented in the *third chapter* called Frame of Reference. These theories create the base for the work. In this chapter also MES is explained. Giving a good help for the reader to achieve a further understanding in what MES is and what kind of possibilities this system creates.

Regulatory compliance concerning GMP and FDA rules that are specific for pharmaceutical industry and MES are presented in the *fourth chapter*.

In the *fifth chapter* the results from the empirical studies are revealed. The material flow, workflow, and information flow is presented. A deeper presentation of the Final Packaging Department and their requirements is made.

The theories and Empirical Results are analysed in the *sixth chapter*. It is also presented a solution of how a MES pilot system could be implemented in the Final Packaging Department. This is done with a possible MES workflow presentation as well as a case description. Finally the benefits and the costs that can be reached are listed as well as an estimated payback time of the investment.

In the last and *seventh chapter* generalisations are made and conclusions are discussed. In this chapter examples of further studies are suggested.

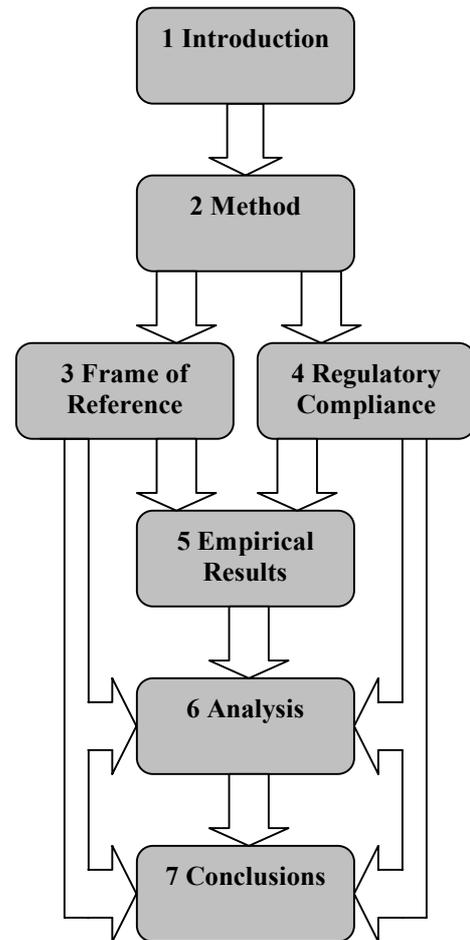


Figure 1.1 Disposition¹¹

¹¹ Own

1.7 Company description

1.7.1 Aventis¹²

“Aventis is dedicated to improving life through the discovery and development of innovative pharmaceutical products”

Aventis Homepage, 2002-09-19

As the statement above indicates is Aventis a Pharmaceutical company. It was established as late as December 1999 by the business combination of Hoechst AG and Rhône-Poulenc S.A., two pharmaceutical companies with long histories and large product portfolios.

Aventis core businesses is Prescription Drugs and Human Vaccines as well as the 50% equity interest in the animal health business Merial, a 50-50 joint venture with Merck & Co. Non core businesses are Aventis Behring, Dystar, Rhodia and Wacker. In figure 1.2 below an overview of the different branches of the Aventis Corporation is visualised.

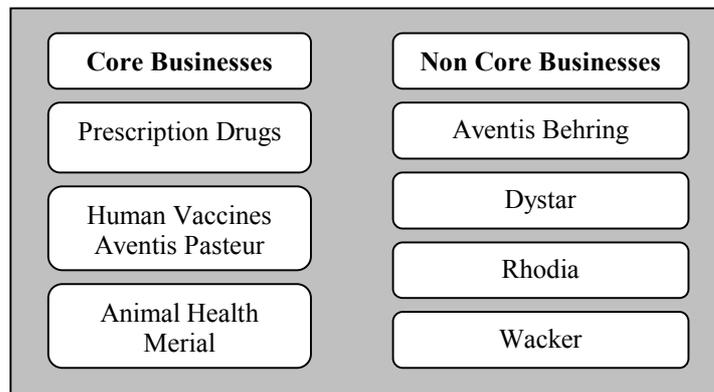


Figure 1.2 Aventis Organisational Structure¹³

In figure 1.3 relevant facts and figures are presented to create a picture of the company size.

Aventis is working on the worldwide market, but primary markets are United States, France, Germany and Japan. Major products offered are for example Allegra, Lovenox, Delix, Amaryl, Actonel and Lantus.

Sales (2001)	€ 18 billion
Research and Development Investments (2001)	€ 3,5 billion
Headquarters	Strasbourg, France
Other major sites	Bridgewater, USA Paris, France Frankfurt, Germany Tokyo, Japan
Employed core businesses (2001)	67,500
Employed total (2001)	90 000

Figure 1.3 Aventis facts and figures.¹⁴

¹² Aventis homepage, www.aventis.com, 2002-09-29

¹³ IBID

¹⁴ IBID

1.7.2 Aventis Behring

As described above Aventis Behring is a part of the Aventis Corporation. Aventis Behring is a world leading plasma producer. Even though Aventis Behring is a fairly new established corporation the company has a long history. The Behring name originates from its establisher Emil von Behring born in 1854. He began his medical path in the German army, 1889 when he was an assistant at the Institute of Hygiene Berlin, he discovered that it was possible to immunise against diphtheria and tetanus. Due to his discovery it became possible to mass-produce medicine, which could be used against different infections.¹⁵

In 1901 Emil von Behring got the first Nobel Prize in Physiology and Medicine for his discovery of serum against diphtheria. This made him famous worldwide and the money he received was used to finance his further studies and later on to build the Behring pharmaceutical company. He constructed his first production and research facilities 1904 in Marburg, Germany. Emil von Behring died in 1917 and the company was transformed into a stock company. The Hoechst AG became the Mother Company of Aventis Behring in 1945.¹⁶



Figure 1.4 Photo Emil von Behring¹⁷

The overall objectives of Aventis Behring are:¹⁸

1. The predictability and reliability of our investment

“We must eliminate the kind of surprises in our operations that keep us from reaching our performance objectives.”

2. The cost structure of our organisation

“Our expense base was built assuming a faster-growing and more profitable business. During 2002, we must take steps to reduce the level of expenditure until our performance improves.”

3. Bring new products in our pipeline

“The lack of new products in our pipeline will be an area of focus for our R&D and Business Development groups.”

4. Avoiding any failures in compliance

This is a mandate that forces us to maintain every aspect of our operations in tight control.

Aventis Behring is headquartered in King of Prussia, Pennsylvania, with corporate functions in both the United States and Germany. The company employs approximately 4,500 people worldwide, and operates manufacturing facilities in Kankakee, Illinois; Marburg, Germany; Barcelona, Spain and Vienna, Austria.¹⁹

¹⁵ Aventis Behring intranet, *intranet*, 2002-09-20

¹⁶ IBID

¹⁷ Infoscience homepage, *www.infoscience.fr*, 2002-10-22

¹⁸ Aventis Behring intranet, *intranet*, 2002-09-20

¹⁹ IBID

The company has a wide range of different plasma products to offer; treating different blood related diseases and disorders, which in many cases are lifesaving. For example Aventis Behring has products that help patients with complex coagulation disorders and Immunglobuline to treat disorders in the immune system. Aventis Behring also produces wound-healing products that help the healing after surgeries, burns, etc. The different products are marketed under names such as Humanalbumin, Fibrogamin, Beriate, Venimmun and Beriplex.²⁰

The more than three million litres of human blood plasma, which is needed in the production every year, are either bought from competing blood collectors or collected by the company themselves. Aventis Behring has for this task its own network of 80 plasma collecting centres in USA and 10 in Germany. This part of the company is its own subsidy, operated under the name Aventis Bio-services.²¹

²⁰ Aventis Behring intranet, *intranet*, 2002-09-20

²¹ IBID



2 Method

This chapter describes how the purpose of this master thesis is fulfilled. First is a short introduction to the method concept given. Fundamental theories are discussed and explained as well as how these theories have been used and how the actual work has proceeded is clarified. At the end of the chapter thoughts are given about the validity and reliability of the study.

2.1 Method introduction

“To get where you want, you have to know where you want to go.”

Abraham Lincoln²²

According to Eriksson & Wiedersheim-Paul the first step in research work is to define the purpose and the approach of the study, declaring what you want to do.²³ This has been done in the first part of this chapter and it is in this part the method is defined, explaining how the purpose will be fulfilled.

An investigation should be interesting, trustworthy and understandable.²⁴ These are aims that this study will try to achieve.

“Before I know what I should study I can not know how I should do it.”

Fog, 1979

According to Patel and Tebelius every researcher has to first identify the problem and then choose the method that best fits the purpose.²⁵ It is not always possible to say that one method is the best. Either can a survey be used, which usually means several observations and few aspects, or a case study can be done, which generates many different aspects but only a few observations.

The case study is more often qualitative and theory generating than quantitative and hypothesis testing according to Merriam, Sharan.²⁶ The qualitative and quantitative approaches will be further described below in this chapter.

²² Eriksson, Lars, Wiedersheim-Paul, Finn (1997) *Att Utreda Forska och Rapportera*, Page 11.

²³ IBID, Page 11.

²⁴ IBID, Page 35.

²⁵ Patel, Runa & Tabelius, Ulla (1997) *Grundbok i forskningsmetodik*.

²⁶ Merriam, Sharan (1994) *Fallstudien som forskningsmetod*, Page 19.

In this thesis a case study was performed. This is done to make sure that a deep understanding of the situation is reached. A case study is also better, when you do not know exactly what is important to look for²⁷.

2.2 Research approach

There are three different research approaches according to Arbnor & Bjerke, analytical approach, system approach and actor approach. Which approach that is used depends on what reality opinion and ideal the researcher has.²⁸

2.2.1 Analytical approach

The following quotation characterises the analytical approach:

“The entirety is equal to the sum of the parts. The knowledge should be independent of the individual. The parts are explained from verified judgements.”

Ingeman Abnor & Björn Bjerke, 1994

This approach is trying to explain an objective reality as far as possible. It is built on additive characteristic, meaning the entirety is equal to the sum of the different parts. Existing theories and techniques are used to verify or discard arranged hypothesis about reality. Verified or discarded hypotheses map out facts as a part of reality. Through the summary a broader picture of reality can be created. One can try to explain an effect through finding its cause. This approach is an assumption about reality, given that the more proven causes, the better explanation of the situation.²⁹

The results achieved with this analytical approach are cause and effect relations this is further illustrated in figure 2.1. The results should be able to generalise and use to create new knowledge.³⁰

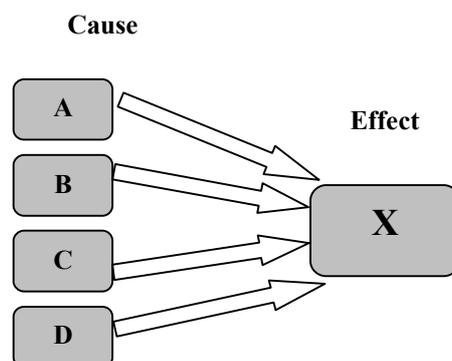


Figure 2.1 The analytical approach³¹

²⁷ Patel, Runa & Tabelius, Ulla (1997) *Grundbok i forskningsmetodik*.

²⁸ Abnor, Ingeman, Bjerke, Björn (1994) *Företagsekonomisk metodlära*, Page 240.

²⁹ IBID

³⁰ IBID, Page 65-95.

³¹ IBID, Page 78.

2.2.2 System approach

The following quotation characterises the system approach:

“The entirety differs from the sum of the parts. The knowledge is dependent of the system. The parts are explained from characteristics of the entirety.”

Ingeman Abnor & Björn Bjerke, 1994

As the quotation above indicates, this approach is an assumption that reality is arranged and the entirety differs from the sum of the parts. The relationship between the parts of the entirety is instead what is essential, one tries to find the forces in the system that causes an effect. A system can either be open or closed see figure 2.2. In an open system there are components that are not taken into account, even though they are causing an effect. In a closed system there are no surrounding components affecting the system.³²

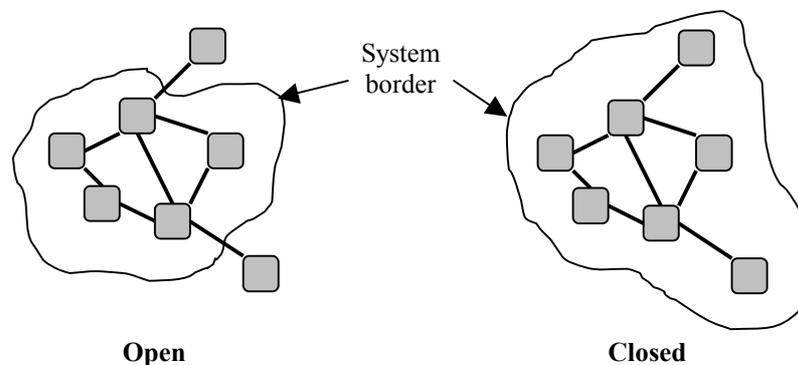


Figure 2.2 Open and closed systems³³

2.2.3 Actor approach

The following quotation characterises the actor approach:

“The entirety exists only as structures of meanings, which was socially constructed. Knowledge becomes dependent of the individual. The entirety is understood on the basis of the actors reality image.”

Ingeman Abnor & Björn Bjerke, 1994

The entirety is understood through the actors reality images. In this approach reality is identified as a social construction. To reach understanding one tries to understand the relation between the interpretations from different actors. The relations searched are how different interpretations and factors affect each other.³⁴

³² Abnor, Ingeman, Bjerke, Björn (1994) *Företagsekonomisk metodlära*, Page 125-136.

³³ IBID, Page 128.

³⁴ IBID, Page 175-185.

2.2.4 The method approach in this study

The open system approach is used in this study. The open system approach has been chosen because the Final Packaging Department can be seen as a systems containing several different components that are linked to and affecting each other. The entire system can be described through analysing the different parts.

The boundaries of the system of Final Packaging Department are clear. But it is not possible to exclude it from the environment. It has connections with several other systems and functions. In figure 2.3 below a rough illustration over the system that is used in this study is made. All the components are not fully evaluated in this study. The dotted box symbolises the border of the Final Packaging Department system. The elements not included in the box are other systems that are affecting the Final Packaging Department in some way.

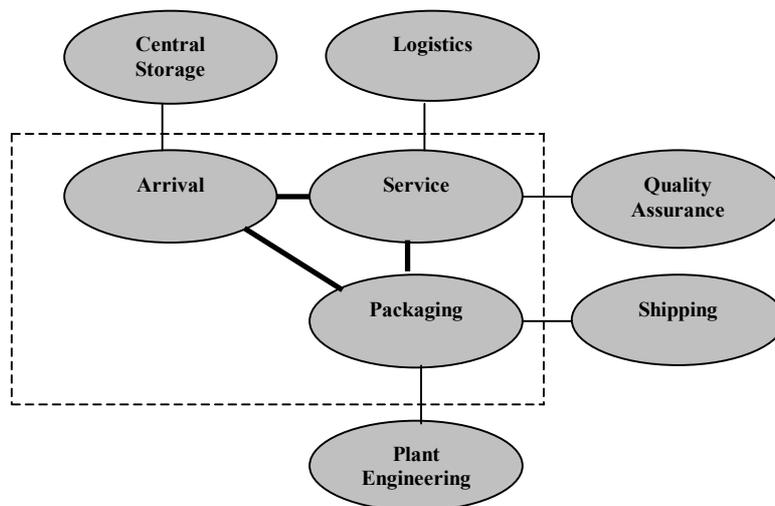


Figure 2.3 The open system of this study³⁵

The main components of the system are Arrival, Service, Packaging and the connection between the different parts. The sub components are Central Storage, Logistics, Quality Assurance, Shipping and Plant Engineering. The sub components will only be considered how they affect the open system. A deeper presentation of the different components is made in the chapter Empirical Results.

2.3 Quantitative and Qualitative studies

You can distinguish between quantitative and qualitative studies when making a research. The differences between these two methods are important to understand to make sure that the work is carried out by the most appropriate technique. It is important that the chosen method supports the purpose of the master thesis. But it is also essential to underline that it is not always possible to use a strict qualitative or quantitative approach, in many cases a combination of both is to prefer.³⁶ For example quantitative studies are often followed by verbal analyses.³⁷

³⁵ Own

³⁶ Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Page 14.

³⁷ Repstad, Pal (1993) *Närhet och Distans; Kvalitativa metoder i samhällsvetenskap*, Page 8.

2.3.1 Qualitative study

“Qualitative method is about characterising.”

Pal Repstad, 1993

Repstad interprets the qualitative method as a way to describe a situation.³⁸ In qualitative studies verbal analysis methods are used. The purpose of this method is to give an understanding with a low level of formalisation. It is central to collect information to achieve a deeper understanding of the object that is investigated. This gives the possibility to describe the overall picture and the context where the object is acting.³⁹ Merriam explains that the qualitative study has as main purpose to explain the meaning of a special phenomenon or experience.⁴⁰

Holme and Solvang describe the strengths with qualitative research as; the total picture of the phenomenon is created, a close contact to the object is formed and deeper understanding will be achieved. This type of study is characterised with a high level of flexibility.⁴¹

2.3.2 Quantitative study

In quantitative studies statistical methods are used and the results are presented in numerical figures. This method is also more formalised and structured, giving the researcher a higher level of control.⁴² The reliability of the research is accentuated which is further described below in this chapter. Other characteristics are distance to the object observed and selection method. The respondent is often randomly selected and the questions are asked without considering if the respondents think it is significant or not.⁴³

Merriam describes that the main purpose of the quantitative study is to break down a phenomenon in its components, which are transformed into variables that are then studied.⁴⁴ The strength in this approach is that generalisations are enabled through the structured way the data is collected. But instead there is a significant risk that the information collected is irrelevant.⁴⁵

2.3.3 This study

This study is a qualitative case study. The object observed is rather complex and deeper understanding is needed to make suitable conclusions. It is also not possible to use a quantitative study because only one system is observed and there are limited individuals within the system that have the required knowledge. The qualitative study was also chosen to keep a high level of flexibility.

³⁸ Repstad, Pal (1993) *Närhet och Distans; Kvalitativa metoder i samhällsvetenskap*, Page 8.

³⁹ Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Page 14.

⁴⁰ Merriam, Sharan (1994) *Fallstudien som forskningsmetod*, Page 30.

⁴¹ Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Page 80.

⁴² IBID, Page 14.

⁴³ IBID, Page 82.

⁴⁴ Merriam, Sharan (1994) *Fallstudien som forskningsmetod*, Page 30.

⁴⁵ Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Page 81.

2.4 Validity and Reliability

2.4.1 Validity

Eriksson and Wiedersheim-Paul define validity as a measurement tool's ability to measure what one intends to measure.⁴⁶ Further Lundal and Skärvad describe validity, as a way to make sure that the study does not contain any systematic errors.⁴⁷

For example the validity is high if the study addresses relevant questions without missing any central elements. The question should catch the reality as it is. You want to make sure that the questions asked correspond with the answers given. This is difficult to measure and sometimes even impossible, because you do not know what the right answer is supposed to be.⁴⁸

2.4.2 Reliability

Reliability is a measurement of how trustworthy the study is. A study is reliable if the same results would be reached if repeated with a different choice in the population and by a different researcher.⁴⁹ The Reliability is grounded on the assumption that there is only one reality and this will give the same result if the study of this reality is repeated.⁵⁰

Validity and Reliability relationship

You often think of reliability and validity as separate ideas but, in fact, they are related to each other. In figure 2.4 this is illustrated.

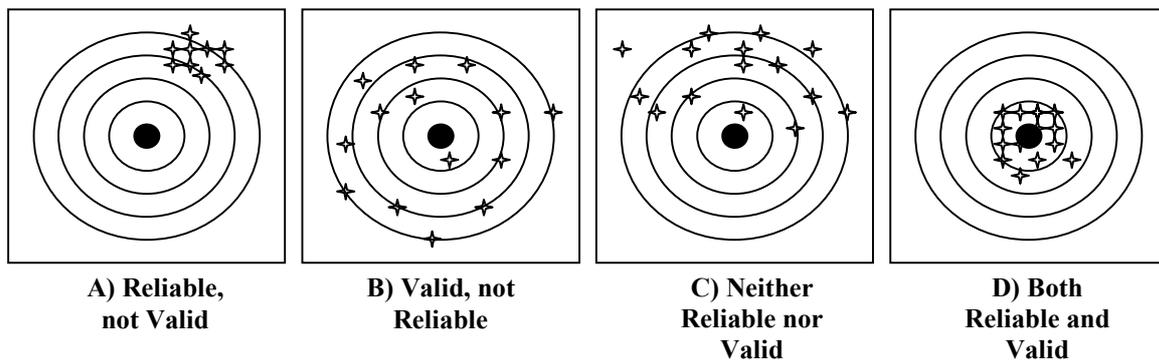


Figure 2.4 The relationship between reliability and validity⁵¹

One metaphor for the relationship between reliability that is often used is the one of the target. The centre of the target is the concept, which you are trying to measure. The figure above shows four possible situations. In the first one (A), the target is hit consistently, but the centre of the target is missed. That happens when measuring consistently and systematically the wrong value for all respondents. This measure is reliable, but no valid.

The second situation (B) shows hits that are randomly spread across the target. The centre of the target is seldom hit but as average you are getting the right answer for the group. In this case, you get a valid group estimate, but you are inconsistent.

⁴⁶ Eriksson, Lars T., Wiedersheim-Paul, Finn (1997) *Att Utreda Forska och Rapportera*, Page 38.

⁴⁷ Lundahl, U. och Skärvad, P-H. (1992) *Utredningsmetodik för samhällsvetare och ekonomer*

⁴⁸ Merriam, Sharan (1994) *Fallstudien som forskningsmetod*, Page 176.

⁴⁹ Eriksson, Lars T., Wiedersheim-Paul, Finn (1997) *Att Utreda Forska och Rapportera*, Page 39.

⁵⁰ Merriam, Sharan (1994) *Fallstudien som forskningsmetod*, Page 176.

⁵¹ Abnor, Ingeman, Bjerke, Björn (1994) *Företagsekonomisk metodlära*, Page 250.

The third scenario (C) shows a case where the hits are spread across the target and the centre is consistently missed. The measure in this case is neither reliable nor valid.

Finally (B), we see the scenario where the centre target is hit consistently. The measure is both reliable and valid.

The qualitative study gives a high validity due to the fact that one can secure a deep understanding with few respondents. On the other hand this type of study has low reliability. The quantitative study has instead the possibility to secure high reliability, this because many respondents are used in this study and better understanding for different factors can be achieved.⁵²

2.4.3 The validity and reliability of this study

How has this study been carried out to make sure that the centre of the target is hit consistently? This study is a qualitative case study giving a high validity. During the time spent in the Final Packaging Department a deeper understanding was created.

The reliability on the other hand has its weakness in the qualitative study. It has been my intention to make the study as reliable as possible, trying to be objective in my observations, using several respondents as well as discussing the relevance of my results with my supervisors.

Spending most of the time directly in the Final Packaging Department has increased the reliability of the study. It has appeared that observations made in an initial phase later were shown to be false or misunderstood. These incorrect observations would not have been identified if the main time of the study was not spent in the production.

2.5 Data collection

When collecting data two different ways can be used. These are:⁵³

- *Using already collected data (secondary information)*
- *Collecting new data (primary information)*

Collecting new data can be done in three different ways:⁵⁴

- *Observations*
- *Interviews*
- *Experiments*

2.5.1 Observation

Observations can either be direct or indirect. In the direct observation the researcher collects the data him/herself through observations for example watching how a work process is done. When secondary data are collected it is called indirect observations.⁵⁵ The observations can also be open or hidden. In an open observation the respondents are aware that they are observed which can result in that they act differently from how they usually do. The

⁵² Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Page 94.

⁵³ Abnor, Ingeman, Bjerke, Björn (1994) *Företagsekonomisk metodlära*, Page 240.

⁵⁴ IBID, Page 240.

⁵⁵ Eriksson, Lars T., Wiedersheim-Paul, Finn (1997) *Att Utreda Forska och Rapportera*, Page 16.

respondents do not know that they are observed in a hidden observation. This could instead lead to a conflict because the respondents have not been informed in advance.⁵⁶

2.5.2 Interview

Before making the interview or the questions to the interview, one has to decide what type of interview that should be used and in what form.⁵⁷

The interview could be either:

- *Standardised (everyone receives the same question)*
- *Not-steered (the questions have a low level of standardisation)*

The questions could be either:

- *Open (no answer alternatives)*
- *Closed (answer alternatives)*

The interview is not a simple task to perform there are many different aspects that have to be taken into account to make it suitable. Using an interview manual is an excellent way to prepare an interview. The interview manuals do not only include the questions asked but also what one want to get to know from each question. Follow up questions are used to lead the respondent on the right track.

One aspect that has to be taken into account is the interview situation. Is the respondent able to be anonymous if needed, where does the interview take place? Using a video recorder or a type recorder has advantages when collecting the data but it can also be disturbing to the respondent. Recording not only the verbal answers but also acts and motions with paper and pen is also an option.⁵⁸

All these aspects have to be considered when making an interview. There is not a right or a wrong way. Instead the researcher has to consider what aspects suit the best in every situation.

The interview could also be more or less guided. In a guided interview the researcher presents answers options, which provide control. Instead a not guided interview give the respondent the opportunity to bring forward the aspect he or she feel is significant.

2.5.3 Information handling

It is not sure that the collected data is useful. Firstly one has to make sure that the appropriate persons have responded, possessing the information wanted. The respondents must also have understood the questions correctly. If this is not the case the researcher has to get in contact with the respondents and clarify what was meant.⁵⁹

⁵⁶ Repstad, Pal (1993) *Närhet och Distans; Kvalitativa metoder i samhällsvetenskap*, Page 25-35.

⁵⁷ Abnor, Ingeman, Bjerke, Björn (1994) *Företagsekonomisk metodlära*, Page 242.

⁵⁸ Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Page 99-107.

⁵⁹ Eriksson, Lars T., Wiedersheim-Paul, Finn (1997) *Att Utreda Forska och Rapportera*, Page 85-87.

2.5.4 My data collection

Primary information

The primary information has been collected through observations and interviews.

Most of the time writing this master thesis has been done in or nearby the Final Packaging Department. This has made it possible to make continuous observations of the processes taking place. It has given an insight in the work processes and the problems that occur. If this thesis had been written at one other location the insight would not have been obtained. Spending so much time in the Final Packaging Department has created an open and friendly relationship to the respondents as well as reducing the risk for the respondents to be different from how they really are.

Interviews have been done with many different respondents in several departments. Most of the respondents have been asked questions more than once. In figure 2.5 a summary of the different departments and the amount of persons that has been interviewed within each department is presented.

Department	Amount
Final Packaging	9
Compliance	1
Quality	3
Shipping	2
Plant Engineering	1
Logistics	2
Information Solutions	1

Figure 2.5 Amount of respondents interviewed at each department⁶⁰

The questions have often been open and follow-up questions have been formulated to lead the respondents if necessary. Open questions have been chosen to make sure that no important information was left out. When writing the questions I tried to consider the purpose of the question. This was used as a support during the interview making sure that the respondent answered the question as intended.

Similar questions were asked to different respondents, this to make sure that as little information as possible was left out. It made it also more likely to confirm specific answers and increasing the reliability. The information from the interviews was recorded on paper trying to make sure that no information was neglected.

Secondary information

As secondary information literature and company information has been used.

To create deeper understanding of MES and relevant theories literature has been studied. Since MES is a rather new subject only little information was found in books. The most information about MES is therefore collected from electronic databases. The libraries at the Lund University and the Philips University in Marburg have been used to reach these databases.

On the Internet has search engines as Google, Evreka and Altavista been used to find specific information.

⁶⁰ Own

2.5.5 Frame of Reference

In the Frame of Reference, theories have been chosen that are concerning MES and different regulations. As indicated in the introduction, this study aimed for individuals with some basic knowledge in logistics and therefore are such theories not presented in this Frame of Reference. The theories chosen were picked out to be a base for the further studies as well as giving the reader a deeper understanding of MES and relevant FDA and GMP regulations.

2.5.6 Regulatory Compliance

In the pharmaceutical industries regulatory compliance is an important issue as stated in the initial chapter. An extra chapter is therefore included in this study treating this issue. This is made not only to give an understanding what regulatory compliance concerns but also to identify what makes pharmaceutical industries different from other industries. Such a discussion enables a broader generalisation of MES in the final chapter.

2.6 Analysing tools

2.6.1 Aeneis

The software Aeneis, made by Atoss, has been used as an analysing tool. In this software it is possible to model processes and make simulation of different cases. Further Aeneis can be used as a tool to calculate costs. The processes within the Final Packaging Department were already modelled in Aeneis. My task was then to make a new model where process changes due to an implementation of MES were made. Simulating the two different models gave an estimation of the potential benefits that can be reached when implementing MES in the Final Packaging Department.

2.6.2 Net Present Value

To evaluate if it is profitable to invest in a MES the Net Present Value method has been used. With this formula below it is possible to calculate how long time it takes until the investment has paid itself. It is in this formula possible to take inflation, return on investment as well as varied profit into account.⁶¹

$$t=0 \sum^n (Ft / (1 + k)^t)$$

$t=0 \sum^n$ = the sum of the formula $(F_t / (1 + k)^t)$ within the interval $t=0$ to $t=n$

F_t = the cash flow at the time t

k = the sum of the inflation and expected return of the investment.

⁶¹ Kungliga Tekniska Högskolans homepage, www.isk.kth.se.

2.7 Resource distribution

The resources given to this master thesis corresponds to six months work. In figure 2.6 below a Gantt-scheme is presented, showing how the resources are distributed over time. The darker areas in figure correspond to when the main work was carried out.

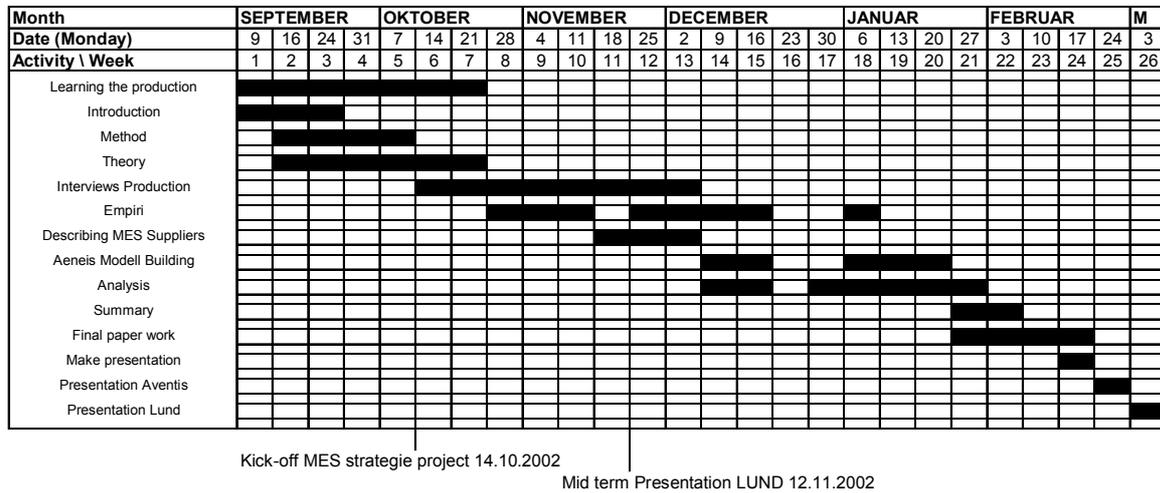


Figure 2.6 Resource distribution in a Gantt-scheme⁶²

⁶² Own

2.8 Model

The different elements that this master thesis constitutes of and how they are connected with each other is presented in the following model see figure 2.7. This model is used as a support for the actual work as well as help for the reader to understand the structure of the report.

The current situation in Aventis Behring Final Packaging Department is described through a material flow, information flow and workflow as well as different problems are identified.

It is not only the requirements from the production and organisation that has to be taken into account when implementing MES in pharmaceutical industries. It also has to be analysed what Regulatory Compliance demand on the system.

An explanation of how MES solution could be made in the Final Packaging Department is made. From this knowledge and the comparison with the current situation advantages and disadvantages can be identified as well as MES aspects identified.

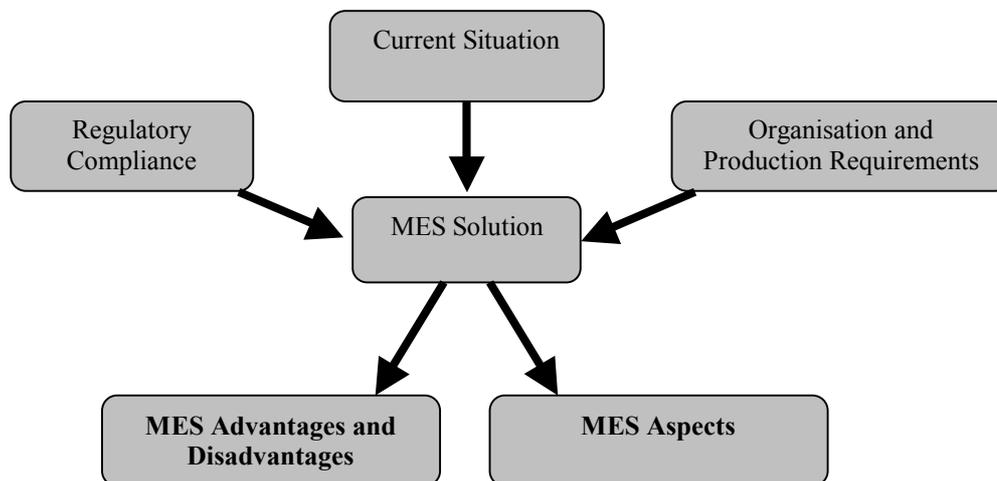


Figure 2.7 The thesis model⁶³

⁶³ Own

3 Frame of Reference

The theories used in this master thesis are presented in this chapter. A explanation of control system as well as a presentation of MES is made.

3.1 Planning, Execution and Control

As long as manufacturing has occurred there has been some kind of way to distribute the resources, perform the skills and control the processes. You firstly have to plan where, when and with what resources the product should be manufactured. It is obvious that some kind of planning and controlling has to be made to produce a product, even if it this is done without any written procedures it is still planning, execution and control.⁶⁴

It was first in the 1920's when decision makers began to put an increased weight on the liquidity of assets that planning and control became an important issue. Fast turnover became a goal in many organisations. Since the produced products have become more complicated, the demands on the planning, execution and control has increased.⁶⁵

Planning is described as a way of guiding for future actions and dedicating resources in time to perform defined activities.⁶⁶ Dietger Hahn separates planning into four different categories:⁶⁷

1. *General goal planning* – This category is treating overall goals on corporate level
2. *Strategic planning* – This is a lower level considering planning in a specific area for example research and development or environmental issues
3. *Operative planning* – is going into detail concerning how the operations should act.
4. *Entire business outcome and finance planning* – is where financial performances of the company is planned.

Pottoff and Trescher declare that it is difficult to find the right level of planning. They say that it is possible to under-plan or over-plan. When under-planning is made a better planning would generate increased benefits to the process. When over planning the costs for performing the detailed plan is larger than the benefits received. It is therefore important to try

⁶⁴ Silver, Edward, Peterson, Rein (1985) Decision Systems for Inventory Management and Production Planning, Page 3-12.

⁶⁵ IBID, Page 3-12.

⁶⁶ Heinen, Edmund (1991) *Industrie Betriebs Lehre*.

⁶⁷ Hahn, Dietger (1994) *PUK – Controlling Konzepte*.

to make the planning complete and catch relevant aspects.⁶⁸ According to Hahn one also has to be careful not to over plan because this reduces the co-worker motivation.

One other important aspect in planning according to Hahn is the flexibility. It is important that the system can easily adjust to changes in the plan.⁶⁹

Control is described as an extension of the planning where a comparison is made between how it should be and how it currently is. In this way deviations can be identified.⁷⁰ Control is made to rule, link, steer and regulate processes according to Peter Horvath.⁷¹ Dietger Hahn describes the main goal of control to make sure that the plan is fulfilled and to improve the management process. He further defines four secondary goals of planning:⁷²

1. Goal orientation and coordination
2. Find and reduce risks
3. Decrease the complexity
4. Increase the flexibility

Also by control it is possible to have a too high or a too low level. Control comes to a point where the costs of further control are higher than the benefits achieved.⁷³

As described above planning and control is closely linked or as Edmund Heinen describes it:⁷⁴

“Planning without control is senseless and control without planning impossible”

Edmund Heinen, 1991

According to Anthony and Govindarajan every control system has at least four elements:⁷⁵

5. Detector
6. Assessor
7. Effector
8. Communication network

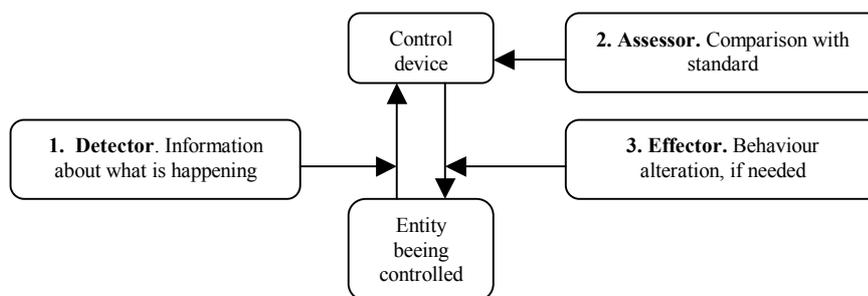


Figure 3.1 Basic elements of any control system⁷⁶

The detector is measuring what actually is happening see figure 3.1. The assessor is a device that determines the significance of what is happening. To do this it compares what is

⁶⁸ Potthoff, Erich and Trescher Karl (1986) *Controlling in der Personalwirtschaft*

⁶⁹ Hahn, Dietger (1994) *PUK – Controlling Konzepte*.

⁷⁰ Hahn, Dietger (1994) *PUK – Controlling Konzepte*.

⁷¹ Horvath, Peter (1991) *Controlling*.

⁷² Hahn, Dietger (1994) *PUK – Controlling Konzepte*.

⁷³ Heinen, Edmund (1991) *Industrie Betriebs Lehre*.

⁷⁴ Heinen, Edmund (1991) *Industrie Betriebs Lehre*.

⁷⁵ Anthony, Robert (2000) *Management Control Systems*, Page 1-3

⁷⁶ IBID, Page 2

happening with some standard or expectation of what should happen. Feedback is done through the effector, which alters the behaviour if the assessor indicates the need to do so. A communication network is needed to transmit the information between the different devices.

3.2 Computer systems

With the introduction of computers new possibilities has been obtained. It is now possible to manage complex systems with different computer software. A widely used manufacturing control system is Manufacturing Resource Planning (MRP). It is estimated that somewhere in-between 30 000 and 70 000 systems are installed around the world.⁷⁷ This is making it the dominant manufacturing management methodology in the world. In the beginning this system was not intended to include so many different functions. In fact, the standard system has evolved to include so many functionalities and manufacturing plants that many vendors now market their MRP products as Enterprise Resource Planning systems (ERP).⁷⁸

In the late 1980's and early 1990's, another generation of control systems became available. These systems attempted to solve the "islands of information problem" by providing broad comprehensive solutions. MRP systems became Enterprise Resource Planning. Distribution Resource Planning became Supply Chain Management Systems and the shop floor solutions evolved into integrated MES systems. At the control level an evolution took place, where computers gradually replaced manual controls, process and machine management became increasingly sophisticated. There was a need for rapid management of information and control; real time execution became a keyword.⁷⁹

Today the boundaries between the traditional systems are not as clear, many of the functions that were specific for one system is today adopted by other systems.⁸⁰

But also other systems are used in different areas. Below some major manufacturing systems categories are listed.⁸¹

- *Enterprise Resources Planning (ERP)*- used for materials planning and similar functions.
- *Supply Chain Management (SCM)* - includes forecasting, distribution and logistics.
- *Sales and Service Management (SSM)* – Software used by the sales force.
- *Product and Process Engineering (P/PE)* – is (CAD/CAM), process modelling, and Product Data Management.
- *Controls* – are usually distributed control systems (DCS), programmable logic controllers. (PLC), distributed numerical control (DNC), supervisory control and data acquisition (SCADA) systems.

Each of these system categories includes various functions and product types.⁸²

One significant benefit that is reached through computerized planning and control systems is the possibility to get different performance data from the systems. Through this data

⁷⁷ Hakansson, Bill (1997) "Execution-Driven Manufacturing Management for Competitive Advantage", Page 3-5.

⁷⁸ IBID, Page 3-5.

⁷⁹ Hakansson, Bill (1997) "Execution-Driven Manufacturing Management for Competitive Advantage", Page 3-5.

⁸⁰ IBID, Page 3-5.

⁸¹ Hakansson, Bill, Schaeffer, Julie (1997) "MES Explained: A High Level Vision", Page 14.

⁸² IBID, Page 14.

improvements of the process can be made reducing excess inventories, excess capacity, excess labour costs and lead times.⁸³

3.3 Manufacturing Execution System (MES)

3.3.1 History

As described above is MRP a widely used manufacturing control system. It was in this context the MES evolved, first developed by the semiconductor industry in the 1980s to improve manufacturing performance and flexibility.⁸⁴

According to Michael McClellan was the purpose of the first generation of MES to⁸⁵:

- *Reduce past due orders*
- *Reduce inventory levels*
- *Reduce lead times*
- *Improve information flow*
- *Eliminate repetitive tasks*

The Manufacturing Execution Systems Association (MESA) was formed in 1992 by the leading Manufacturing Execution System software vendors. The non-profit association provided a legal forum for competitors to work together to expand awareness and use of manufacturing technology, particularly MES.⁸⁶

3.3.2 What is MES

Adler et al briefly explains MES as the link between production planning and production process control⁸⁷. Young means that one should view MES as glue that binds the business planning systems with real-time process control systems. He illustrates this in a simple illustration, also presented here as figure 3.2. The Business system is working with a time frame of weeks, days or hours. MES becomes a bridge to the control system that is working in real time.⁸⁸

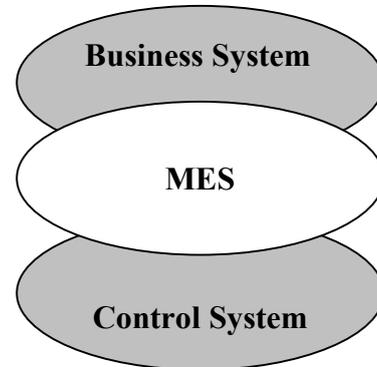


Figure 3.2 Simple MES model⁸⁹

⁸³ Vollman, T. et al (1988) *Manufacturing and Control Systems*, Page 5.

⁸⁴ Scott, Douglas (1996) "Comparative Advantage Through Manufacturing Execution System", Page 180.

⁸⁵ McClellan, Michael (1997) *Applying Manufacturing Execution Systems*, Page 115-16.

⁸⁶ MESA homepage, www.mesa.org

⁸⁷ Adler, David J. (1995) Execution System reduce the cost of production for bulk pharmaceuticals" Page 343.

⁸⁸ Young, Stephen L. (1995) "Technology... The enabler for tomorrow's agile enterprise", Page 335.

⁸⁹ IBID, Page 336.

MESA International deeply defines MES as:⁹⁰

“Manufacturing Execution Systems (MES) deliver information that enables the optimisation of production activities from order launch to finished goods. Using current and accurate data, MES guides, initiates, responds to, and reports on plant activities as they occur. The resulting rapid response to changing conditions, coupled with a focus on reducing non value-added activities, drives effective plant operations and processes. MES improves the return on operational assets as well as on-time delivery, inventory turns, gross margin, and cash flow performance. MES provides mission-critical information about production activities across the enterprise and supply chain via bi-directional communications.”

MESA International, 1997

MES is a software program that supports the manufacturing process. Making it more efficient through removing and reducing a large amount of the paper work, which in many industries captures more and more of the resources available. MES simplifies this work.

A key word in MES is transparency, making the information available throughout the company and sometimes also to other parts of the value chain. This is enabled because parts of the work that was former recorded on paper, now is recorded electronically. It is with the electronic form easy to distribute the relevant information to the right place at the right time. The increased transparency gives support to different company functions, not only for managers and supervisors but also to the shop floor operators, through giving them information that is essential for making the right decisions at all times.

One other keyword is real time. The manufacturing processes are surveillanced automatically and directly by MES, recording real time data. Real time data is especially important in process industries where defects have to be recorded quickly so that immediate action can be taken. If this does not happen quickly a large amounts of products will be produced, which has to be discarded.

MES is giving the opportunity to a higher level of Track and Trace. Before it was only possible to identify that the products where in production. MES gives the opportunity to trace products within the production process. Supply chain pressures demand that many manufacturers have an accurate view of where products and materials are at all times, in order to effectively supply customers with product Just In Time.

⁹⁰ Hakansson, Bill, Schaeffer, Julie (1997) “MES Explained: A High Level Vision“, Page 3.

3.3.3 MES users

It is difficult to list every type of business where MES is applicable. But Michael McClelland lists in his book a couple of potential candidates. Some of the candidates are as follows:⁹¹

- *Manufacturers of aircraft equipment*
- *Appliance Manufacturers*
- *Automotive industries*
- *Breweries and soft-drink processing*
- *Electronics and computer equipment manufacturers*
- *Food processing companies*
- *Printing operations*
- *Pharmaceutical, chemical and petroleum industries*

The primary users of the MES data within the factories is personnel that are focusing on manufacturing productivity. This is for example personnel such as plant-, materials-, maintenance-, quality-, and scheduling- managers. But also personal, such as operators and technicians, has use for the information that MES provides to optimise the production.

3.3.4 MES connected with other manufacturing systems

MES is only one of several major information system types aimed for manufacturing companies as described above. MES touches all of these categories of systems (see figure 3.3). Integration between MES and the other management systems is a key to gain benefits not only of MES, but also of these other systems. MES becomes the link between the various systems, providing the other systems with information.

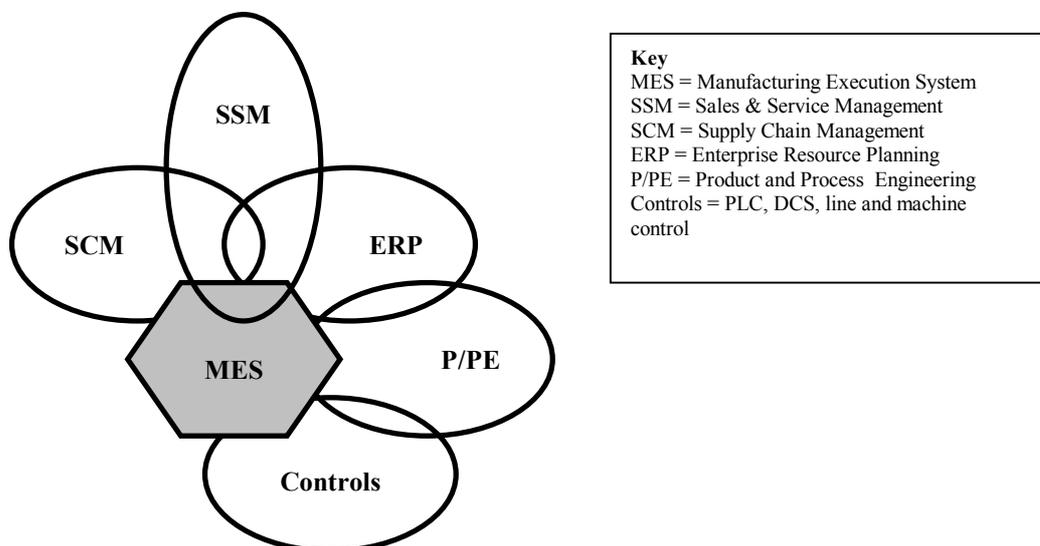


Figure 3.3 MES context model⁹²

From MES ERP receives information such as: costs, cycle times, throughput and other production performance Data. MES supplies the SCM system with data about actual order status, production capacities and capabilities. Sales and Service Management applications is linked to MES, to get the latest information about the production process. Product and Process

⁹¹ McClelland, Michael (1997) *Applying Manufacturing Execution Systems*, Page 22-23.

⁹² Hakansson, Bill, Schaeffer, Julie (1997) "MES Explained: A High Level Vision", Page 14.

Engineering is tuned, based on the product yield and quality measured by the MES. Controls receive instructions that reflect the facilities optimum way to run at a given moment.

But of course MES does also receive data from these other systems, ensuring that their information is transparent through the factory. This makes it also able for MES to rapidly distribute the information from one part of the system to another.

Sometimes overlapping functions will occur. For example, either ERP or MES can dispatch work to the floor, both supply chain management and MES include scheduling and process plans. Documents can be created either by the product/process engineering or by the MES.

Data acquisition and collection functions in control systems generally aim at improving the individual process or line under control, while in MES, this function aims to analyse how effectively a given process is contributing to the overall performance of the plant. This gives the possibility to reach a total view of the effectiveness in the plant.

3.3.5 Functions⁹³

MESA international has defined eleven functions, which are performed by MES. These eleven functions provide the core information base to run almost any type of plant. The functions are:

1. Resource Allocation and Status

The Resource Allocation and Status function manages the resources including; machines, tools labour skills, materials, equipment and other entities such as documents that must be available in order make work start at a specific operation. MES provides a history of resources and ensures that equipment is properly set-up for processing. This function provides the real time status of the resources.

2. Operations/Detail Scheduling

This function provides sequencing and timing to optimise the plant performance. It is finite and it recognises alternative and overlapping/ parallel operations in order to calculate the exact time in detail.

3. Dispatching Production Units

MES manages the flow of production units. This is done with this function through guiding jobs, orders, orders, lots, and work orders. It gives the command to send materials or orders enabling the process to start. Dispatch information is presented in sequence, in which the work needs to be done and changes in real time, as events are occurring on the factory floor. It has the ability to alter a prescribed schedule on the factory floor. Through this function it is able to control the amount of Work In Progress at any point.

4. Document Control

Records that must be maintained within the production unit are managed by MES. This includes for example work instructions, recipes, drawings, standard operation procedures, batch records and shift-to-shift communication. This function sends instructions to the operations, including providing data to operators or recipes to device controls. Environmental, health and safety regulations, and information such as corrective action procedures are also included.

⁹³ Hakansson, Bill (1997) "MES Functionalities & MRP to MES Data Flow Possibilities", Page 6-7.

5. Data Collection/Acquisition

The data is collected from the factory floor, either manually or automatically from equipment, in an up to a minute time frame. The function provides a link to obtain the intra operational production. It is this function that enables the creation Electronic Batch Records (EBR).

6. Labour Management

This function traces and directs the personnel in a real time frame. This includes time and attendance reporting, as well as certification tracking. This data can then be used as a basis for Activity Based Costing. The MES function can also suggest resource allocation to determine optimal assignments.

7. Quality Management

Quality management provides real time analysis of measurements and data, collected from manufacturing to assure proper product quality control. This function can also recommend actions that should be taken to correct a problem. In this part Laboratory Information Management Systems (LIMS) also could be included, which simplifies the offline inspections.

8. Process Management

The Process Management monitors the production and either automatically or provides decision support to operators to correct and improve the in-process activities. The function also direct the flow of work within the plant based on planned and actual production activities. It may include alarm management to make sure factory persons are aware of changes and disturbances in the production.

9. Maintenance Management

This function tracks and directs the activities to maintain the equipment and tools to insure their availability for manufacturing and insure scheduling for periodic or preventive maintenance. Of course a history is also maintained.

10. Product Tracking and Genealogy

Product Tracking and Genealogy provides the visibility to where work is at all times. Included information is for example who is working on it, components by supplier, lot, serial number, current production conditions and any alarms, rework or other exceptions related to the product. This function gives the opportunity to create a historical record as well.

11. Performance Analysis

This function provides reports of actual manufacturing operation results along with the comparison to past history and estimated results. Performance results include such measurements such as resource utilisation, resource availability and cycle time.

As described above these eleven functions constitute the base for information, making it possible to run almost any type of factory. But the MES can also consist of any combination of these eleven basic MES functions making the system as suitable and beneficial as possible.

3.3.6 Benefits

The Manufacturing Execution Systems Association (MESA) has performed a research concerning actual benefits that manufacturers have realised when implementing MES. This study, titled “Report From The Field,” was carried out in 1993 and 1996. This study notes that ninety percent of the respondents consider MES to be one of their top three priorities and one in three consider it as the top priority. Payback periods ranged from 6 to 18 months and overall life cycle costs were dramatically reduced. The following figure 3.4 presents some of the benefits MESA observed.⁹⁴

Benefit Studied	Average Reduction
Reduces manufacturing cycle time	45%
Reduces or eliminates data entry time	75%
Reduces Work in Progress (WIP)	17%
Reduces/eliminates paperwork between shifts	56%
Reduces lead times	32%
Improves product quality (reduces defects)	15%
Reduces/eliminates lost paperwork/blueprints	57%

Figure 3.4 MESA study results on operational level⁹⁵

The benefits presented above are on the operational level. Other benefits that were observed at this level were empowered employees, rapid process upgrades and informed decision support. On the corporate level the study observed higher return on assets, improved customer service, regulatory compliance, lower operating costs, reduced capital expenses, reduced product liability, delivery reliability, lower inventory carrying costs and reduced floor space.

Adler et al accentuate that the work spent on handling documents can be significantly reduced. But they also underline that additional staff is needed to maintain the new system.⁹⁶ It has also been observed that the users of MES have seen a significant increase in the benefits over time.⁹⁷

3.3.7 Costs

According to Adler et al the major costs to implement a MES system are the design costs, purchase costs and installation costs. Further the authors underline that you should not forget the costs for reengineering the business process. The initial costs concern evaluation and propose reengineering activities. Then the new business process has to be evaluated as well as which software and hardware that best supports the process.⁹⁸ The Adler et al pronounce that it is clear that MES has benefits but one should not forget that the expenses also could be considerable and difficult to estimate. When deciding to implement a MES system it is

⁹⁴ Hakansson, Bill (1997) “The Benefits of MES: A Report from the Field”, Page1-9.

⁹⁵ IBID

⁹⁶ Adler, David J. (1995) ”Execution System reduce the cost of production for bulk pharmaceuticals”, Page 345-346.

⁹⁷ Hakansson, Bill, Schaeffer, Julie (1997) “MES Explained: A High Level Vision“, Page 8.

⁹⁸ Adler, David J. (1995) ”Execution System reduce the cost of production for bulk pharmaceuticals”, Page 346-347.

therefore important to weigh the pros versus the cons. It is also essential to find a vendor that best supply the tools needed to achieve a profitable MES system.⁹⁹

Scott, Douglas underlines that the hardware and software costs are only a small part, normally 10-20% of the total costs of a MES system. Other costs that have to be taken into account are for example; configuration management, customisation, initial implementation, training the users, support, integration with other systems, installing new releases, testing and validation, database loading, performance tuning, backup and security management.¹⁰⁰

3.3.8 Evaluation¹⁰¹

There are not two similar plants and therefore every plant needs to have its own MES applications. Therefore a deep evaluation of the manufacturing process has to be done to be able to configure the software so that it matches the specific plant model.

There are also many suppliers of MES with a variety of different products. It is central for potential buyers to first evaluate their own needs carefully.

There are two major dimensions of choice in MES:

- *Functional Scope*
- *Functional Operation*

Functional Scope

This dimension is focusing on the needs of the plant and the software products that serve them. Different combinations of functionality are included as described above. Firstly the special needs in each plant are located. Then it is established which combination of functions that best fulfils these needs. Some plants will only need a few of the different function; others will need all eleven. In the functional scope the focus is to find standard MES components to solve a problem.

Functional Operation

The functional operation is looking deeper into the processes. It is often essential variations in how similar processes are carried out in different plants. For example, companies in a regulated industry such as pharmaceutical or medical devices will need a level of product tracking that is troublesome. In the functional operation one goes further and customises the standard components to fit special needs. Such customisation can be costly.

Software vendors also have varied approaches to MES. Some have focused narrow and deep others have tried to cover all of the MES functionalities. One industry that uses most of the functionalities successfully is the semiconductor industry. Due to the various supplier approaches it is important to carefully investigate what vendors best suits the needs.

⁹⁹ Adler, David J. (1995) "Execution System reduce the cost of production for bulk pharmaceuticals" Page 346-347.

¹⁰⁰ Scott, Douglas (1996) "Comparative Advantage Through Manufacturing Execution System", Page 181.

¹⁰¹ Hakansson, Bill, Schaeffer, Julie (1997) "MES Explained: A High Level Vision", Page 7-8.

4 Regulatory Compliance

In this chapter regulatory compliance specific, for the pharmaceutical industry is presented. The focus has been to highlight areas that are concerning MES and the Final Packaging Department. This is done to give an understanding for the special circumstances in which the pharmaceutical industry is operating.

4.1 FDA Regulations

The Food and Drug Administration (FDA) regulates the pharmaceutical industries that market products in the United States. FDA is giving regulations and directions in what way the industry should work. These directions and regulations are used as guidelines when FDA is evaluating these pharmaceutical companies

4.1.1 Electronic Records

In response to the pharmaceutical industries request to use paperless record systems, FDA issued new regulations in the 21 Code of Federal Regulations (CFR) part 11, titled; Electronic Records; Electronic Signatures, Maintenance of Electronic Records. This regulation is a guideline, which explains what criteria have to be fulfilled to make FDA consider the electronic records equivalent to paper records. This guideline is therefore not forcing anyone to start using paperless recording systems.

The regulation is mainly concerned about the authenticity and readability of the electronic records created.

FDA requirements

The regulation concerning electronic records is divided into several different sections, which will be further described here below.

In section 11.10, titled *controls for closed systems*, it is stated that the authenticity, integrity and the confidentiality of electronic records have to be ensured. The system also has to ensure that the signer cannot readily reject the signed record as not genuine. This section is only applicable to closed systems.

To satisfy this requirement the procedures and controls shall include the following:

“Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.”¹⁰²

“The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the agency.”¹⁰³

“Protection of records to enable their accurate and ready retrieval throughout the records retention period.”¹⁰⁴

To protect the records, procedures should be written describing:¹⁰⁵

- How electronic records will be maintained
- Storage conditions and precautions
- Retrieval and access restrictions
- The technical approach for long term electronic record storage
- Which personnel that are responsible for relevant tasks

“Limiting system access to authorised individuals.”¹⁰⁶

“Use of secure, computer-generated, time-stamped audit trails that, among other things, shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.”¹⁰⁷

As it is stated here, there is a need for an audit trail. This data has to be computer generated. It is not allowed to store this data on paper and the data has to be stored as long as the file exists.¹⁰⁸

Controls for open systems or section 11.30 deals with additional measures that has to be considered if the system is open. Measures as for example, encryption and use of appropriate digital signature standards, is to make sure that confidentiality, integrity and record authenticity are kept.¹⁰⁹

The signed electronic records should contain the following information, the printed name of the signer, when the signature was executed with date and time and why the signature was made. This is stated in section 11.50 *Signature manifestation*.¹¹⁰

In section 11.70 *Signature / record linking*, it is written that electronic signatures and hand-written signatures executed to electronic records must be linked to their respectively records,

¹⁰² Food and Drug Administration (1997) “Electronic Records, Electronic signature“.

¹⁰³ IBID

¹⁰⁴ IBID

¹⁰⁵ Food and Drug Administration (2002) “Guidance for Industry 21 CFR Part 11; Electronic Records; Electronic Signatures Maintenance of Electronic Records”, Page 8.

¹⁰⁶ Food and Drug Administration (1997) “Electronic Records, Electronic signature“.

¹⁰⁷ IBID

¹⁰⁸ ABB home page, www.abb.com.

¹⁰⁹ Food and Drug Administration (2002) “Guidance for Industry 21 CFR Part 11; Electronic Records; Electronic Signatures Maintenance of Electronic Records”, Page 8.

¹¹⁰ IBID, Page 8.

so that signatures cannot be excised, copied or otherwise transferred to falsify an electronic record by ordinary means.¹¹¹

Under the section 11.100, is stated that each signature must be unique to one individual and must not be reused by anyone else.¹¹²

Section 11.200 present that electronic signatures, not based on biometrics, must employ at least two identification components such as an identification code and password. It is also required that the electronic signature is only used by the genuine owner. This makes it more difficult for anyone to forge a signature.¹¹³

In 11.300, it is stated that signature controls shall ensure that there is not two individuals that have the same password and identification code. Further also the password should be remade periodically to ensure that ageing does not occur. Cards and tokens etc. must be possible to block, to ensure that no unauthorised person gets access, which could be the case if for example a card is lost or stolen. If any unauthorised use is detected this should be automatically recorded.¹¹⁴

*Further FDA guidelines*¹¹⁵

In the guidelines, set by the FDA, it is also given considerations about how the maintenance of the electronic records should be made. In this guideline it is said that:

One should identify the factors that can affect the reliability of the records. These should be controlled while the records are preserved. Examples of things to control are, the software and hardware status as well as the processes of extracting and presenting information. If the factors are not controlled properly the information might not be accurate, usable or complete.

One should ensure that the information has availability and readability. With this it is meant that one should periodically access the records to ensure that the information is recorded. How frequent this has to be done depends on what is recorded, if there is a backup and what type of media is used. It is also advised that a backup of the most important information is kept.

The storage of the records should be done under appropriate environmental conditions. To make sure that the records are preserved one has to consider for example temperature, humidity, dust, vibration and sources of electromagnetic and radio frequency interference. These factors should then continuously be monitored and controlled.

The ability to process the information throughout its retention period should be preserved. By being able to process the information it is meant the ability to effectively and efficiently reconstruct events. It is further important that the records are in such a form that they are suitable for FDA to review, inspect and copy.

Accurate copy processes are essential to ensure that no data is vanished while replicated. To ensure this the copy system used, has to have a built in copy verification mechanism that prevents inaccurate or incomplete copy from being made.

¹¹¹ Food and Drug Administration (2002) "Guidance for Industry 21 CFR Part 11; Electronic Records; Electronic Signatures Maintenance of Electronic Records"

¹¹² IBID

¹¹³ IBID

¹¹⁴ IBID

¹¹⁵ IBID

4.2 Good Manufacturing Practice

Good Manufacturing Practice (GMP) include regulations and guidelines that should help industries to produce safe products. The GMP is used internationally to describe a set of principles and procedures that, when followed by manufacturers, helps to ensure that the products manufactured have the required quality. A basic rule of GMP is that quality cannot be tested into a batch of product, but must be built into each batch of product during all stages of the manufacturing process.

GMP covers all aspects of production, from the starting materials, buildings and equipment to the training and personal hygiene of the staff. Detailed written procedures are essential for each process that could affect the quality of the finished product. There must be systems to provide documented proof that correct procedures are consistently being followed at each step in the manufacturing process.

In order to be a GMP compliant manufacturer one has to write Standard Operating Procedures (SOPs). The purpose of a Standard Operating Procedure is to describe the performance of a controlled process. Compliance with SOPs ensures that activities are conducted in a standardised and consistent way, thus reducing the variability of how a specific process is performed. SOPs are based on the idea that consistency in performing a specific process that is designed in full compliance with regulatory requirements will increase the likelihood of providing an end product of consistently high quality.¹¹⁶

In US the FDA create the regulations and guidelines, the same is done in the European Union by the EU-commission. Because of this two different systems were created, one for the US and one for the European market. Even though the two systems have similar content, it is creating problems for manufacturers that are marketing their products on both markets. Therefore the FDA and the EU-commission are trying to agree on a general standard.¹¹⁷

The regulations are treating aspects for example equipment, facilities, containers, and different parts of the production process. In this part of the theory chapter will only a few of the regulations in 21 part 211 Code of Federal Regulations be discussed. The regulations chosen are those that have an impact on the Final Packaging Department and this master thesis.

4.2.1 Subpart G, Packaging and Labelling Control¹¹⁸

Subpart G concerns how materials shall be examined, labelled, issued, operated, inspected and expiry dated.

Also in the packaging and labelling controls the procedures shall be written. It is important that any change in these procedures is recorded. In this subpart is stated exactly what such written procedures shall include, for example weighing, identification and supervision procedures.

Procedures about calculation of the yield are also treated. It is essential that such calculations are independently verified by a second person.

¹¹⁶ Food and Drug Administration (2002) "Guidance for Industry 21 CFR Part 11; Electronic Records; Electronic Signatures Maintenance of Electronic Records"

¹¹⁷ GMP Publications Inc., homepage, www.fda.com

¹¹⁸ IBID

Identification of the major equipment and storage points shall be done, ensuring that the content can be identified at all times.

To ensure that the production process is uniform, continual examination shall be carried out, monitoring the work progress. The data shall be recorded and maintained for each shipment, indicating receipt, examination and whether accepted or rejected. This is also made to ensure that the containers and products are labelled correctly.

It is stated in this subpart that all excess packages and labels shall be destroyed.

The product shall be marked with expiry date, a date that has been determined by appropriate stability testing.

4.2.2 Subpart J, Records and Reports¹¹⁹

In this subpart is described how long records shall be kept, where and in what kind form. It is important that the records are kept in such a way that they are available for authorized inspection.

Records shall be kept concerning the cleaning of equipment, data from each shipment, records from controls, laboratory records, etc.

¹¹⁹ GMP Publications Inc., homepage, www.fda.com



5 Empirical Results

In this section of the master thesis a deeper presentation of the Final Packaging Department is given as well as a brief presentation of linked systems. The standard work-, material- and information flow is described. As a base for the analysis and simulation of benefits in the Aeneis software, the activities are listed and the estimated time used is presented. This chapter corresponds to the current situation illustrated in the thesis model see figure 2.7.

5.1 Description of Final Packaging Department

5.1.1 Organisation

The Final Packaging Department has 53 co-workers and is run by Thomas Schwartz.¹²⁰ The department is divided into five groups illustrated in figure 4.1. The support group is called Production Service. This group includes five co-workers and is lead by H. Klingelhöfer. Three different groups perform the packaging work and are lead by E. Engelbach, B. Baum and H. Lapp. In each group eight to eleven co-workers are employed. The Arrival / Labelling group is the largest group with 14 co-workers. This group is lead by P. Rupp.

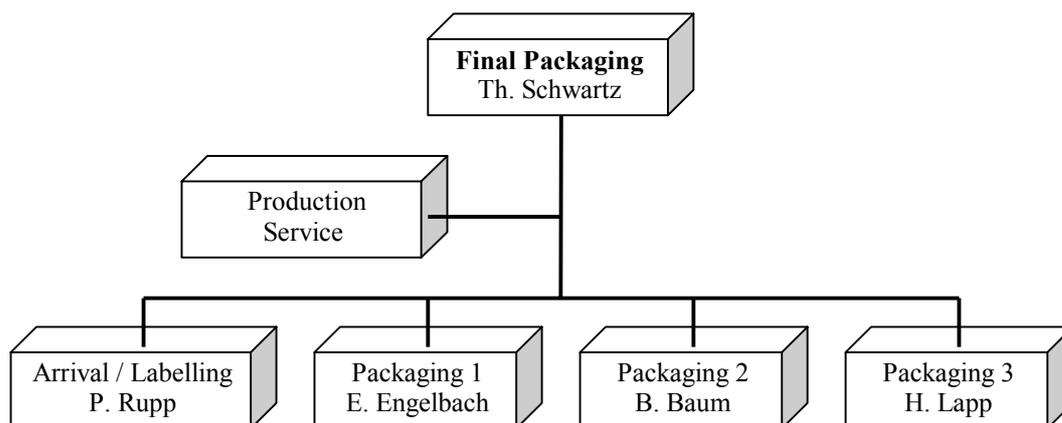


Figure 4.1 Final Packaging Department¹²¹

¹²⁰ Personal interview, Thomas Schwarz

¹²¹ Aventis Behring Intranet

5.1.2 Production

The production is normally done in one shift. But when there are peaks in the customer demand are either extra labour employed or the work is carried out in two shifts.¹²²

The production is located on two different levels in the same building namely the second and fourth floor. An overview of these two floors can be observed in appendix I and II.¹²³ On the second floor labelling and folding machines, printers, fridge facilities and several packaging lines are located. On the fourth floor no fridge facilities are located, but the same workflow is present on both floors.

The packaging lines are more or less fully mechanised. The least mechanised packaging lines only constitute of a table where the packaging is carried out by hand. In the most mechanised lines the machine does almost everything. The personnel only load new material and observe the process. Usually some parts of the packaging are done by hand. The fully mechanised packaging lines are used when the complexity of the product packed allows this and the order size is large enough to carry the set-up costs. For small order sizes it is not economical beneficial to set up a mechanised production line, instead the work is done by hand. If the packaging process is too complicated and the product has many different components it also has to be packed by hand.

Other workstations in the Final Packaging Department are Printing, Labelling and Folding. These are further described in the workflow below.

5.1.3 Production facts

The Final Packaging Department processes 3000 orders each year, the size of each order varies from a few to thousands to only a couple of units.¹²⁴ During the latest years the customer orders have become smaller and more frequent a tendency that one think will continue also in the future.¹²⁵ There are 60 different products packed in the department. Due to different country specifications, package sizes etc. the 60 different products can be packaged in 760 packaging variations.¹²⁶ To process one order takes an average of 27 days including storage time.

As Business System Aventis Behring uses SAP R/3 (SAP), so also in the Final Packaging Department. To help record the information into SAP is a barcode system used, even though in a small scale.

Orders	3000 per year
Product variety	60
Order variety	760
Cycle time	27 days
Produced value	34 million €
Business system	SAP R/3
Warehouse system	PROBAS

In the department is a fridged highbay warehouse located, which uses a warehouse system called PROBAS to keep track on the components stored. This warehouse system has in the present situation no interface with SAP. In figure 4.2 the production facts are summarised.

Figure 4.2 production facts¹²⁷

¹²² Personal interview, Thomas Schwarz

¹²³ Aventis Behring Intranet

¹²⁴ Personal interview, Thomas Schwarz

¹²⁵ IBID

¹²⁶ IBID

¹²⁷ IBID

5.1.4 Description linked Systems

Here is a description made of other systems that are linked to the Final Packaging Department. These systems, which are affecting the Final Packaging Department in some way, are illustrated in figure 4.3 below.

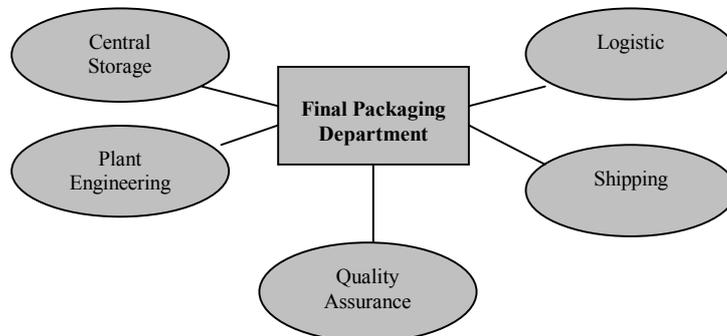


Figure 4.3 Systems linked to Final Packaging Department¹²⁸

Logistic

The Logistic Department is the link to customers, which is either an Aventis market company or an independent customer. From the customer the Logistic Department receives orders. It is then estimated when the order can be delivered. A rough work plan is outlined in SAP stating roughly how and when the work should be done in the Final Packaging Department.

Central Storage

In the Central Storage all the material needed for processing the order are stored. The material is delivered with forklifts to the Final Packaging Department when requested by a supervisor in SAP.

Plant Engineering

The maintenance of the equipment in the Final Packaging Department is managed by the Plant Engineering Department. They perform regular services and reparations on the equipment. The Plant Engineering personnel also do the set up of the machines. Data about when maintenance should be made and reparations has been done is kept in SAP.

Shipping

The Shipping Department receives the finished products after they have been processed in the Final Packaging Department. They prepare the delivery of the goods and load the palettes onto trailers for delivery to the customer.

Quality Assurance Department

The Quality Assurance Department is working with quality issues and control the processes in the Final Packaging Department. One task the Quality Assurance Department has is to check that the batch records fulfil GMP requirements.

¹²⁸ Own

5.2 Workflow

In the following figure 4.4 the Final Packaging workflow is presented. This is the standard workflow without any considerations taken to deviations that might occur.

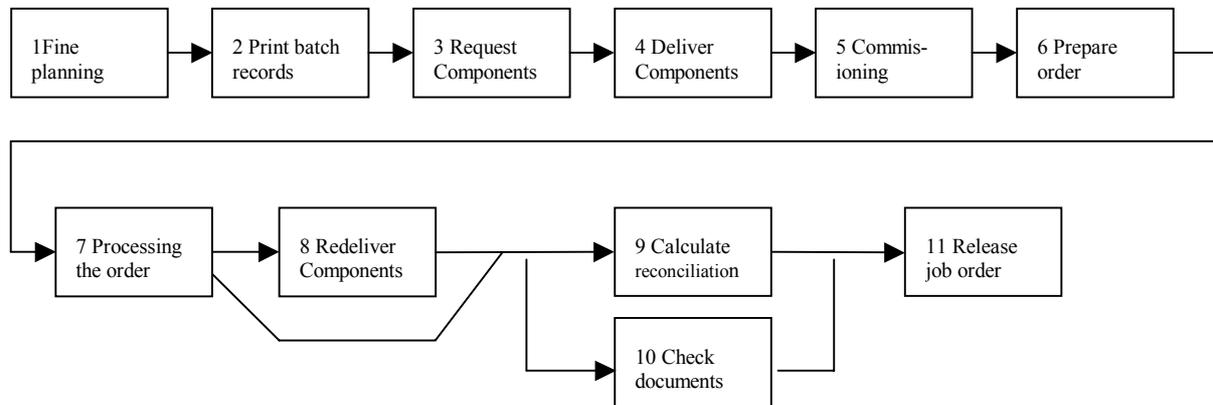


Figure 4.4 Workflow¹²⁹

5.2.1 Fine planning

The first step of the workflow is fine planning (1) the resource usage. This is done in SAP mostly by one co-worker from the Production Service group. The main focus here is to make sure that the customer orders given from the Logistics Department is finished on time. If the timeframe cannot be kept, this is reported to the Logistic Department by mail. Another purpose of the fine planning is to simplify the work. This is done through gathering orders that are similar into one batch, which saves set-up time.

5.2.2 Print batch (order) records

In the next step the production records are printed (2) and checked by the Production Service. All the printed batch records are kept in a order folder.

5.2.3 Request Components

The supervisor requests the needed components (3) in SAP. To do this it is needed to calculate the volumes needed. Extra units are added to ensure that there will be enough material for setting up the equipment.

5.2.4 Deliver Components

The components are delivered to the Final Packaging Department (4) from the Central Storage. When the goods arrive it is checked by the arrival personnel to make sure that the right products and the correct amounts are delivered.

¹²⁹ Own

5.2.5 Commissioning

Before the packaging process is started the needed material is commissioned (5) in the arrival area on palletes, in order to gather the material needed to perform the next production step.

5.2.6 Prepare order

The next activity is to prepare the order (6). The supervisor is informed about the planned packaging processes through SAP. From this information the supervisor knows what materials should be compiled and placed it in the holding zone close to the signed workstation. If a set up of the equipment is needed this information is given to the Plant Engineering Department, who then performs the set up. The supervisor also assigns the work tasks to specific operators.

Before the job process can be started someone from the personnel checks that all and the right components have been delivered. The printed batch records are also sorted and the material dedicated pages for the order being processed are taken out from the batch record folder.

5.2.7 Processing the order

There are four different production processes (7) in the Final Packaging Department, namely:

- *Printing*
- *Labelling*
- *Folding*
- *Packaging*

Printing means, that order and country specific data (e.g. lot no, exp. Date) are overprinted from the batch record onto the labelling material. The printing is either done directly on the cartons or on blank labels. The printed labels are then applied on the packages in the labelling process or in some cases directly at the packaging lines. In some cases an insert follows the product. The insert is folded in the folding process. The packaging is done at the packaging lines, the operators and the machines puts the different components into the consumer packages as well as larger shipping boxes.

5.2.8 Redeliver material

The active components (drugs) that have not been used are redelivered (8) to the Central Storage. All other material is discarded.

5.2.9 Calculate reconciliation and check documents

When the production processes are finished the Production Service makes sure that the documents are filled out correctly (10) and calculates (9) the usage of material, also called reconciliation. The data is entered into the SAP and in an extra excel sheet for internally usage and temporarily for evaluation.

5.2.10 Release order

The director finally examines and signs (11) each batch record, in order to finally release the finished products and enable the customer delivery to take place.

5.3 Material Flow

In figure 4.5 below the material flow of the Final Packaging Department is illustrated.

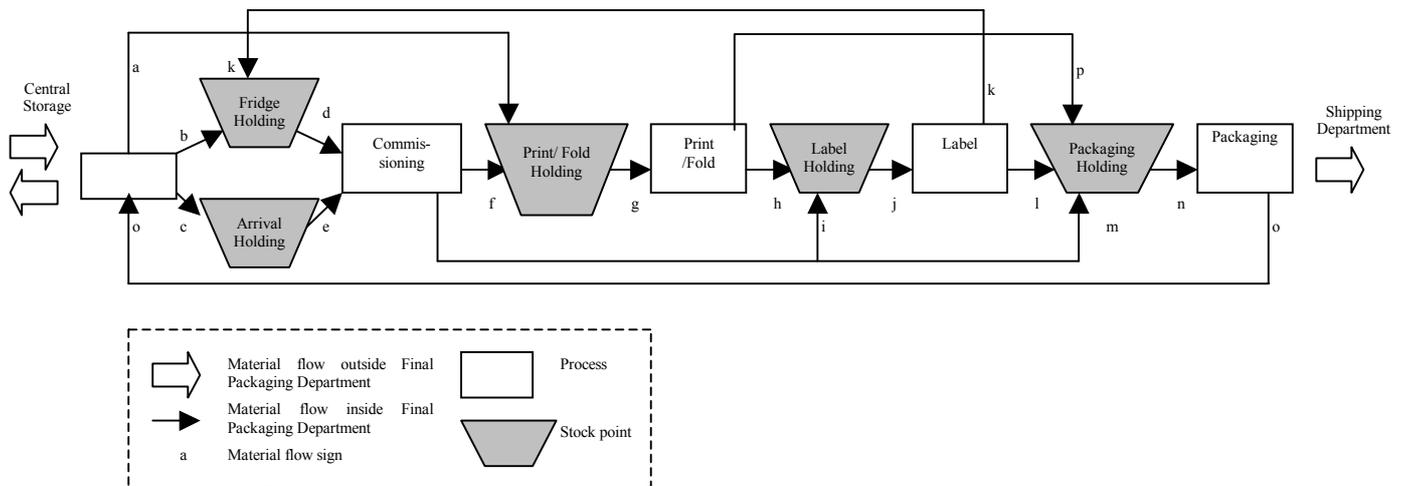


Figure 4.5 Material flow of the Final Packaging Department.¹³⁰

Requested material is delivered from the *Central Storage* to the *Arrival*. There are three different types of material delivered:

- *Medical devices (single use items)*
- *Active components (drugs)*
- *Printed and unprinted packaging material.*

It is stated that this delivery from the *Central Storage* to *Arrival* should not take more than 24 hours from when the supervisor in SAP requested it until the delivery is made.

After *Arrival* the material is sent to three different stock points (a,b,c) depending on the type of material and what intention it has. The three locations are:

- *Print/Fold Holding*
- *Fridge Holding*
- *Arrival Holding*

To the *Print/Fold Holding* blank labels are brought directly from *Arrival* (a). These labels are stored in close range from the printing machines and can easily be reached by the operator when needed.

In the *Fridge Holding* the active components are stored (b), also active components that actually do not need low temperature are stored in the *Fridge Holding*. This is done to make sure that no temperature sensitive active components by accident are stored in room temperature.

Unprinted and printed packaging material as well as medical devices are brought to and stored in the *Arrival Holding*(c).

Before a production process is started the components needed are *commissioned* on palettes. The personnel commissioning the components or the supervisor brings the palettes to the designated workstation holding zone (f,i,m), *Print Holding*, *Label Holding* or *Packaging Holding*.

¹³⁰ Own

In the *Print/ Fold Holding* packaging material and insert are taken (f).

The insert is folded and print is applied on blank labels or directly on the packaging material. If the material need to be labelled it is sent from the *Print/Fold process* to the *Labelling Holding* (h), if not it is sent directly to the *Packaging Holding* (p).

When the active components have been *commissioned* they are brought to the *Label Holding* (i) if they need to be labelled otherwise directly to the *Packaging Holding* (m). If the labelled active components are temperature sensitive and are not going to be packed in the near future, they are brought back to the *Fridge Holding* (p). The not temperature sensitive active components are sent directly to the *Packaging Holding* (l).

The medical devices and unprinted and printed packaging material are stored in the *Arrival Holding* and moved to the same locations (i,m) as the active components. They are moved to the *Label Holding* (i) if a label is going to be applied otherwise directly to the *Packaging Holding* (m).

At the *Packaging Holding* the material flows emerge together (l,m,p). Components from the *commissioning* (l), the *Print/Fold process* (p) and the *Label process* (m) emerge here.

In the *Packaging process* the components are packed in cartons and finally in shipping boxes. The finished products are handed over to the *Shipping Department* as well as samples that have been taken for quality control.

The spare active components are sent back to the *Arrival* (o), where the *Central Storage* personnel pick them up.

At the moment the entire Final Packaging Department is seen as one large stock point in SAP. It is therefore not possible to distinguish, where specific components are located within the department. Because of this it is difficult to get an overview of where in the packaging process a specific order is. According to some co-workers is it negative to have this large stock point, especially when components are not to be found or when an inventory count is made. On the other hand, having the department seen as one stock point simplifies the transportations, because no notation has to been done in SAP when moving material and components from one location to another.

5.4 Documents

5.4.1 Document description

In the Final Packaging Department a numerous amount of documents are generated and used, each document is filling its own purpose. There are two different categories of documents created. The first category originates from SAP and is designated to a specific order. Most of these documents have a standard header illustrated in figure 4.6. The other category is specific for different workstations.

Dok.-Nr.: EF00002 EF 600A	Gültig: 07.08.01	Protokolldruck: 10.12.2001 04:11	Seite: 17/ 19
Aventis Behring Endfertigungsprotokoll Testdruck			
Stückliste			
Auftragsnummer: 1054502 Aventis Behring		 (Auftragsnummer)	
Fertigwaren-Bez.: HUMATE-P 1000IU			
Fertigungsvorschrift: F-666			
Fertigungsplan Nr.: 1680			
Land-Bezeichnung: USA			
Termin: 14.12.2001			
Material-Nr. der FW	Ch. Bez.	Sollmenge	ME
OBKC455540	18466611A	936,000	PAK
			Herstelldatum
			28.09.2001
			Verfalldatum
			28.09.2003
Hinweise: Schnellstmöglich verpacken!!! 6 Muster ziehen!!! Charge 184 aufbrauchen, nichts zurücklagern!!!			

Figure 4.6 Final Packaging Department standard header¹³¹

The documents that originates from SAP are:

- *Production accompanying list*
- *Accompanying list medical devices*
- *Accompanying list Packaging Material*
- *Accompanying list active components*
- *Accompanying list for exemplification and quality control*
- *Pallet card*
- *Bill of Material*
- *Hand over ready goods to shipping*
- *Assignment closure Final Packaging*
- *Transport order*

The *production accompanying list* is a document where all the production phases are listed. In this list the operators at each production phase records the time the process was started, ended, as well as disruption times. The supervisor uses this information to calculate and record in SAP the times that have been utilized for each production process step.

The other *accompanying lists* follows the products through the entire process, used as a base for different controls and to attach samples and control stickers. An example of a control sticker is presented in figure 4.7. The service group uses the last part of these documents for reconciliation.

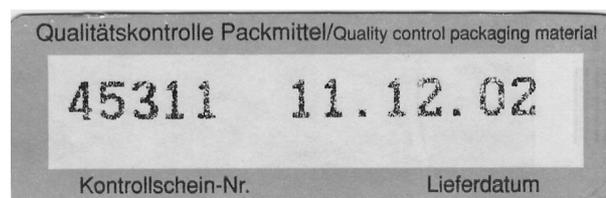


Figure 4.7 Control sticker¹³²

¹³¹ Aventis Behring

¹³² IBID

With each pallet handed over to the Shipping Department a *pallet card* is followed. The Service Group prints this document in one original, if the goods are piled on several pallets the card is copied so that each palette receives a card. This is the only document allowed to be copied in the Final Packaging Department. The document contains information about what product, material number and in what amount the product should be delivered.

In the *bill of material* all the material that is used to finish one specific order are listed. It includes information concerning the type and amount of material needed. Also information about when the components expire is included. In this document normally no information is recorded.

In the *hand over ready goods to shipping* document, for each pallet handed over to the Shipping Department it is recorded what order and quantity it contains. The products can either be designated for the Shipping Department or the Quality Assurance Department, which also is recorded.

The Service Group uses the *assignment closure document* when they are closing the order and performing the reconciliation. For final release of the finished order, this page is signed by the director of the department (responsible person production), the Quality Assurance Department and the Control Manager (responsible persons Quality control)

When a transport is needed between the Arrival and Central Storage a transport order is created in SAP. The transport order is either printed in the Central Storage or at the Arrival. It is printed at the Central Storage when a transport to the Final Packaging Department is needed. The Arrival personnel print it when active components are redelivered to the Central Storage.

The workstation specific documents are:

- *Line clearance*
- *Checklist control devices*
- *Operator verification*
- *IPK test certificate*
- *Workstation protocol (use log)*

These documents are from the beginning not specific for each order instead they are dedicated to a specific workstation. The supervisor when needed prints these protocols.

The *line clearance* document has the purpose to make sure that the workstation is clear from products, packaging material and that the station is cleaned. Two co-workers are always responsible for the line clearance. Information about where and how things should be tested is included in this document.

Before a process is started at a workstation it is checked that the set up of the equipment is properly made. For this task the *checklist control devices* is used.

The *operator verification* is a document where the co-workers record what task they have been doing at a specific workstation. This document is only needed at those workstations where more than one co-worker is working simultaneously.

There are two different types of In Process Controls (IPK) made in the Final Packaging Department. One of these controls is performed at each workstation and is only recorded on the accompanying lists described above. The other one is made as a final step before the products are handed over to the Shipping Department. Here the *IPK test certificate* is used. One co-worker that has not been taken part of the current packaging process makes the IPK test.

To keep track on the events happening at each workstation a *use log* is written. This document makes it possible to track the actions that have been taken place at each workstation.

5.4.2 Document problems

Through interviews with personnel within the Final Packaging Department as well as other Departments linked to the Final Packaging Department, such as Shipping and Quality Assurance Department, a number of problems related to the documents described above could be identified.

The documents were mostly considered to be difficult to overview and fill out and often do the same parameters have to be filled out in different documents. In the interviews were nine problems identified, below these are listed and described.

Information missing

It is often occurring that parameters are not filled out, this due to that the documents are complex and the co-workers do not pay enough attention when filling out the form. This is a very common and large problem in most of the documents used.

Unreadable

It is not always possible to read what is written, this due to that the co-workers are in a hurry and do not write properly or the space where notes and explanations are recorded is too small.

Incorrect document used

It has happened that the wrong document has been filled out. For example for the line clearance document it has happened that the wrong document is filled out, using a form from another workstation.

Incorrect note used

It has reoccurred that the co-workers do not fill out the documents according to the guidelines that have been given. It is important that the documents are filled out correctly so that they are easy to interpret and difficult to forge. Often co-workers fill out the documents with their own notations, which is not acceptable.

Incorrect calculations

The calculations are done by hand and it is of course possible that these calculations are not done correctly due to the human factor. It seems not crucial if a few and small mistakes are made, but calculations (reconciliation) are performed to avoid mix-ups with other material/batches and on the other hand in the long run this can have a negative affect on the stock levels.

Not possible to see if forgotten to fill out

In the operation verification and the use log the operators record their names. It is not possible, in an easy way, to check if somebody has forgotten to record him or herself.

No distinct areas for all notes

There are not always distinct areas for all notes and samples. This makes it easy to forget to record specific parameters as well as difficult to control if something was forgotten.

Not chronological order

In the workstation protocol it happens that the operator does not remember to record the data, and then does this later. If other orders have been produced at the workstation in between there will not be a chronological order of the data in the workstation protocol. This is not seen as a major problem but could cause confusion when authorities (e.g. FDA) do a review.

Lost documents

It has happened that documents are lost in the production process. This is a risk, even if it is not large, that is taken with all documents. It has also occurred that the lost documents could not be found again.

In figure 4.8 are the documents as well as the problems that occur with each document listed.

Document \ Problem	Information missing	Not readable	Incorrect document used	Incorrect note used	Incorrect calculations	Not possible to see if forgotten	Not distinctive areas for all notes	Not chronological order	Lost documents
	Production accompanying list								
Accompanying list one-time item									
Accompanying list Packaging Material									
Accompanying list semi finished									
Accompanying list exemplification									
Pallet card									
Transport order									
Parts list									
Line clearance									
Checklist control devices									
Operation verification									
IPK test certificate									
Hand over ready goods to shipping									
Assignment closure Final Packaging									
Work station protocol									

Figure 4.8 Summary of the Document problems¹³³

All these problems are creating irritation in the organisation. The rework is time consuming, not only for the Service Group and the Quality Assurance Department, but also for the production personnel that has to be involved.

¹³³ Own

5.5 Information and Document Flow

The information and document flow is illustrated in figure 4.9. The dotted line in the figure symbolises the border between the Final Packaging Department and other areas.

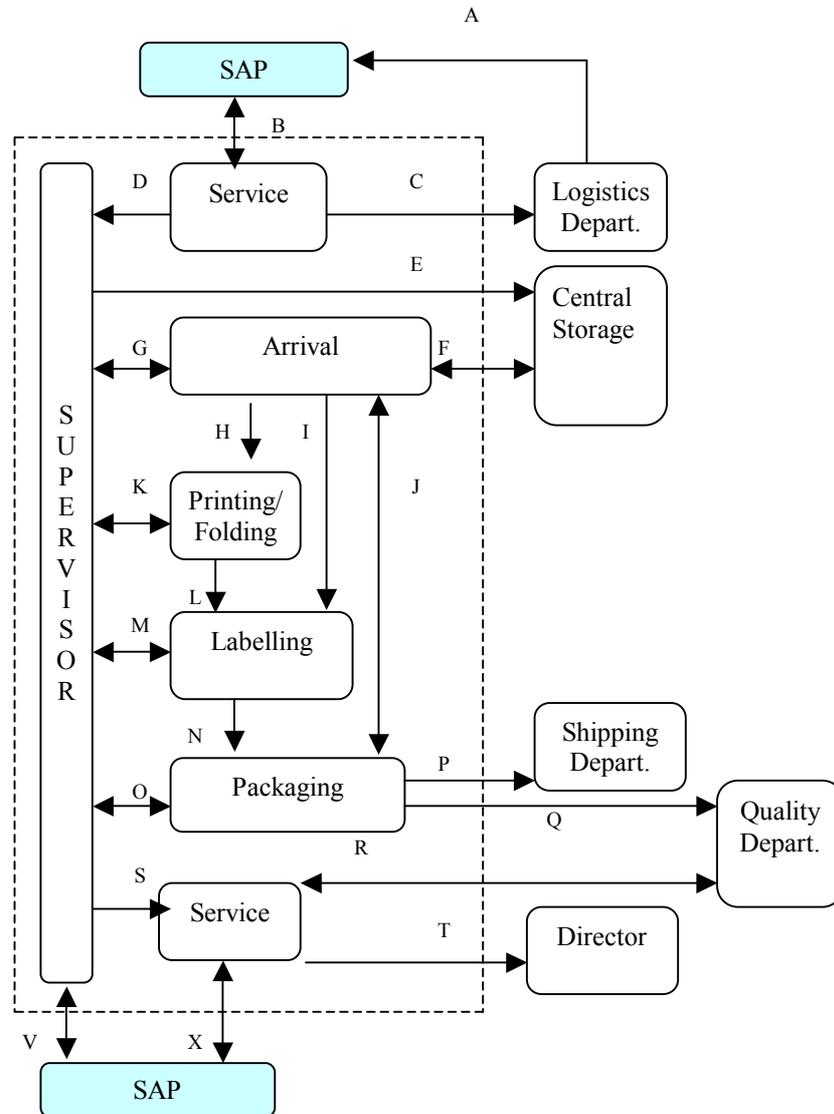


Figure 4.9 Information and document flow¹³⁴

The *Service Group* receives the order through SAP from the *Logistics Department* (A,B). Information about priority orders and batches that will not be ready within the time limits are sent back to the *Logistics Department* by e-mail (C).

The *Service Group* prints the batch record (production accompanying list, accompanying list medical devices, accompanying list packaging material, accompanying list semi finished products, accompanying list for exemplification and quality control, pallet card, Bill of

¹³⁴ Own

material and hand over finished products to shipping and assignment closures). These documents are handed over to the *supervisor* who is signed to process the order (D).

The *supervisor* receives information from *SAP* about how much material is needed to process the order (V). The amount is recalculated, adding extra units, and a new request of the components is made in *SAP* (V). This request is then sent to the *Central Storage* (E).

Between the *Central Storage* and the *Arrival* transport orders are sent in both directions (F). From the *Central Storage* when components are delivered to the *Final Packaging Department* and from the *Arrival* when spare active components are redelivered.

The *supervisors* give the *Arrival* personnel the different accompanying lists, which are need when the delivered goods are checked (G). These lists then follow the commissioned pallets during the entire production process. In figure 4.9 this is illustrated as arrows connecting *Arrival*, *Printing/Folding*, *Labelling* and *Packaging* (H,I,J,L,N)

At each process step the *supervisor* gives the co-worker a production accompanying list (K,M,O). The packaging accompanying list is given back to the *supervisor* after the work is finished, including information about how the work has proceeded. (K,M,O) At each workstation a dedicated line clearance document is filled out, which is also handed over to the *supervisor* (K,M,O).

To the *Packaging process* the *supervisor* hands over the entire order folder with all the documents received from the *Service Group* (O). Taken out and used from this folder is the accompanying list, accompanying list for exemplification and quality control, pallet card, Bill of Material, operation verification and hand over ready goods to shipping document.

The pallet card is sent with the products to the *Shipping Department* (P). The accompanying list for exemplification and quality control follows the product samples to the *Quality Assurance Department*. This document is signed and sent back to the *Service Group* (R).

After the *packaging process* is finished the folder is returned to the *supervisor* who makes sure that all documents are filled out correctly (O).

Continuously, when one process step is finished the *supervisor* enters the utilised manpower hours into *SAP* (V).

All the remaining documents in the folder are then handed over to the *Service Group* (S). The *Service Group* performs the reconciliation and checks the documents. In *SAP* the obtained information is recorded (X).

When the *Service Group* has calculated the reconciliation and made the control, the documents are collected in the order folder and handed over to the director who releases the order with his signature (T).

The information flow in the *Final Packaging Department* is as seen above rather complex. The personnel feels it is difficult to distribute the information mainly because difficulties to know where persons are at the moment. It is also seen as difficult to get an overview of where different documents are located. Where *SAP* is used this has been seen as a good support for the information flow.

5.6 Case Activities

When describing the detailed activities taking place in the Final Packaging Department a specific order was used as case study. This case is built on the order 1076075 carried out in august 2002. In the appendix III the activities that where carried out is listed, what documents that were used and estimated time needed to perform the activity. This case is considered to be an average order processed in the Final Packaging Department.¹³⁵ In the business case the received productive working time was 17.58 hours. The average total cycle time in the department is 27 days. This gives the result that only 8.7% of the cycle time is productive time.

5.7 Regulatory Compliance

Aventis Behring is following GMP and FDA regulations and guidelines. All work steps in the Final Packaging Department are described in SOPs. These SOPs are kept in paper form both by the different workstations as well as the supervisors. The co-workers continuously receive qualification in the SOPs. Without qualification the operators are not allowed to operate specific tasks. The grade of education every co-worker has is saved in SAP. In the current system it is difficult for the supervisor to get an overview of who has the accurate qualification to operate different equipment.

¹³⁵ Thomas Schwarz

6 Analysis

In this section different MES solutions and functions are discussed, which would be possible to implement in the Final Packaging Department. Organisation and production requirements are considered as well as the costs and benefits a MES would generate.

6.1 MES Functions

As described in the Frame of Reference, MESA has defined 11 MES functions. To describe the MES solution that should be implemented it has to be defined which of these functions should be considered. The functions interesting to implement in the first phase of MES are:

- *Operations/Detail Scheduling*
- *Document Control*
- *Data Collection/Acquisition*
- *Product Tracking and Genealogy*
- *Performance Analysis*

6.1.1 Why these functions

Operations/Detail Scheduling

A capacity planning system already exists in SAP, but this system does not automatically respond to status changes in the production process or propose alternative resources when needed. The scheduling function would have to have access to real-time information from the production units and the job orders in order to be efficient. It would therefore not be relevant to include this function without implementing a Data Collection/Acquisition function. The Operations/Detail Scheduling function would help improve the planning system and provide the following features:

- *Fine planning reacting to changes*
- *Fine planning proposing alternative resources*
- *Automatic distribution of information*

Document Control

The Document Control function would make it possible to transform paper documents such as SOPs and recipes into electronic form. It will provide the operators with relevant information for a specific task such as SOPs, recipes and safety regulations. The information transparency, which was one of the problems observed, will be improved through this function.

Features received when implementing these functions are:

- *Electronic documents for SOPs, recipes and safety instructions*
- *Automatic distribution of information*

Data Collection/Acquisition

Implementing the Data Collection/Acquisition function would make it possible to transform the paper based batch records into Electronic Batch Records (EBR). The administrative work and the documents problems would be reduced with this function. As described in the Regulatory Compliance chapter control, EBR and audit trail are central issues in pharmaceutical industries. This is seen the priority problem to solve and it is consequently essential to implement this function.

Features provided are:

- *Electronic Batch Record*
- *Audit trail*
- *Automatic time acquisition*
- *Validity check of manually recorded data*
- *Automatic distribution of information*
- *Automatic calculations of reconciliation*
- *Check if personnel has required qualification*
- *Electronic signatures*
- *Automatic acquisition of use log and operation verification.*

Product Tracking and Genealogy

Implementing a Product Tracking and Genealogy function would support the compliance with FDA and GMP regulations as well as improve the information transparency. It will be possible in real time to know exactly where all components in the department are located. The information could be recorded and be saved in the Electronic Batch Record making it possible to retrieve exactly where and when different components has been moved or stored. Through such a function it is also easily to control that temperature sensitive components are not stored in room temperature for to long.

This function would provide the following features:

- *Electronic Batch Record*
- *Audit trail*
- *Automatic distribution of information*
- *Acquisition and documentation of the material flow*
- *Electronic signatures*

Performance Analysis

Implementing the functions described above would give new data concerning the internal performance. Through introducing the performance analysis function this data can be transformed to valuable information, which can be used to evaluate and improve the process. According to the Frame of Reference chapter this makes it possible to reduce excess inventories, capacity and labour costs. Performance analysis is today made in SAP where Key Performance Indexes (KPI) are calculated. These KPIs in SAP are mainly evaluating the Final Packaging Department as a whole. The Performance Analysis function can give more detailed KPIs about the internal activities and would be a valuable addition to the other functions. This function should therefore be implemented in the first phase of MES.

Feature and Function Summary

In the following figure 5.1 the functions and the features are listed.

Feature \ Function		Scheduling	Document Control	Data Collection	Tracking and Genealogy	Performance analysis
Electronic Batch Record						
Audit trail						
Electronic SOPs, recipes and safety instructions						
Automatic time acquisition						
Validity check of manually recorded data						
Automatic distribution of information						
Automatic calculations of reconciliation						
Check if personnel has required qualification						
Fine planning reacting to changes						
Fine planning proposing secondary resources						
Acquisition and documentation of the material flow						
Electronic signatures						
Automatic acquisition of use log and operation verification.						
Key Performance Indexes						

Figure 5.1 Summary of features and functions¹³⁶

6.1.2 Why not the other functions

Resource Allocation and Status

The Resource Allocation and Status function would provide real time data, collected from manufacturing equipment to assure proper quality control as described in the Frame of Reference. Currently the Resource Allocation is made satisfactorily in SAP. This function can be an option in a further expansion of MES within the department to improve the efficiency of the Resource Allocation and Status. This function is not going to be implemented in the first phase of MES.

¹³⁶ Own

Dispatching Production Units

The Dispatching Production Units function is managing the material flow in the production. This is an interesting function, which is applicable in factories with defined production locations and stock points. In the Final Packaging Department it would be necessary to define the locations and record status data at real time. Even if the locations will be defined the Dispatch Product Units function has not a high priority in a first phase of MES. This because managing the material flow has not been seen as a major problem in the department.

Labour Management

The Labour Management function can help calculate the costs for each order through activity based costing. In the current situation this is managed by SAP. This function will not be further considered in this study.

Quality Management

A Quality Management function would provide real time measurements collected from manufacturing to assure proper quality control. In the Final Packaging Department are the parameters controlled by the Quality Assurance Department limited. It would be preferred to implement this function at all departments at once, this to not complicate the work at the Quality Assurance Department. The Quality Assurance Departments are running a LIMS System as a Quality Management tool. Due to this, the Quality Management module of a MES has a low priority and is also not listed as one of the interesting features presented above.

Process Management

The process management function monitors the production. In the first phase of MES it would not be relevant to implement such a function. In the current situation the supervisors manage the process manually and can also do so in the future. This function is therefore not considered in first phase of MES in the Final Packaging Department. But it is important that the other implemented functions are flexible enabling the supervisors to manage the packaging process manually.

Maintenance Management

The maintenance of the equipment currently managed by the SAP. Maintenance module is also not seen as a major issue for the Final Packaging Department. The maintenance activities are therefore not going to be further evaluated in this study.

6.2 Description MES workflow

In this part a suggestion of how the workflow could be made with the considered MES functions. It is described how different work steps would change if MES were implemented.

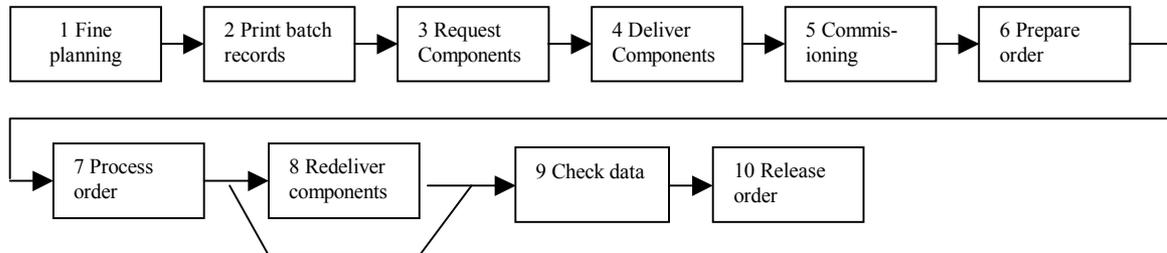


Figure 5.2 MES workflow¹³⁷

Through analysing each work step it is possible to give an estimation of the benefits that can be achieved. As base the current workflow presented in chapter Empirical Results is used. In figure 5.2 the possible MES workflow is presented.

6.2.1 Fine planning

The fine planning (1) would become easier in MES. The system would be able to self adjust the plan when changes and disturbances in the production occur. The time used for rework would be minimized as well as improved accuracy of when orders are finished. MES would also be able to suggest alternative equipment if the primary equipment has a breakdown or too many orders are scheduled. E-mails can automatically be sent to the Logistics Department when an order will not be finished within the time limit. The time used for fine planning will be reduced and the information transparency increased.

6.2.2 Print batch records

This function (2) would be more or less excluded when the batch records are managed electronically. It could still be relevant to have a function where the Service Group releases the electronic documents after the fine planning is made. It may also be the case that some documents are left in paper form and new documents have to be created as described in the reengineering part of this chapter. These documents will still have to be printed.

6.2.3 Request Components

The components have to be requested (3) by the supervisor in SAP even after MES is implemented. This due to extra units has to be manually added, units used for samples taken and equipment set-ups. But MES could be a support in the calculations and help acquire the information needed.

¹³⁷ Own

6.2.4 Deliver Components

The components will still be delivered (4) with forklifts from the Central Storage with the help of a transport order. The arrival procedure can be simplified through using a handheld computer, which scans the barcodes of the delivered components. Through this operation the MES makes sure that the right components are delivered. The co-worker does not have to record any information. The amount delivered, the date and signature will automatically be recorded through a password confirmation.

6.2.5 Commissioning

With a barcode system as well as a handheld computer the commissioning (5) would be simplified. The arrival personnel will receive the information about components to be commissioned directly on the display. The scanner would control that the right components are picked and inform when all need components are scanned. No extra notations or documents will be needed. The system will finally print labels, which are attached on the commissioned components. This label will have a barcode that carries information what material it contains what amount and where it should be delivered.

6.2.6 Prepare order

When preparing an order (6) it would be helpful to use a handheld computer and scanner. With the handheld computer the co-worker checking the material will scan the barcodes on the delivered components. The system would inform the co-worker if not all or wrong components have been delivered to the workstation. The co-worker will no longer have to sort the paper documents in the order folder. The MES will automatically present the needed screen for the operator. This reduces the amount of data to be recorded, the risk for human mistakes and the time needed to carry out this work step.

6.2.7 Process order

During the order processing (7) the information former recorded on paper based batch records is now recorded on a computer terminal. The same data is in the current system noted on several different documents. In MES these notations only have to be made once, the system then distributes the information to the designated locations when needed.

It is in MES possible to control that only qualified personnel are able to work on specific tasks in the system, which increases the regulatory compliance. It also possible to make sure that the process only starts if preset conditions are fulfilled. This is further described in the benefits part of this chapter.

When a work step has been processed it will be necessary to print a new label to identify the processes components. If no major change has been made on the components it might be possible to keep the label printed in the previous step.

MES will automatically record utilised work hours the supervisor will then no longer have to record this information in SAP. The use log and operation verification can also be automatically created by the system if requested.

6.2.8 Redeliver components

The redelivery of spare active components (8) will be slightly simplified with MES. Transport orders will still have to be requested in SAP by the arrival personnel but the information needed can be received automatically from MES. The personnel will still have to make sure that the amount redelivered is corresponding to the amount the system identifies.

6.2.9 Calculate reconciliation

The operators at each workstation record the losses and produced amounts directly in MES. The calculation of the reconciliation is then also easily managed in MES as well as the reporting to SAP. This work step can therefore be excluded and the risk for human errors eliminated. Reconciliation is performed by MES in real time, due to this any discrepancies are notified immediately, this improves both GMP compliance and stock of inventory.

6.2.10 Check data

Through MES the amount of documents will be reduced used and thereby several of the checks and SAP bookings performed by Production Service no longer have to be made. The MES can make a large part of the checks, which are made manually in the current system for example plausibility checks. But still it could be necessary to partly examine the data that was recorded, trying to find mistakes the computer cannot locate.

6.2.11 Release order

The director could release the order directly on a personal computer. The difference from releasing, with a signature on the paper documents will not be significant.

6.3 Material flow

The actual material flow will not be changed when introducing MES. But new activities will have to be considered when transporting material and components within the department. It will also be necessary to fix defined and labelled stock points and equipment within the department to support the Product Tracking and Genealogy function, further described in the reengineering part below.

6.3.1 Transportation

The locations will be identified with a name as well as a barcode. When transporting from one location to another a handheld barcode scanner will be used. The person carrying out the transportation will first be identified through a login. With the barcode scanner the operator scans the location as well as the materials moved. At the new location the material is scanned again as well as the new location.

This makes it possible to identify where all material is located or transported in real time. Through the login it will also be possible to identify who has performed the transportations. Scan the barcodes is simple and should not be seen as a difficult activity to implement. But this reengineering will slightly increase the time required to carry out the transportation.

6.4 MES case activities

In appendix IV the case activities described in Empirical Results are remodelled. Activity and time adjustments are made with consideration to an implemented MES. The times presented are rough estimations, representing the time the activity might take.

The total time saved in the case is 304 min or 5.1 hours. In this estimation no consideration has been taken if some of the time saved is carried out while the operator is waiting for the process to finish. Through model simulation in the Aeneis software the time saved when implementing MES was 4.7 hours. These figures will be used when calculating the Net Present Value of the MES investment in this chapter.

6.5 Interfaces

In the Frame of Reference chapter is described that MES can be used as information bridge between different computer systems such as MRP and SCM. Further is described that MES can link different departments within the company to improve the information flow. In some cases MES is even supporting the distribution of information in the entire supply chain.

In the Final Packaging Department there are seven interfaces that have to be considered when implementing MES as a pilot project namely: Logistics Department, Central Storage, Plant Engineering, Quality Assurance Department, Shipping Department, SAP and the Final Packaging Fridge warehouse system, see figure 5.3.

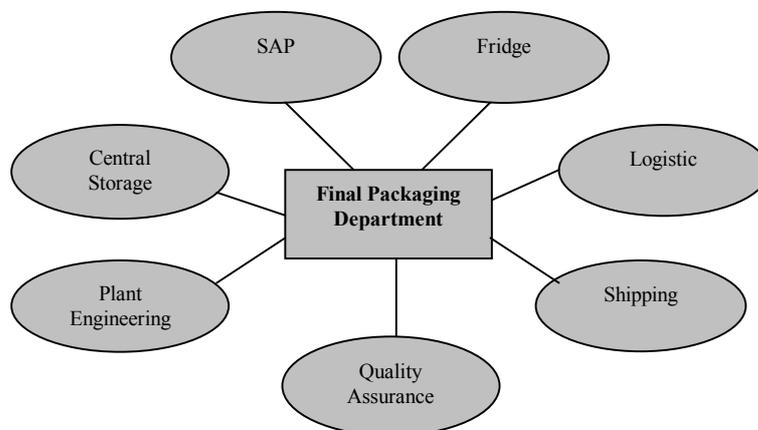


Figure 5.3 System interfaces

Logistics Department

The interface between the Final Packaging Department and the *Logistics Department* is managed by SAP and e-mail in the current process. If implementing a MES fine planning function it would be necessary to create an interface between MES and SAP. The MES receives the rough capacity planning information, performed by the Logistics Department. in SAP. From master receipts and current capacity status information MES creates a detailed packaging schedule, within the given timeframe. It is in MES also possible to automatically send information to the Logistics Department when an order will not to be processed within the given timeframe. This interface is often a standard MES software interface and would then be simple to establish.

Central Storage

It will not be necessary to make any changes in the interface with the *Central Storage*. The transportation orders can be printed and discarded as usual. SAP will be the system where the transport information between the different departments is recorded, distributed and saved.

Plant Engineering

It will not be necessary to make any changes in the interface with Plant Engineering in the first phase of MES. This is because no maintenance function will be implemented in this phase. In the current process the information is exchanged verbally or over SAP and can so be done also in the future. In a future MES phase it might be interesting to obtain information about when maintenance is planned directly in the MES fine planning tool.

Quality Assurance Department

The Quality Assurance Department is examining that the documents are filled out according to current GMP guidelines, with implementation of a EBR, it will not be necessary to do immense control of all parameters. This because some of the parameters will be checked by MES as described above. But still some control has to be made and it will therefore be required to give this department access to the MES system. If the department should not be included in the MES pilot project it will still be possible to run the MES as a hybrid system, where the batch record is first made electronically and then printed out for further process steps.

Shipping Department

The interface with the Shipping Department is more complicated than the other interfaces. In the current process there are documents that are given to and/or signed by the personnel in this department namely the pallet card, accompanying list for exemplification and quality control and handing over ready goods for shipping. It would be difficult to transform these records into electronic form without imposing MES on this department. There are different things that can be made to solve this problem; either can these documents still be kept in paper form, as they are today or the shipping personnel could record the information needed directly in the MES.

SAP

SAP is a software system where it is required to have an interface with MES, in many different areas. MES will need to get information from SAP such as recipes and order information. SAP will receive information about production statuses from MES. Interface with SAP is a standard feature, which most MES system manages. With a SAP interface it will be possible for other departments using SAP to receive information of the real time production and order statuses.

Final Packaging Fridge

As described in chapters the fridge warehouse system (PROBAS) in the Final Packaging Department does not have an interface with SAP. MES could here act as a bridge between SAP and the fridge warehouse system. Making it possible to identify, which active components are stored in the stock point. It is not likely that the vendors have a standard interface to the fridge warehouse system, which is a rather unique system. It would then be required to develop a customised solution for this interface. From the fridge it would also be interesting to automatically log the temperature into the MES. It can then be traced at what temperature different active components have been stored.

6.6 Organisation and production requirements

6.6.1 Business Reengineering

It will not be possible to implement MES in the Final Packaging Department without some kind of business reengineering as described in the Frame of Reference. New activities will be added and some activities will no longer have to be made. An example of how an order could be processed and activities changed is presented in the appendix IV.

Several of the existing documents will be transformed to electronic form. The layout of the electronic documentation and the recording of the information can be done in a rather similar way as in the current system. It will then be necessary to change from component orientated documentation to process orientated.

In the present batch record several different samples are attached. These will be difficult to attach in the EBR. There are solutions provided where the samples are scanned and only the file is saved. This should be compliant with FDA and GMP regulations but the system is a rather new and should therefore be seen with some uncertainty. It is instead recommended to introduce a new document where the samples taken are attached and linked to the process order. Some of the documents that are used by other departments might also have to be kept in paper form. If not it will be necessary for these departments to at least partly use MES.

Before the MES can be implemented all the master recipes will have to be rebuilt in the system. In MES it will be necessary to define exactly where different activities are taking place as well as where information should be recorded in order to produce the final product. It might be possible to get the base of the master recipes from SAP but still this rebuilding will demand considerable resources.

6.6.2 Defined equipment and stock points

It will be required to have well defined and well marked equipment and stock points. This to make sure the implemented functions are effective and confusions where components are stored reduced. In the current situation the stock points are not well defined and only partly marked. It is recommended that the stock points are either marked with lines on the floor or with ropes. Ropes are already used in some of the current stock points. Each stock point must have an individual name according to GMP regulations. Barcodes should be used to reduce the time required to record information when moving material from one location to another.

6.6.3 Personnel

As stated in the Frame of Reference introducing MES to an organisation sets new demands on the personnel. A new system within a department is more or less creating stress to the organisation. MES would demand the personnel in the Final Packaging Department to adapt to change. As described above business reengineering is needed and the personnel will have to learn to do the production processes in new ways. MES is computer based and would force the personnel to use new equipment such as barcode scanners as well as PCs and handheld computers.

The main part of the Personnel has been working within the department under a long period of time. They are used to the ways things are and introducing new systems can be met with limited approval. The personnel also have limited computer knowledge, which could cause problems. But there is also a frustration over the existing administration that has to be done with each order and an understanding that something has to be done.

An understanding for the need of change has to be established in the organisation. This could be done through communicating the importance of the change as well as letting some of the co-workers take part of the pilot project. In the Frame of Reference it is also noted that training will be needed when implementing MES. The personnel will need to receive accurate education and support, when introducing the system. The education and support should reflect the need of each individual

It would be beneficial in the beginning to first introduce a small scale MES parallel to the existing work system. For example introducing MES at one workstation and for one product, in this way it would be possible to reduce the risk for large disturbances in the production while the personnel learn the systems. Such disturbances can cause the personnel to regard the system as unpleasant. The operator menu should also be made as simple as possible to use for the operators. The menu can have a similar layout as the current paper documents “so called paper on glass”. It will then be easier for the personnel to use the system and understand what they are supposed to record.

MES will make it possible to reduce the administrative tasks. But it will also be required to build a new organisation that supports and maintains the system, which is also emphasized in the Frame of Reference chapter.

6.6.4 Regulatory Compliance

As described in the regulatory compliance chapter, FDA and GMP set restrictions and guidelines specific for the pharmaceutical industry, when using a MES. Some of these are directly concerning the MES software. Other are concerning the organisation and the production. It is therefore essential to make sure that the chosen vendor can offer a system that is compliant with FDA and GMP regulations. This can be made by checking if the FDA has approved the system or already used in other pharmaceutical companies.

Regulations concerning the software system are for example the following topics:

- *Ensure authentic records*
- *Generate copies*
- *Have different levels of access*
- *Secure login, logoff and signatures*
- *Use encryption*
- *Audit trail*

But there are also guidelines and restrictions that put requirements on the organisation and the production for example new aspects have to be considered concerning:

- *Maintaining electronic records*
- *Storage conditions and precautions*
- *Retrieval and access restrictions*
- *The technical approach to long term electronic record storage*
- *Which personnel are responsible for relevant tasks*
- *How to make sure that the records are preserved and can be read*

When reengineering the process it is central to have the GMP guidelines in mind concerning how the packaging process has to be managed and supported. If this is not done correctly the process might not be compliant.

Using a small part of the entire packaging process in an initial phase of the pilot project would also from a compliance point of view be preferred. It would then be possible to test if the system is compliant before it is further expanded.

6.6.5 Flexibility

The work in the Final Packaging Department is flexible. It is possible, in short notice to use alternative workstations to process a specific order. In the Frame of Reference is stated that MES is increasing the flexibility. In some way this is correct for example enables the system to quickly react to changes in the customer demand. But on the other hand there is a risk that the system sets restrictions in how the work process is currently managed. For example choosing alternative workstations should be easily made as well as acquire needed information at different computers. The option that currently exists within the department has to be summarised and modelled in the system to make sure that the packaging process remains flexible.

6.7 Benefits

6.7.1 Increased Information transparency

The information transparency will be increased through MES. It will be possible to present the relevant information needed at a specific location or by a specific operator. Information not only concerning the specific order processed is available but also SOPs, safety instructions and recipes will be presented. Increased information transparency in the organisation is also achieved because MES communicates with other systems such as SAP. From the real time information it becomes possible to present accurate information to the customer about status of specific orders.

Through the Electronic Batch Recording (EBR) detailed information about a specific order from the past can be retrieved as well as all orders containing a specific value or parameter. In pharmaceutical industries audit trail is an important issue as stated in previous chapters. In MES it is possible to list all changes that have been made in an order or in a specific time frame, which satisfies the audit trail issue.

MES can also be connected to a mail system and automatically distribute information to an e-mail account. This can be made when warnings in the system are generated. This should be allowed in restricted extent to avoid information overload.

6.7.2 Cycle time and lead-time reduction

In the Frame of Reference it is described that MESA has observed an average reduction in the cycle time of 45 % and in the lead-time of 32 %.

As seen in the description of the current situation the actual time to process the order is only a small part of the total cycle time. Not before the batch record is released as a final work step the completed products can be delivered to the customer. There is therefore a considerable potential to reduce the cycle time with MES within the department and also reduce the total lead-time.

It is not only the less time needed to entry the data, find the right document and transport the documents that is reducing the lead-time. It will also be possible to analyse where in the information, material and workflow the bottlenecks are. Bottlenecks that have to be considerable when comparing the time used to processes an order and the total cycle-time.

Of course an improvement in the cycle-time will also give a reduction of Work In Progress as well as a lower level of stored components.

The benefit of lower levels of components can be quantified. The total worth of products produced passing through the department is 34,000,000 € and the current cycle time 27 days. Assuming an interest rate of 6 % would generate a benefit of 5,600 €¹³⁸ per year by only reducing the cycle-time by one day.

6.7.3 Improved planning and scheduling

The fine planning will be improved through MES as described above in the Operations/Detail Scheduling function description.

6.7.4 Increased regulatory compliance

The regulatory compliance will be increased when implementing MES, because many of the human mistakes will be eliminated or reduced. Not only mistakes concerning the information flow but also a safer material and workflow will be attained.

Through MES most of the document compliance problems can be reduced, which is further described below.

The regulatory compliance will increase when all stock points within the department are marked and identified with a barcode. It will reduce the risk for material to be switched in the process. It is stated in 21 part 211 Code of Federal Regulations, Packaging and Labelling Control, that identification of the major equipment and storage points shall be done, ensuring that the content can be identified at all times. Dividing the Final Packaging Department into many stock points would be compliant with this regulation.

The actual processes will also be improved. For example warnings or limited access can be given to the operators if a line clearance has not been made at the workstation.

Through login it would be possible to control that only persons with authorisation have access to specific workstation or MES functions. The access could be limited to those who have accurate qualification for the specific work task. In the present situation it is difficult to have an overview on who has the accurate training and who does not even if this information exists in SAP. Further the login also increases the ability secure that information is not given to unauthorized individuals, which would be in compliance with GMP and FDA.

6.7.5 Documentation problem reduction

Introducing a MES where most of the documents are transformed to electronic form would significantly reduce the document problems that have been observed in the Final Packaging Department:

1. With MES it would not be possible for the operator to *miss recording information*. When a notation in a field is not recorded the system will make the operator aware of this before the task is completed. If information should not be recorded a notation should be done stating that this is not required in this specific situation.
2. That the recorded information is unreadable would be eliminated for documents transformed electronically. The data recorded will always be readable as long as there are no hardware or software problems.
3. MES would provide the operator with the right documents needed at the workstation. It would reduce the risk that the wrong document is used. It is valuable to have the

¹³⁸ $((34\ 000\ 000 / (364/27)) - (34\ 000\ 000 / (364/26))) \times 0,06 = 5604$

opportunity to retrieve all documents at all workstation if requested to maintain the flexibility.

4. Through the use of validity checks it is possible to reduce the risk that an *incorrect note is used*. In MES it is possible to define in what range or exact notation that should be approved in a specific field. If another value than allowed is recorded in the system this will be notified by the system, the operator either has to correct the recorded information or confirm the already recorded value. Of course the system does not know exactly what is supposed to be recorded and it will still be possible for the operator to make mistakes within the defined intervals and limits.
5. The calculations will not longer be made by hand, which will make sure that the actual *calculation is made correctly*. As described above it is possible for the operator to record an incorrect value. The value retrieved after the calculations will then also be incorrect, but this not due to faults in the calculation process.
6. If all the operators working at the workstation uses log in and log of when processing an order the use log is automatically up dated. If personnel is missing at the workstation this also should be recorded in the system with a short explanation. The risk that someone is *not recorded* in the use log would then be significantly reduced.
7. That there are *no distinct areas for all notes* is something that one has to try to improve not only in MES but also in the kept paper documents. In an electronic form it would be possible to make almost unlimited space for notes.
8. MES will as described above notify the operator when data is not recorded in a specific field. Data will then only be possible to record in *chronological order* or when a notation is done why the order was changed.
9. It would be difficult to *lose electronic production* documents within the Final Packaging Department. But there is instead a risk that data is lost due to hardware and software problems, one has to try preventing this to happen. In this matter it is recommended to follow the guidelines and regulations set by FDA and GMP concerning how electronic data should be kept as described in previous chapters.

Other benefits with MES are that when an operator has logged in he/she does not have to sign for every notation made this can be made automatically. The recording of dates and times can also be excluded, the MES will automatically note when a notation was made. In many cases the same data is recorded more than once or do not have to be recorded at all. The distribution of the information would be managed by MES making it necessary only once to record the information. In figure 5.4 the estimated notation reduction for each document is listed when using MES in one order. For the estimation the documents used in the business case Haemate as described in the chapter Empirical Results has been used.

Document (amount in case)	Current notations	MES Notations	Notation reduction
Production accompanying list (1)	18	0	100 %
Accompanying list medical devices (0)	-	-	-
Accompanying list Packaging Material (5)	256	20	91 %
Accompanying list semi finished – TG (2)	51	3	94 %
Accompanying list for exemplification and quality control (1)	8	-	0 %
Pallet card (1)	3	1	67 %
Transport order (6)	12	12	0 %
Bill of Material (1)	3	1	67 %
Line clearance (6)	132	108	18 %
Operation verification (1)	24	0	100 %
IPK test certificate (1)	31	23	26 %
Hand over ready goods to shipping (1)	31	2	94 %
Assignment closure Final Packaging (1)	13	4	69 %
Workstation protocol (6)	54	0	100 %
New sample document (1)	-	44	-
Total	636	218	66 %

Figure 5.4 estimated notation reduction¹³⁹

The result was that 66% of notations could be excluded with MES. MESA has also seen improvements in the data entry time with 75%. The estimation is based on the use of scanners, login and log of when entering and leaving the system. These activities are not considered as notations in this estimation.

In the regulatory compliance chapter was stated that it shall not be possible to forge or cancel the initial recordings made. MES can be formed so that it is impossible forge the data recorded, but still it has to be possible to make changes and notations without cancelling the recorded data and there should not be any restrictions in how large and how many these notations are.

6.7.6 Defect reduction

MESA has observed defect reduction of 15% when implementing MES. The number of defects due to problems in the Final Packaging Department is limited but the value of the components processed is considerable. Discarding one order due to mistakes can therefore be costly. Aventis Behring knows that some of the past discarded orders could have been avoided if MES had been implemented.

6.7.7 MES supports the company objectives

As described in the Frame of Reference MES should help support the companies goals and objectives. MES would help Aventis Behring to improve some of the objectives they have stated. These objectives are described in the first chapter of this study.

MES gives closer real time updated performance information from the operation, which is reducing the risk for surprises. This is supporting the first objective.

A new MES system is a large initial investment but has as purpose to reduce the overall level of expenditure, which is in accordance with Aventis Behrings second objective.

MES cannot help in the development of new products as the third objective emphasises.

Avoiding failures in compliance as the fourth objective states is one of the benefits that MES supports and together with the process improvement the most important objective.

¹³⁹ Own

6.7.8 Benefit summary

In figure 5.5 is summary made over the benefits and the functions suggested summarised.

Function \ Benefit	Information transparency	Lead-time	Order location information	Planning & scheduling	Regulatory compliance	Document problems	Support company objectives
Operations/Detail Scheduling	■	■		■			■
Document Control					■		
Data Collection/Acquisition	■	■	■	■	■	■	■
Product Tracking and Genealogy	■		■		■		■
Performance analysis		■					■

Figure 5.5 Summary of functions and benefits achieved¹⁴⁰

In figure 5.2 and 5.5 can be observed that the *Data Collection/Acquisition* function would provide significant benefits. This is an important function because it reduces the document problems. *Operational /Detail Scheduling*, *Document Control*, *Performance analysis* and *Product Tracking and Genealogy* functions are also beneficial but in a lower extent.

6.8 Costs

Costs associated with the acquisition of hardware and software is not difficult to estimate when implementing MES as described in the Frame of Reference. These costs can easily be attained through proposals from different vendors. Through such proposal one can estimate the costs of the design, purchase and installation. It might also be possible to make an estimation of the support costs. But often these costs are just a small part of the total MES costs as stated in the Frame of Reference chapter.

The software costs will be dependent on the number of functions implemented. It is likely to believe that the first functions implemented are more expensive then later implemented functions not only within the own department but also when extending the system. This because the base for the system is then built and additional functions are easier to apply.

Other resource demanding are activities according to the Frame of Reference reengineering the business process, configuration management, customisation, training the users, integration with other systems, installing new releases, testing and validation, database loading, performance tuning, backup and security management. These are costs that are more difficult to estimate. Also by the Final Packaging Department these activities will be resource demanding.

To create an efficient MES system one has to invest in appropriate hardware as described in previous chapters. Several handheld and personal computers will be needed. It is recommended to have one computer for each workstation to reduce the risk for confusion and

¹⁴⁰ Own

the risk to mix the recording of different orders. Handheld computers are needed for the arrival personnel when receiving components from the Central Storage as well as for the co-workers preparing the orders. Hardware is also needed to store the information recorded. According to the regulatory compliance chapter the data should be stored in a proper way reducing the risk for data to be lost. Aventis Behring has to consider if the existing hardware systems to save data within is fulfilling the regulatory requirements. If so these hardware systems are only need to be expanded. The investment of hardware is only a small part of the total MES investment as stated in the Frame of Reference chapter.

There is always a risk that there are problems in the hardware and the software system. It therefore has to be evaluated what the consequences are if such problems would occur. A total break down would stop the work in the department with extra costs as result.

To implement the first phase with the functions *Operations/Detail Scheduling, Document Control, Data Collection/Acquisition, Product Tracking and Genealogy and Performance analysis* are the following costs estimated:¹⁴¹

- Software costs including customisation and validation 300 000 € initially
- Hardware costs (including 50 000 for data storage) 150 000 € initially
- Training and business reengineering 300 000 € initially
- Support and Maintenance costs 40 000 € each year¹⁴²
- One hour of breakdown in Final Packaging Department costs 728 € /hour

¹⁴¹ Based on vendor proposals and own estimations.

¹⁴² Based on 20% of the license costs

6.9 Net Present Value

Making an estimation of the payback time of the investment is not easy because some of the benefits and costs are either difficult to estimate or difficult to quantify as described above. I will still make a rough estimation on the Net Present Value of the investment. The results are to be seen as guidance and not as an absolute value. The costs are based on data given by the vendors and own estimations. The benefit is based on the time reduced in the process as well as lower stock levels and Work In Progress. The time saved has been retrieved both from the Excel calculations in appendix IV and from the simulation in the Aeneis software. In figure 5.4 the data used in the calculations are listed. The Net Present Value calculations are presented in appendix V.

Element	Unit
Inflation	3 %
Return on investment	10 %
Investment costs	750 000 €
Maintenance costs	40 000 € /year
Benefit (Excel value)	370 400 € /year
Benefit (Aeneis value)	344 400 € /year
Payback time (max)	5 years
Breakdown costs	728 € / hour

Figure 5.4 calculation data¹⁴³

After 5 years the Net Present Value would be 412 000 € of the investment with the Excel benefit and 319 000 € with the Aeneis benefit.

In the Excel benefit the investment achieve break-even after 2-3 years. With the Aeneis benefit breakeven is reached after 3-4 years.

Using a simple payback method¹⁴⁴ without considering inflation and return on investment gives a payback period of = 2.0 years with the Excel benefit and 2,5 years with the Aeneis benefit. In the Frame of Reference was the payback time estimated to be 6-18 months, which is not remote from the payback time received in the calculations for this investment.

This could be considered as a profitable investment. Even if several estimations have been done. It also has to be considered that only the reduced time, lower stock levels and Work In Progress have been considered and not all other benefits presented above taken into account.

A risk analysis was also performed calculating how much different parameters could be change without risking not reaching breakeven within five years.

The time saved could be reduced to 3.5 hours per order or the annual costs could increase to 157 000 € and the investment would reach breakeven after 5 years with the Excel benefit. With the Aeneis benefit the saved time is the same but the costs can only increase to 131 000 €. Breakeven is also reached after five years even if the costs increase and the benefits decrease by 19 % with the Excel benefit and 15 % with the Aeneis benefit.

¹⁴³ Own

¹⁴⁴ Payback period = Investment costs / (Benefit - Maintenance costs)



The system can have an average of 9 breakdown hours per month with the Excel benefit and 7 hours with the Aeneis benefit. Through this observation it can be observed that rather large changes in the estimated data can be made and the investment can still be seen as profitable.



7 Conclusions

In this final chapter a general discussion of the advantages and disadvantages of MES as well as aspects that has to be considered when deciding to implement the system. In the final part of this chapter a solution for Aventis Behring as well as suggestions for further studies is presented.

7.1 Advantages and disadvantages

7.1.1 MES advantages

Functionality

One advantage MES has is that it consists of several different standard functions. It is then possible to combine the best set of functions to support the needs of one department. At other departments within the same company another set of function might be profitable and can then be implemented. This makes it possible to create a large patchwork of functions that suits the needs of the entire company. The MES functionality also enables the creation of small testing systems where evaluation can be made and knowledge generated further described below. If deciding to expand the system new functions easily can be added.

Beneficial

In the previous chapter several different benefits with MES were identified. These benefits can all be seen as advantages of the system. It will not be once more described how these benefits are created through MES but a summary is made in the following list:

- *Improved regulatory compliance*
- *Improved planning, execution and control*
- *Safer material flow*
- *Improved component location information*
- *Knowledge generation*
- *Improved customer satisfaction*
- *Increased transparency*
- *Improved information flow*
- *Documentation problem reduction*
- *Improved retrieval of historical data*
- *Reduced lead-time*
- *Reduced cycle time*
- *Reduced past due orders*

- *Reduced stock levels and work in progress*
- *Increased quality*
- *Reduced administrative work*
- *Better support of company objectives*
- *Improved evaluation possibilities*

As seen above the list of benefits identified in this study is large. Thereby not said that these benefits would be attained in all departments and all companies.

Even if only a few of these benefits were quantified and used in Net Present Value calculations it is shown that the MES has considerable advantages.

7.1.2 MES disadvantages

Functionality

The functionality is not always a benefit it also has its weaknesses. Often one thinks that one only will need a couple of the defined MESA functions to receive a sufficient MES. But the problem that has to be solved is often complex and will therefore need several of the different functions to be solved even if only small parts of each are actually used.

It is also not possible to take the standard functions as they are without some kind of customisation. The vendors have developed a standard system and to make it perfectly fit the own process customisation is needed. How much is depending on the process and which functions that are chosen. The level of customisation has to be tried to keep as low as possible to avoid a considerable increase in costs. This can be made through evaluating how different vendor solutions best fits the own process.

Qualitative issues difficult to quantify

Several of the benefits that are observed with MES are of a qualitative nature that is difficult to quantify. It is therefore impossible to make calculations where it can be said how beneficial MES is to implement. Due to these qualitative benefits it is also difficult in the future to quantify the advantages MES has brought.

Uncertainty

Introducing a new system such as MES is related with a high level of uncertainty. Estimations have to be done in both costs and benefits.

Training is requiring different amount of resources for different individuals. It will therefore need different amount of support and time to learn the new way of working for different co-workers. It is therefore problematical to estimate the effort for the organisation to transform to the new situation.

It is also difficult to know what the costs are dependent of. There might be a reduction in costs when implementing the system in other departments and the benefits might increase over time.

Risk exposure

There is also a risk in the stability of the MES. A breakdown in the system can have disastrous consequences. Of course an alternative plan should be made in such occasions. But due to regulatory compliance it is not allowed to use paper documents as back up and therefore it is not possible to let the processes proceed. Long periods of system problems where the process stops could therefore be extremely costly and can make the difference from an investment success to an investment disaster

If pilot project not profitable

If it would be shown that a MES pilot project is not profitable it is easy to come to the conclusion that the system should not be further expanded. Such a decision could be unfavourable. It is possible that MES first becomes profitable when it has been expanded into several departments to be able to take full advantage of the benefits. This because adding additional functions can make the system more complete. In a large system it is also possible to distribute the fixed costs on more units, which could make a difference in the profitability.

There are also lower implementation costs when applying MES in other departments because knowledge has been generated as described below.

7.2 MES Aspects

7.2.1 How to save the generated and existing knowledge

Evaluating if MES should be implemented in a company generates knowledge and a deeper understanding of the processes is obtained. This knowledge would be helpful in an implementation phase of MES. One has to try to use this knowledge to support the construction of the new system. This can be done through letting the same individuals involved in the evaluation work also take part in the implementation phase. Documents, models and information created in initial phases should be saved. It should be considered what value these could have in the future work.

In the implementation phase new knowledge is also created. Knowledge that is useful in a further expansion of MES within the own department or other sections. The knowledge can also be valuable in other projects where a system is implemented. To save this knowledge it could be beneficial to form a project group where some of the members are following to the next organisation as well.

When implementing MES an understanding for the own process is created. It is then an excellent opportunity to improve the process. In this way a higher efficiency can be created not only because of the MES system but also because of the process reengineering.

The MES can be seen as a way of saving the existing knowledge in the process. Many processes are managed by the co-workers skills and are passed verbally between different individuals. Only a few key persons have a total overview of the entire process. If these persons should finish working in the organisation important knowledge is lost, which takes time to rebuild. In MES the process is modelled and thereby a detailed description of how the work should proceed is obtained. This makes it easier to introduce new co-workers and the organisation becomes less dependent of key individuals.

7.2.2 Customer orientation

As described in the first chapter there is a focus on globalisation and customisation in enterprises of today and I believe this focus is going to increase also in the future. The orders will become more customer specific and contain a smaller quantity. In this context it is important to reduce the administration costs and increase the flexibility. With MES it will be possible to have larger customer focus. The lead-time will be reduced and the production process can quickly adapt to changes from the customer. MES also reduces the administration costs making it easier to produce smaller orders without immense increase in costs. An

improved planning system also enables quick and flexible reactions to demands from the customer. With MES you can improve your customer orientation.

7.2.3 Flexibility versus control

When implementing MES it is easy to achieve an increased level of control making sure that all work steps follow a defined path. The risks for mistakes in such a system is low. But if you are not careful in the modelling of the process the increased control can cause loss in flexibility within the department. Manual adjustment and changes that is considered as obvious in the current system might no longer be an option. Especially in processes where many different alternatives are present this can be a problem. The implementation of MES has to be made careful to not lose flexibility in the search for increased control and regulatory compliance.

7.2.4 Interfacing

MES is described by many authors as a way of linking different systems and departments together, sometimes even the entire supply chain. This is made to improve the information flow in the organisation. This is correct in a large MES system involving many different departments. But in a small MES system, like the pilot project several company intern interfaces has to be managed.

Software integration is easily managed through standard interfaces received in the MES. In some cases customisation will be needed. But these interfaces are not changing the way the users are working in other departments. But instead problems with the software upgrades can follow. It can be the case that when one of the systems are upgraded that the interface does not longer work.

MES also has to be integrated with other departments. It is difficult to create a system that totally covers one department without imposing the system partly on other departments. These departments will then have to manage both the MES and the current system, which is illustrated in figure 7.1.

If instead a MES with borders within the department is created it is difficult to exclude all current activities in the own organisation as illustrated in figure 7.2. For example this can make it necessary to leave some of the documents used by other departments in paper form.

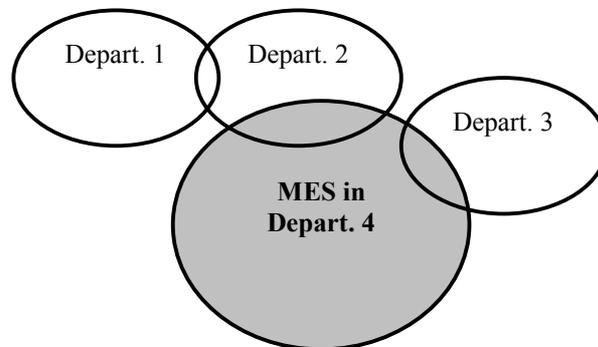


Figure 7.1 MES imposed on other departments

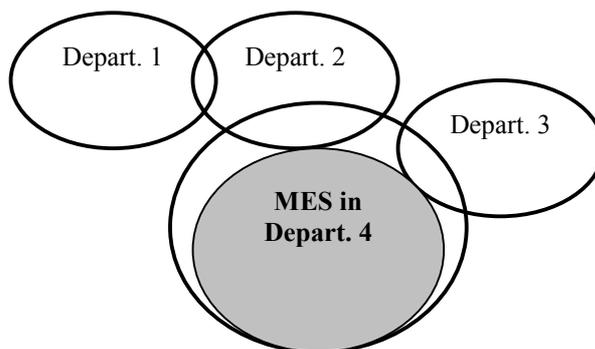


Figure 7.2 MES with borders within the department

Which interface that should be used has to be considered in each case. In some cases it is more beneficial to keep the current interface in others it is better to let the other department partly use the MES.

7.2.5 Information improvement or information overload

The MES is described as a way of improving the information flow and information transparency. But the MES is also automatically recording much more data than a manual system. From this data it can be difficult to find important matters even if different filters in the system can be used.

Through the use of different alarms and automatic distribution of warnings the information overload soon can become immense. Such overloads can make the operator frustrated as well as not attentive when important information is distributed. The operator then might confirm different warnings without paying attention to what they really mean.

7.2.6 Regulatory Compliance changes

FDA and GMP are dynamical in the way of developing guidelines and regulations. As the time evolves technology gives new possibilities. It is then also likely that new regulations and guidelines will be formed putting larger restrictions on companies, not only in pharmaceutical industries. In the future it might be required by FDA to have a computer system that is managing different aspects of the quality field, to reduce the risk for human errors. It is therefore recommended to act in advance trying to fulfil more than minimum required. This reduces the risk for unpleasant surprises where a system has to be implemented with little thought. Implementing the system in advance also makes it possible to take advantage of the benefits during a longer period of time. On the other hand being the first to implement a new system can create problems when FDA and GMP do not consider it to satisfy the regulatory requirements.

7.2.7 Financing a pilot project

A pilot project is not only beneficial for the involved department. Through testing the system in one area, decisions about further implementation on corporate level can be made. Such an investment should not have the same requirements on the return as other investments. If only safe investments were implemented it would not be possible to evaluate systems with high potential and risk. A pilot project like MES should therefore be partly financed or at least secured on corporate level.

7.3 MES in a planning, execution and control context.

In the Frame of Reference chapter planning execution and control was presented. Different authors described the relationship between these elements. The way they looked at the relationship between these can be regard as static.

First planning is set to guide for further actions. Then execution is made to carry out the plan. Control is made at the end to compare the obtained value with the planned to find deviations. Control is also made during the execution to check if the plan is followed. This way of looking at the elements is illustrated in figure 7.3.

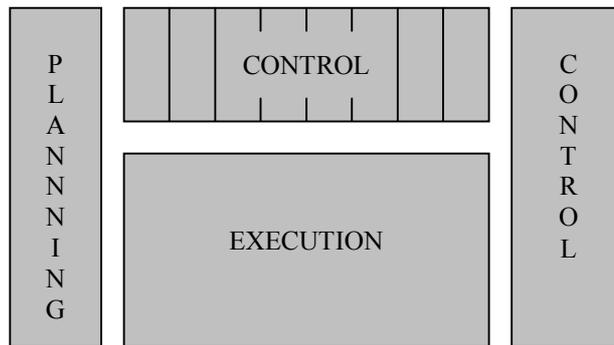


Figure 7.3 Static planning, execution and control¹⁴⁵

With MES these borders are lighten and the elements become more dynamic. Planning is continuously updated and changed to the current situation. The control is made continuously with immediate impact on the execution. In this way the size of the deviations can be reduced and almost excluded. The control function is not longer only a comparison between the current and planned situation. Instead it is guiding the execution continuously creating a better regulation of the process. Through continues control the final control loses some of its purpose. The updated plan is at the end of the execution equal to the existing situation. Of course a comparison with the original plan can be made. The dynamic MES is illustrated in figure 7.4 below.

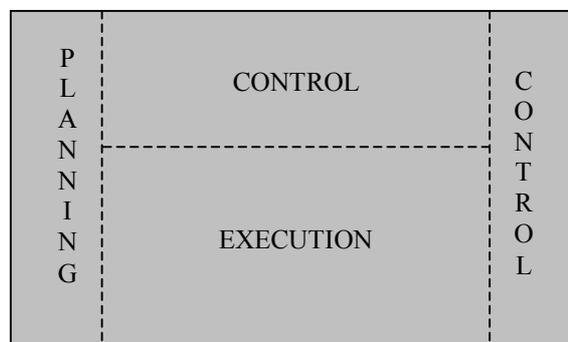


Figure 7.4 Dynamic planning, execution and control¹⁴⁶

¹⁴⁵ Own

¹⁴⁶ Own

MES also changes the way of looking at over planning and under planning as well as how to find the right level of control. When data is automatically recorded in MES it is possible to increase the control with only small changes in the cost. The same can be seen in the planning where a rigorous plan can be made with numerous updates and notable increases in costs. With MES the importance of these aspects are reduced.

7.4 MES in other industries

In this study many different advantages, disadvantages and aspects has been identified, which can be reached when implementing MES in pharmaceutical industries. But will the same benefits and costs be seen when implementing the system in other industries? One aspect that makes pharmaceutical industries exceptional is the high level of control and regulatory requirements. The products produced have also often a high value. Therefore an immediate generalisation can consequently not be made.

The high level of control and regulatory compliance in pharmaceutical industries makes it extra beneficial to implement MES. This advantage is only obtained in similar industries such as food and beverage. In these industries control and safety is also an important issue. In non-compliant industries this benefit is not obtained. But regulatory compliance also set requirements on the system and the organisation causing an increase in costs. For example is special procedures needed to maintain the system as well special hardware to ensures a safe storage of the data. These are costs that the non-compliant industries can avoid if introducing MES.

The high value of the raw material as well as the final product in pharmaceutical industries makes a reducing of the defects more advantages here then in industries with low product value.

Even if pharmaceutical industries are especially suitable for a MES system the return of the investment seen is so remarkable that it should also be profitable in other areas. MES is also a rather new system and it is likely to believe that the costs for the system will decline in the coming years. Declining costs might make it interesting to apply MES in industries in the future where the current profitability is considered to low.

7.5 Final solution

Through the discussion from costs and benefits it is recommend that Aventis Behring implement all the considered functions. This because they all would be profitable and would be working efficiently as one unit. The total benefit of the functions are also larger then the benefit of every single one. This due to that some benefits increases when the functions are combined. The difference in costs from implementing one function or all is also limited.

Through the introduction of EBR the most of the benefits used in these calculations are received and thereby should the focus be to introduce the *Data Collection/Acquisition* function first.

The other four functions have a lower priority because the benefits are smaller in relation to the effort for the first implementation. But adding these functions after or simultaneously with the EBR function is only increasing the costs in limited extent.

7.5.1 Strategy

Recommendations for the implementation phase for the Final Packaging Department as well as the entire Aventis Behring Corporation is listed below.

1. Decide to implement MES as a pilot project in the Final Packaging Department as intended.
2. Form a project group for the implementation, containing co-workers from the Final Packaging Department as well as personnel with computer and MES knowledge.
3. Chose a suitable vendor with a regulatory compliant system.
4. Use the knowledge created in the evaluation phase when implementing the system.
5. Make a solid evaluation of the current work process, trying to identify where problems can be located.
6. Reengineer the current process ensuring both control and flexibility.
7. Define stock points and equipment
8. Create a test system within the pilot system
9. Use the test system for training
10. Use the test system for modification and compliance validation
11. Try to avoid information overload.
12. Save the knowledge created in the implementation process
13. Evaluate the profitability of the investment.
14. Continue implementing MES into other departments.

7.6 Further studies

Here below are four examples of topics that could be used in further studies.

Evaluate the implemented MES pilot project.

As base for further MES investments decisions within the Final Packaging Department or other parts of the Aventis Behring it is essential to evaluate the implemented MES project. From this information it is then possible to compare if the estimated benefits and costs that became a reality. This information can be used as a base for further decisions about the expansion of the system.

Evaluate other departments where MES could be beneficial

A similar study as this one could be done at other departments not only within Aventis Behring but also in other companies. Such studies could give a better support to the results received in this master thesis

Identify what functions a second phase should include.

Within the Final Packaging Department it could also be interesting identify what functions might be beneficial to implement in a second phase of MES.



8 References

8.1 Published Sources

- Abnor, Ingeman, Bjerke, Björn (1994) *Företagsekonomisk metodlära*, Studentlitteratur, Lund.
- Adler, David J., Herkamp, Joe, Henricks, Dan, Moss, Richard (1995) "Does a Manufacturing Execution System reduce the cost of production for bulk pharmaceuticals" *ISA Transactions*, Vol 34, Elsevier Science, Indianapolis, IN, USA.
- Anthony, Robert N. (2000) *Management Control Systems*, McGraw and Hill, New York.
- Cross, Peter (1997) "MES and ADC: A Dynamic Duo for Execution Excellence", *Automatic I.D News*, July.
- Eriksson, Lars T., Wiedersheim-Paul, Finn (1997) *Att Utreda Forska och Rapportera*, Liber Ekonomi, Malmö.
- Fog, Jette (1979) *Om kvantitative metoder i dansk samfundsforskning*, Institutt for organisations- och arbejds sociologi, Copenhagen.
- Food and Drug Administration (2002) "Guidance for Industry 21 CFR Part 11; Electronic Records; Electronic Signatures Maintenance of Electronic Records", Rockville, MD, USA.
- Food and Drug Administration (1997) "Electronic Records, Electronic signature", *Code of Federal Regulations*, Title 21 part 11, USA.
- Hahn, Dietger (1994) *PUK – Controlling Konzepte*, 4th edition, Gabler Verlag, Wiesbaden.
- Hakansson, Bill (1997) "The Benefits of MES: A Report from the Field", *White Paper Number 1*, MESA International, Pittsburg, PA, USA.
- Hakansson, Bill (1997) "MES Functionalities & MRP to MES Data Flow Possibilities", *White Paper Number 2*, MESA International, Pittsburg, PA, USA
- Hakansson, Bill (1997) "Execution-Driven Manufacturing Management for Competitive Advantage", *White Paper Number 5*, MESA International, Pittsburg, PA, USA.
- Hakansson, Bill, Schaeffer, Julie (1997) "MES Explained: A High Level Vision", *White Paper Number 6*, MESA International, Pittsburg, PA, USA.
- Heinen, Edmund (1991) *Industrie Betriebs Lehre*, 9th edition, Gabler Verlag, Wiesbaden.
- Holme, Idar M. & Solvang, Magne K. (1997) *Forskningsmetodik; Om kvalitativa och kvantitativa metoder*, Studentlitteratur, Lund.
- Horvath, Peter (1991) *Controlling*, 6 Edition, Verlag Vahlen, Munich.
- Kaplan Robert S., Cooper Robin (1997) *Cost & Effect; Using Integrated Cost Systems to Drive Profitability and Performance*, Harvard Business School Press, Harvard.
- Kilger, Cristoph & Stadler, Hartmut (2000) *Supply Chain Management and Advanced Planning*, Springer Verlag, Heidelberg, Germany.
- McClellan, Michael (1997) *Applying Manufacturing Execution Systems*, CRC Press LCC. Boca Raton, FL, USA.

- Merriam, Sharan (1994) *Fallstudien som forskningsmetod*, Studentlitteratur, Lund.
- Lange, Lothar, Seifert, Wolf, Jaeger, Halvor, Klingmann, Ingrid(1992) *Good Clinical Practice I*, Institut für Humanpharmalogie, Berlin.
- Lundahl, U. och Skärvad, P-H. (1992) *Utredningsmetodik för samhällsvetare och ekonomer*, Studentlitteratur, Lund.
- Patel, Runa & Tabelius, Ulla (1997) *Grundbok i forskningsmetodik*, Second Edition, Studentlitteratur, Lund.
- Persson, Göran & Virum, Helge (1998) *Logistik för konkurrenskraft*, Liber Ekonomi, Oslo.
- Potthoff, Erich and Trescher Karl (1986) *Controlling in der Personalwirtschaft*, Walter de Guyter, Berlin.
- Repstad, Pal (1993) *Närhet och Distans; Kvalitativa metoder i samhällsvetenskap*, First Edition, Studentlitteratur, Lund.
- Scott, Douglas (1996) “Comparative Advantage Through Manufacturing Execution System”, *Advanced Semiconductor Manufacturing Conference*, Toronto, Ontario, Canada.
- Silver, Edward, Peterson Rein (1985) *Decision Systems for Inventory Management and Production Planning*, second edition, John Wiley & Sons, New York, NY, USA.
- Young, Stephen L. (1995) “Technology... The enabler for tomorrow’s agile enterprise” *ISA Transactions*, Vol 34, Elsevier Sience, Spring House, PA, USA.
- Vollman, Thomas, Berry, William, Whybark, Clay (1988) *Manufacturing and Control Systems*, Irwin, Homewood, IL, USA.
- Wingate, Frank (1997) “Breakthrough Automation Strategies”, *Industrial Engineering Solutions*, Nov, Atlanta, Georgia, USA.

8.2 Company Intern Sources

Aventis, Annual report, May 2002.

8.3 Verbal Sources

- Baum, Bernd, Group Manager, Final Packaging Department, Aventis Behring GmbH, personal interview.
- Bayer, Ulrich, Service, Final Packaging Department, Aventis Behring GmbH, personal interview.
- Burg, Heidemarie, Quality Assurance Department, Aventis Behring GmbH, personal interview.
- Eidam, Horst, Logistic, Aventis Behring GmbH, personal interview.
- Engelbach, Elke, Group Manager, Final Packaging Department, Aventis Behring GmbH, personal interview.
- Kolat, Huelya, Service, Final Packaging Department, Aventis Behring GmbH, personal interview.
- Dr. Christoph, Kraus, Information Solutions, Aventis Behring GmbH, personal interview.

Palm, Dietmar, Plant Engineering, Aventis Behring GmbH, personal interview.

Prieler, Marlene, Aventis Behring GmbH, personal interview.

Rupp, Paula Group Manager, Final Packaging Department, Aventis Behring GmbH, personal interview.

Rösser, Juergen, Logistic Europe, Aventis Behring GmbH, personal interview.

Schmidt, Ernst, Arrival, Final Packaging Department, Aventis Behring GmbH, personal interview.

Schumacher, Marina, Service, Final Packaging Department, Aventis Behring GmbH, personal interview.

Schwarz, Thomas, Department Manager, Aventis Behring GmbH, personal interview.

Schüssler, Joachim, co-worker, Final Packaging Department, Aventis Behring GmbH, personal interview.

Schüssler, Stephan, Arrival, Final Packaging Department, Aventis Behring GmbH, personal interview.

Schäfer, Antje, Manager Quality Assurance, Quality Assurance Department, Aventis Behring GmbH, personal interview.

Schäfer, Axel, Shipping Department Aventis Behring GmbH, personal interview.

Lehnert, Norbert, GMP Assurance Manager, Quality Assurance Department, Aventis Behring GmbH, personal interview.

Trinkl, Mario, GMP Coordinator, Compliance Department, Aventis Behring GmbH, personal interview.

8.4 Electronic Sources

ABB homepage, www.abb.com, 2002-10-08

Aventis homepage, www.aventis.com, 2002-09-12

Aventis Behring intranet, intranet, 2002-10-08

GMP Publications, Inc homepage, www.fda.com, 2002-11-09

Infoscience homepage, www.infoscience.fr, 2002-10-22

Kungliga Tekniska Högskolans homepage, www.isk.kth.se, 2002-12-12

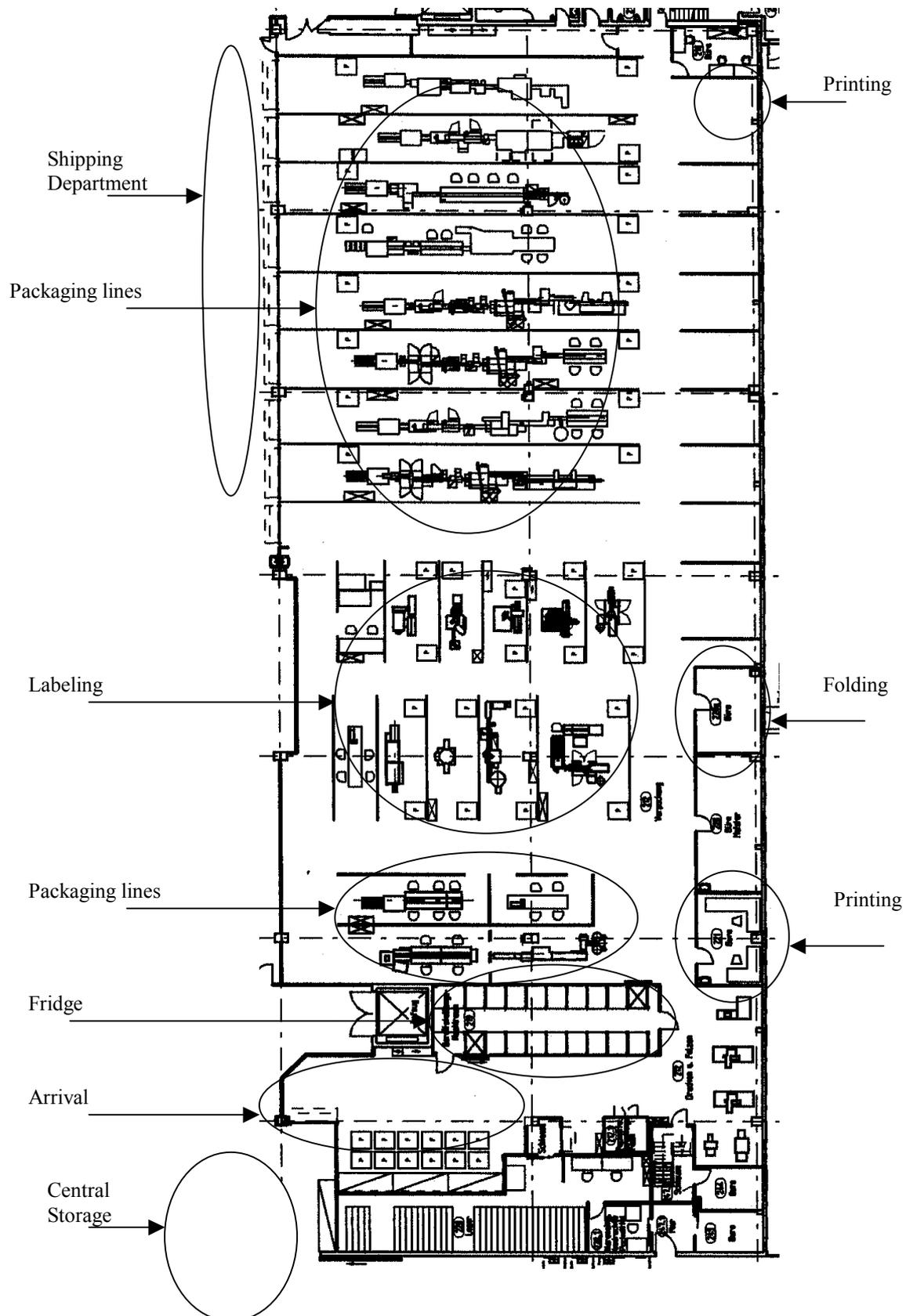
MESA homepage; www.mesa.org, 2002-09-30

Propack Data homepage, www.propack-data.com, 2002-11-25

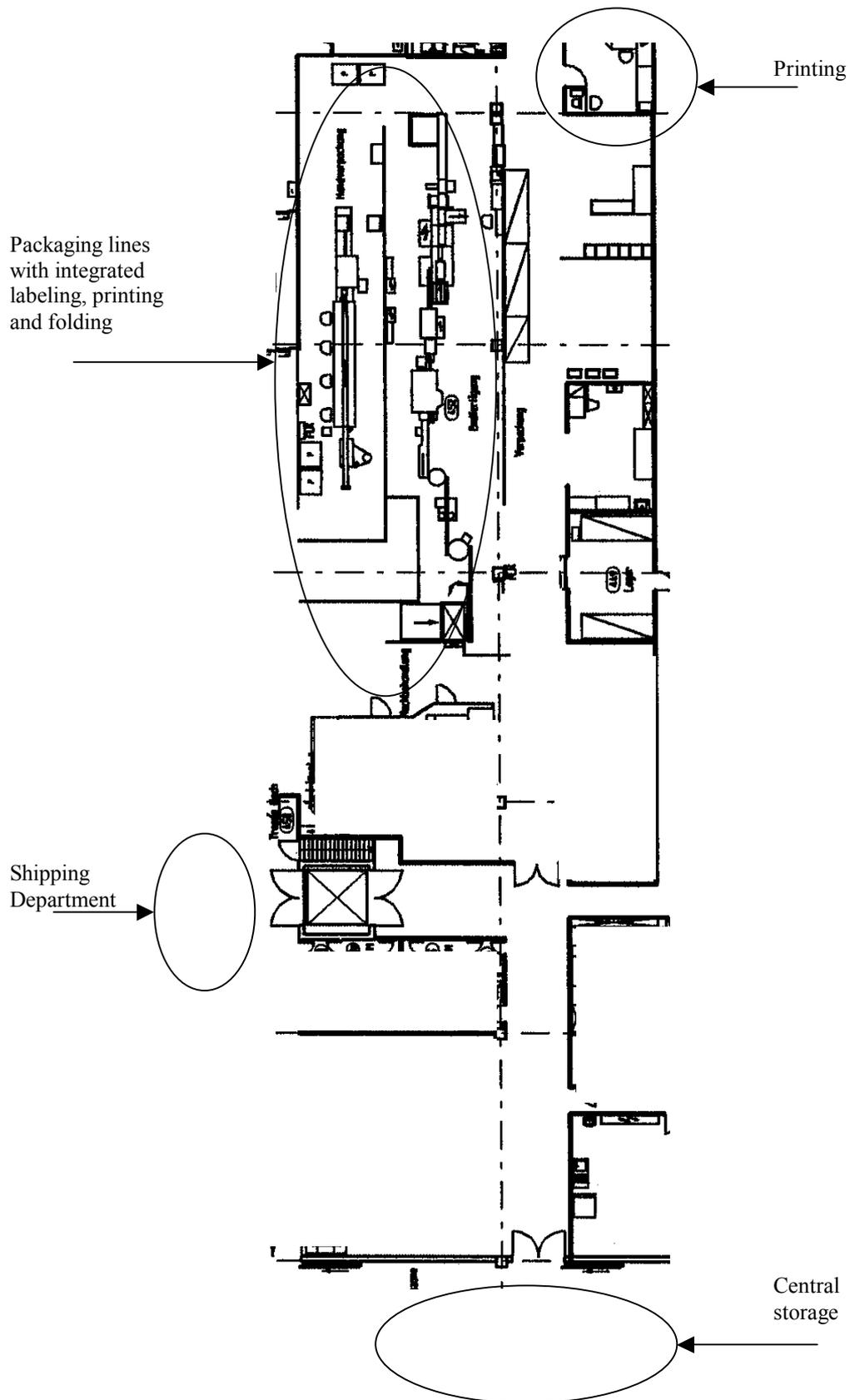
Werum homepage, www.werum.com, 2002-11-25



Appendix I – Final Packaging Department (second floor)



Appendix II - Final Packaging Department (fourth floor)



Appendix III – Current case activities

The documents used in the case are listed and numbered below this is done to assist and simplify activity list.

Documents	Nr	Documents	Nr
Production accompanying list	1	Line clearance	8
Accompanying list active components	2	Operation verification	9
Accompanying list Packaging Material	3	IPK test certificate	10
Accompanying list for exemplification and quality control	4	Hand over ready goods to shipping	11
Pallet card	5	Assignment closure Final Packaging	12
Transport order	6	Workstation protocol (use log)	13
Bill of Material	7		

In this case 10 different components was used to produce the final product. Two of these were active components:

- *Haemate HS TAT/ZUK. 1000IE TG*
- *BEIP.M.30ML WASS.F.INJ.ZW.*

Of the components eight were packaging material.

Printed:

- *VE Haemate (label)*
- *PB Haemate (insert)*
- *FA Haemate (carton)*
- *VI Haemate (label)*
- *NE Haemate (standard package label)*

Unprinted:

- *Folie PE 50x0,05 x700 M*
- *Wellp.Fa 1.40 295x185x220 mm*
- *Klebeb:Pap. 60X200M Antislip*

No medical devices were used in the case.

Description	Doc. Nr.	Location	Aver. time	Comment:
Fine planning		Service	40	
Print batch records	2-4, 7, 10-13	Service	5	
Check batch records	12	Service	5	The documents are handed over to Supervisor
Print Production accompanying list	1	Supervisor	5	
Request Components	SAP	Supervisor	30	In SAP, the amount of material needed to process the order is requested
Receive packaging material	2, 3, 6	Arrival	15	
Receive active components	2, 6	Arrival	10	
Store active components	Fridge	Fridge	10	
Store packaging material			5	
Commissioning	2, 7	Arrival	20	The components are commissioned on palettes.
Fold PB Haemate				
Prepare order	3	Folding	5	The components are checked before used at the workstation.
Line clearance	8, 3	Folding	10	
Fold PB Haemate	-	Folding	15	The actual process
In Process control	3	Folding	10	
Take sample	3	Folding	15	One insert is taken, checked and attached on document 3



Measure and record data	1,3	Folding	10	
Line clearance	8, 3	Folding	10	
Update use log	13	Folding	5	
Record utilised work hours in SAP	1	Supervisor	5	The Production accompanying list is used to calculate the working hours needed.
Print VI Haemate				
Prepare order	3	Printing	5	At the workstation it is checked that the right components were delivered
Line clearance	8,3	Printing	10	
Print VI Haemate	-	Printing	20	The actual process
In Process control	3	Printing	10	
Take sample	3	Printing	15	One label is taken at the beginning and one at the end, attached and checked on document 3
Measure and record data	3,1	Printing	10	
Line clearance	8,3	Printing	10	
Update use log	13	Printing	5	
Record utilised work hours in SAP	1	Supervisor	5	The Production accompanying list is used to calculate the working hours needed.
Label FA Haemate				
Prepare order	3	Labelling	5	The components are checked before used at the workstation
Line clearance	8, 3	Labelling	10	
Label FA Haemate	-	Labelling	50	The actual process
In Process control	3	Labelling	10	
Take sample	3	Labelling	15	One label is taken attached and checked on record 3
Measure and record data	3,1	Labelling	10	
Line clearance	8, 3	Labelling	10	
Update use log	13	Labelling	5	
Record utilised work hours in SAP	1	Supervisor	5	The Production accompanying list is used to calculate the working hours needed.
Print NE Haemate				
Line clearance	8, 7	Printing	10	
Print NE Haemate	-	Printing	15	The actual process
In Process control	3	Printing	10	
Take sample	3	Printing	15	One label is taken at the beginning and one at the end, attached and checked on record 3
Measure and record data	3,1	Printing	10	
Line clearance	8	Printing	10	
Update use log	13	Printing	5	
Record utilised work hours in SAP	1	Supervisor	5	The Production accompanying list is used to calculate the working hours needed.
Print FA Haemate				
Prepare order	14,3	Printing	5	At the workstation it is checked that the right components were delivered
Line clearance	8, 3	Printing	10	
Print FA Haemate	-	Printing	20	The actual process
In Process control	3	Printing	10	
Take sample	3	Printing	15	One sample is taken at the beginning and one at the end, checked and attached on record 3
Measure and record data	3,1	Printing	10	
Line clearance	8	Printing	10	
Update use log	13	Printing	5	
Record utilised work hours in SAP	1	Supervisor	5	The Production accompanying list is used to calculate the working hours needed.
Packaging				
Prepare order	2,3	Packaging	5	The components are checked before used at the workstation one carton label (Kastenzettel) is applied on document 2. One carton is applied on document 3
Line clearance	8	Packaging	10	
Packaging	-	Packaging	95	The actual process
In Process control	3	Packaging	10	
Take sample	3	Packaging	15	One sample is taken of each component.
Fill out record 4		Packaging	5	
Measure and record data	1,3	Packaging	10	
Line clearance	8	Packaging	10	



Load pallets/ record pallet card	5	Packaging	20	If the goods are piled on several pallets the pallet card is copied.
In Process control (IPK) (Final)	10	Packaging	15	
Hand over ready goods to shipping	11, 5	Packaging	5	
Update use log	13	Packaging	5	
Update operation verification	9	Packaging	5	
Record utilised work hours in SAP	1	Supervisor	5	The Production accompanying list is used to calculate the working hours needed.
Redeliver spare active components	6	Arrival	30	A transport order is booked in SAP.
Check batch records	1- 4, 6-13	Service	30	
Calculate reconciliation	2, 3, 17	Service	30	Data recorded in SAP
Sign batch records	18	Service	5	The order folder is handed over to the Quality Assurance Department
Check batch records	1-4 7-13	Quality Dep.	-	order folder is handed over to the Director
Release order	1-4, 7-13	Director	-	
Correct mistakes		-	35	
Planning		Supervisor	80	
Transports		-	20	
Total			1055	

Appendix IV – MES case activities

Description	Current time	Estimated time	Time saved	Comment:
Fine planning	40	25	15	MES reduces the time needed for fine planning.
Print batch records	5	2	3	Is partly not needed in MES
Check batch records	5	3	2	Is partly not needed in MES
Print Production accompanying list	5	0	5	
Request Components	30	30	0	In SAP, the amount of material needed to process the order is requested
Receive packaging material	15	5	10	The activity is simplified with handheld computers and scanners
Receive active components	10	5	5	The activity is simplified with handheld computers and scanners
Store active components	10	10	0	No change
Store packaging material	5	5	0	No change
Commissioning	20	15	5	The activity is simplified with handheld computers and scanners
Folding PB Haemate				
Prepare order	5	2	3	The activity is simplified with handheld computers and scanners
Line clearance	10	7	3	Recorded directly in MES
Folding PB Haemate	15	15	0	No change
In Process control	10	10	0	Recorded directly in MES
Take sample	15	15	0	One insert is taken, checked and attached on sample document
Measure and record data	10	5	5	Recorded directly in MES
Line clearance	10	7	3	Recorded directly in MES
Update use log	5	0	5	Recorded directly in MES
Record utilised work hours in SAP	5	0	5	MES automatically calculates the utilised work hours
Print VI Haemate				
Prepare order	5	2	3	The activity is simplified with handheld computers
Line clearance	10	7	3	Recorded directly in MES
Print VI Haemate	20	20	0	The actual process
In Process control	10	10	0	Recorded directly in MES
Take sample	15	15	0	One label is taken at the beginning and one at the end, attached and checked on sample document
Measure and record data	10	5	5	Recorded directly in MES
Line clearance	10	7	3	Recorded directly in MES
Update use log	5	0	5	Recorded directly in MES
Record utilised work hours in SAP	5	0	5	MES automatically calculates the utilised work hours
Label FA Haemate				
Prepare order	5	2	3	The activity is simplified with handheld computers
Line clearance	10	7	3	Recorded directly in MES
Label FA Haemate	50	50	0	The actual process
In Process control	10	10	0	No change
Take sample	15	15	0	One label is taken attached and checked on the sample document
Measure and record data	10	5	5	Recorded directly in MES
Line clearance	10	7	3	Recorded directly in MES
Update use log	5	0	5	Recorded directly in MES
Record utilised work hours in SAP	5	0	5	MES automatically calculates the utilised work hours
Print NE Haemate				
Line clearance	10	7	3	Recorded directly in MES
Print NE Haemate	15	15	0	The actual process
In Process control	10	10	0	No change
Take sample	15	15	0	One label is taken at the beginning and one at the end, attached and checked on sample document
Measure and record data	10	5	5	Recorded directly in MES
Line clearance	10	7	3	Recorded directly in MES
Update use log	5	0	5	Recorded directly in MES
Record utilised work hours in SAP	5	0	5	MES automatically calculates the utilised work hours



Print FA Haemate				
Prepare order	5	2	3	The activity is simplified with handheld computers and scanners
Line clearance	10	7	3	Recorded directly in MES
Print FA Haemate	20	20	0	No change
In Process control	10	10	0	No change
Take sample	15	15	0	One sample is taken at the beginning and one at the end, checked and attached on sample document
Measure and record data	10	5	5	Recorded directly in MES
Line clearance	10	7	3	Recorded directly in MES
Update use log	5	0	5	Recorded directly in MES
Record utilised work hours in SAP	5	0	5	MES automatically calculates the utilised work hours
Packaging				
Prepare order	5	2	3	Carton label (Kastenzettel) and carton is applied on sample document
Line clearance	10	7	3	Recorded directly in MES
Packaging	95	95	0	No change
In Process control	10	10	0	No change
Take sample	15	15	0	One sample is taken of each component. Attached on sample document
Fill out record 4	5	5	0	Recorded directly in MES
Measure and record data	10	5	5	Recorded directly in MES
Line clearance	10	7	3	Recorded directly in MES
Load pallets/ record pallet card	20	20	0	No change
In Process control (IPK) (Final)	15	12	3	Recorded directly in MES
Hand over ready goods to shipping	5	5	0	Recorded directly in MES
Update use log	5	0	5	Recorded directly in MES
Update operation verification	5	0	5	Recorded directly in MES
Record utilised work hours in SAP	5	0	5	MES automatically calculates the utilised work hours
Redeliver spare active components	30	25	5	No change, MES support
Check batch records	30	10	20	Check the recorded data in MES
Calculate reconciliation	30	0	30	Not needed with MES
Sign batch records	5	0	5	Not needed with MES
Check batch records	-	-	-	Check the recorded data in MES
Release order	-	-	-	Recorded directly in MES
Correct mistakes	35	5	30	
Planning (Supervisor)	80	50	30	The planning process for the supervisor is simplified and more accurate
Transports	20	30	-10	Transports need scanning
Total	1055	751	304	

Appendix V – Net Present Value Calculations

Benefit Excel

Data

Time saved/Batch	Batches/year	Total time saved	Cost per hour	Cost saved
5,07	3000	15200	24,0	364800

Lower stock levels	5600
Total costs saved	370400

NPV

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	750000	0	-750000	-750000	-750000
1	40000	370400	330400	292389	-457611
2	40000	370400	330400	258752	-198859
3	40000	370400	330400	228984	30125
4	40000	370400	330400	202641	232765
5	40000	370400	330400	179328	412093
6	40000	370400	330400	158697	570790
7	40000	370400	330400	140440	711230
8	40000	370400	330400	124283	835514
9	40000	370400	330400	109985	945499

Risk analysis

Benefit change

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	750000	0	-750000	-750000	-750000
1	40000	253236	213236	188704	-561296
2	40000	253236	213236	166995	-394301
3	40000	253236	213236	147783	-246518
4	40000	253236	213236	130781	-115737
5	40000	253236	213236	115736	0
6	40000	253236	213236	102421	102421
7	40000	253236	213236	90638	193059
8	40000	253236	213236	80211	273270
9	40000	253236	213236	70983	344253

Time saved/Batch	Batches/year	Total time saved	Cost per hour	Cost saved
3,52	3000	10551	24	253235

Cost change

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	750000	0	-750000	-750000	-750000
1	157164	370400	213236	188704	-561296
2	157164	370400	213236	166995	-394301
3	157164	370400	213236	147783	-246517
4	157164	370400	213236	130782	-115736
5	157164	370400	213236	115736	0
6	157164	370400	213236	102421	102422
7	157164	370400	213236	90638	193060
8	157164	370400	213236	80211	273271
9	157164	370400	213236	70983	344254

Investment costs
157164

Cost and benefit changes

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	890904	0	-890904	-890904	-890904
1	47515	300812	253297	224157	-666748
2	47515	300812	253297	198369	-468379
3	47515	300812	253297	175548	-292831
4	47515	300812	253297	155352	-137479
5	47515	300812	253297	137480	0
6	47515	300812	253297	121663	121663
7	47515	300812	253297	107667	229330
8	47515	300812	253297	95280	324610
9	47515	300812	253297	84319	408929

Increase in costs and decrease in benefits can be 19%

Total cost saved	Investment costs
300812	890904
	Annually
	47514

Benefit Aeneis

Data

Time saved/Batch	Batches/year	Total time saved	Cost per hour	Cost saved
4,70	3000	14100	24,0	338400

Lower stock levels	5600
Total costs saved	344000

NPV

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	750000	0	-750000	-750000	-750000
1	40000	344000	304000	269027	-480973
2	40000	344000	304000	238077	-242897
3	40000	344000	304000	210687	-32210
4	40000	344000	304000	186449	154239
5	40000	344000	304000	164999	319238
6	40000	344000	304000	146017	465255
7	40000	344000	304000	129218	594474
8	40000	344000	304000	114353	708826
9	40000	344000	304000	101197	810023

Risk analysis

Benefit change

The benefit change is the same as in the Excel benefit calculations.

Cost change

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	750000	0	-750000	-750000	-750000
1	130764	344000	213236	188704	-561296
2	130764	344000	213236	166995	-394301
3	130764	344000	213236	147783	-246517
4	130764	344000	213236	130782	-115736
5	130764	344000	213236	115736	0
6	130764	344000	213236	102421	102422
7	130764	344000	213236	90638	193060
8	130764	344000	213236	80211	273271
9	130764	344000	213236	70983	344254

Investment costs
130764



Cost and benefit changes

Year	Investment costs	Total costs saved/ year	Cash flow	Cash flow today	NPV
0	864406	0	-864406	-864406	-864406
1	46102	291865	245763	217490	-646916
2	46102	291865	245763	192469	-454447
3	46102	291865	245763	170326	-284121
4	46102	291865	245763	150731	-133390
5	46102	291865	245763	133390	0
6	46102	291865	245763	118045	118045
7	46102	291865	245763	104464	222509
8	46102	291865	245763	92446	314956
9	46102	291865	245763	81811	396766

Increase in costs and decrease in benefits can be 15%

Total cost saved	Investment costs
291864,8796	864405,75
	Annually
	46101,64