TALLINN UNIVERSITY OF TECHNOLOGY
SCHOOL OF ENGINEERING
Department of Mechanical and Industrial Engineering

MATERIAL FLOW ANLYSIS AND OPTIMIZATION IN ACINO ESTONIA OÜ

TOOTMISHOONE LIIKUMISVOOGUDE ANALÜÜS JA OPTIMEERIMINE ACINO ESTONIA OÜ NÄITEL

MASTER THESIS

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Tallinn 2022

AUTHOR'S DECLARATION

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No academic degree has been applied for based on this material. All works, major viewpoints and data of the other authors used in this thesis have been referenced.

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Department of Mechanical and Industrial Engineering

THESIS TASK

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Thesis topic:

Material flow analysis and optimization in Acino Estonia OÜ

Tootmishoone liikumisvoogude analüüs ja optimeerimine Acino Estonia OÜ näitel

Thesis main objectives:

1. Determine the most efficient plant layout
2. Optimize flow of material to stay competitive
3. Maintain flexibility of plant arrangement

Thesis tasks and time schedule:

No	Task description	Deadline
1.	A company overview	13.02.2022
2.	Theoretical overview	13.03.2022
3.	Current production layout material flow analysis	17.04.2022
4.	New production layout design and material flow analysis	08.05.2022
5.	Calculations and summary	20.05.2022

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PREFACE

Mariete Popman who works as a production equipment specialist at Acino Estonia OÜ initiated the master thesis "Material flow analysis and optimization in Acino Estonia OÜ".

Facility where human medicines are packed today was built 30 years ago. As production capacity and complexity has increased during those years and will increase in the near future, the current facility layout, including material movements requires improvement to support growth prospective. In spring 2021 company acquired adjacent land which is about 1,8 ha in size. Out-dated facility arrangement and the expansion of company's owned territory encouraged to restructure the plant layout.

Author would like to thank supervisor professor Kristo Karjust for providing feedback during thesis writing and express gratitude to Acino Estonia colleagues in data collection and consultation.

Keywords: material flow, pharmaceutical packaging, Good Manufacturing Practice, master thesis

List of abbreviations and symbols

AHU – air-handling unit

AL – airlock

DAL – document airlock

EBIT – earnings before interest and taxes

FP – finished product

GDP- Good Distribution Practice

GMP – Good Manufacturing Practice

HVAC – heating, ventilation and air conditioning

LPS – Lean Production System

MAL – material airlock

MRA – Medicine Regulatory Affairs

PAL – personnel airlock

PVC – polyvinyl chloride

QC – quality control

SOP – standard operating procedure

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INTRODUCTION

The master thesis is about analysing material flow and optimizing pharmaceutical packaging company's facility layout. Acino Estonia OÜ packages human medicines into bottles and blister packs, production plant is located in south of Estonia. Within the last years, production volumes have grown and will grow in the future. The facility was built 30 years ago which is not meeting current needs and this master thesis will analyse material flow throughout the production area and bring out opportunities for improvement.

Thesis main objectives are to determine the most effective plant layout by optimizing material movements to improve productivity and to stay competitive. As well, it is important to maintain flexibility in a plant layout arrangement to support perspective growth within the facility. To achieve objectives existing production area with current parameters is designed on one floor. Subsequently, multi floor and one floor production areas will be compared.

Material flow in current production area is as practical as possible, but now it is time to consider major changes in plant layout mainly for efficiency purposes. Three-storey facility is not opportune for pharmaceutical packaging for such production volumes. As company acquired last year adjacent land about 1,8 ha in size, expanding the company has already started.

First part of the thesis gives an overview of the company and describes pharmaceutical quality system. As well, facility in general and production area are introduced in this chapter. Next, theoretical background of facility layouts, good manufacturing practice requirements and Lean philosophy is covered. Third part analyses current plant layout and material movements inside the production zone. Material flow in production zone is visualized by using Siemens Tecnomatix Plant Simulation software. Fourth part introduces new pharmaceutical packaging facility layout where production area is designed on the ground floor. Current and new layouts are compared on the basis of material movement distance and time. Thesis last chapter gives an overview of calculations. In closing, results and conclusions are presented in the summary.

1 OVERVIEW OF ACINO ESTONIA OÜ

Acino Estonia OÜ is a Swiss company manufacturing human medicinal products. The company was founded in Switzerland 1836 and its headquarters is located in Zürich. Acino's mission is to develop, manufacture and commercialize high-quality pharmaceuticals for the benefit of patients [1]. Acino's vision is growing fast and making impact for patients in emerging markets [1].

Company has five manufacturing sites located in Estonia, Ukraine, South Africa and 2 factories in Switzerland. Manufacturing site in Põlva, Estonia offers packaging, logistics and warehouse service, business model is contract manufacturing. It means providing outsourcing services to external pharmaceutical or food supplement companies by transferring and manufacturing their oral solid dosage forms [2]. Primary and secondary packaging, serialisation are among the services.

Main business in Põlva site is packaging of oral solid pharmaceuticals, narcotics and food supplements. There are approximately 25 different active substances and 200 medicinal products in packaging portfolio. Medicines are mainly for nervous system, respiratory system, blood and blood forming organs, treating infections. Produced medicines are used to treat psychotic conditions such as schizophrenia and bipolar disorder, to treat mental disorders, Parkinson's, Alzheimer, to relieve severe pain [3].

Facility in Põlva was built at the beginning of 1990s, main area of activity has been since then manufacture of pharmaceutical products for humans. First operating company until 2012 in Jaama 55b Põlva was Nycomed SEFA AS. In 2012, Nycomed was acquired by Japan's biopharmaceutical company named Takeda Pharmaceuticals. Acino AG acquired plant from Takeda in September 2016. Facility photos can be seen in Figure 1.1.

Figure 1.1 Facility in 1990 and in 2020

Acino Estonia consists of a packaging plant together with warehouse and intercompany service centre with 91 employees (as of 20.04.2022). The company has grown steadily - employee growth rate within 5 years is 65%. Acino Estonia functional organizational chart valid as of April 2022 is shown in Figure 1.2.

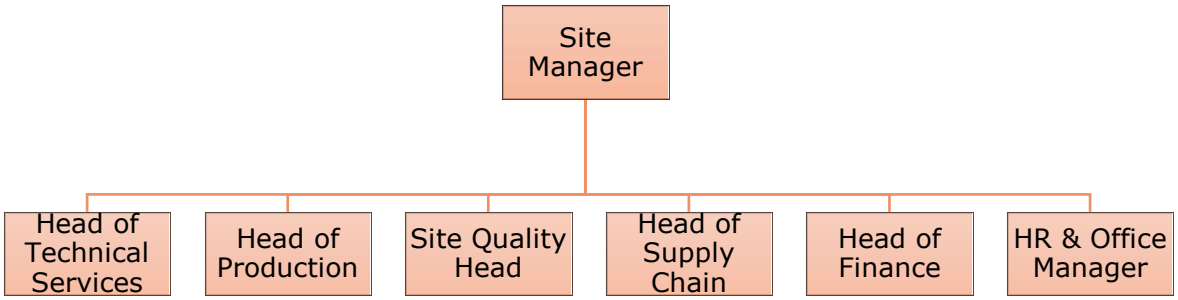


Figure 1.2 Acino Estonia OÜ functional organizational chart

Packaging plant is managed by site manager and company has four representatives. Organisation is divided into six departments: technical services, production, quality, supply chain, finance and human resources (HR). Technical services main functions are maintaining and developing technical systems and production machines. Production department packages pharmaceuticals and this work is done by technicians and operators. Pharmacists and supervisors are documenting and coordinating production activities. Quality department is responsible for overall quality assurance (QA) and quality control (QC), positions are qualified persons (QP), QA and QC officers. Supply chain deals with planning, implementing and monitoring supply chain and logistics. Finance is arranging and developing company's finances. HR find personnel with the corresponding qualification and experience.

Acino Estonia has gained 83% revenue increase during the past 5 years. Revenue growth is mainly driven by customer base upturn. However, main customer contract ending caused decline in operating profit since low-margin products are being produced. Table 1.1 shows the annual revenue and operating profit from 2017 until the end of 2021.

Table 1.1 Acino Estonia OÜ revenue and operating profit [4]

Year	**Revenue (€)**	**EBIT (€)**
2017	4 605 624	712 410
2018	4 780 534	506 309
2019	6 951 760	579 597
2020	7 674 081	348 419
2021	8 415 818	170 550

1.1 Products

Products are oral solid dosage forms of prescription, over the counter medicines and food supplements. Dosage solid forms packaged in Põlva plant are film-coated, sugar coated, uncoated, retard tablets and capsules, as shown in Table 1.2.

Table 1.2 Dosage form examples

Dosage form	Sample picture	Measures (mm)	Usage
Sugar-coated tablet		5,6 x 3,5	Obsessive compulsive disorder
Film-coated tablet		9,0 x 3,4	Heart disease
Retard tablet		9,2 x 3,5	Parkinson’s
Uncoated tablet		7,0 x 3,2	Biotin deficiency
Capsule, hard		23,5 x 7,7	Fungal infections

All packed products are for human use. Põlva plant packages pharmaceuticals in bottle container and into blister pack. Bottle and blister packaging examples presented in Figure 1.3 and Figure 1.4.

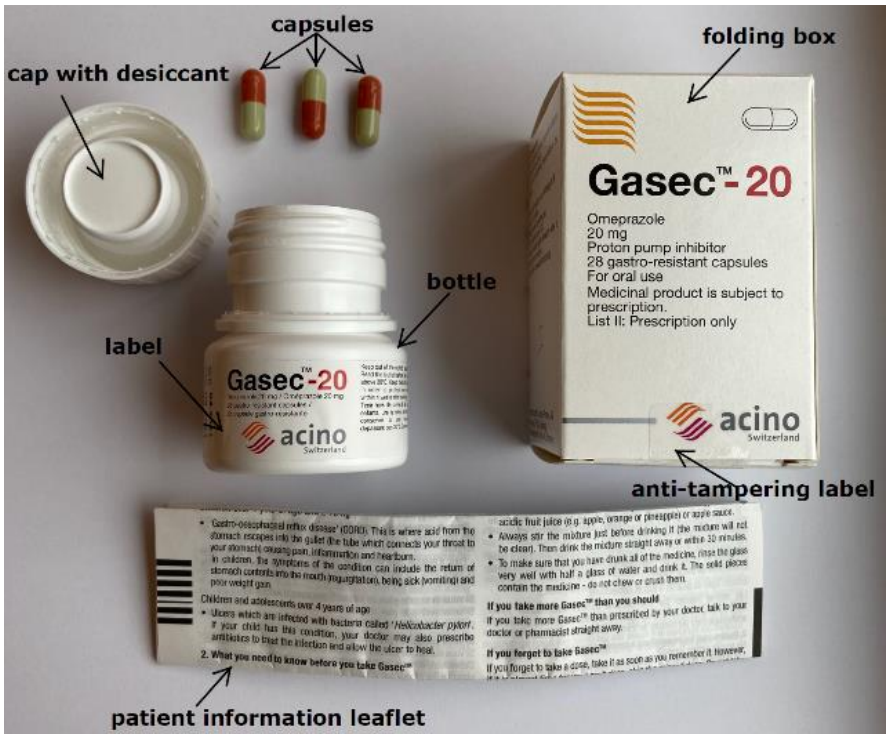


Figure 1.3 Bottle packaging components

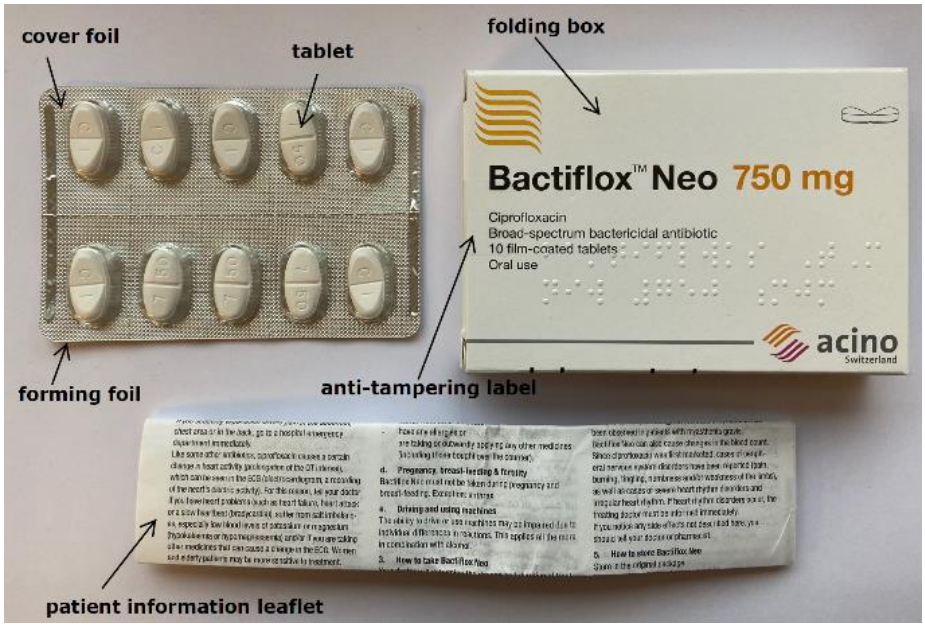


Figure 1.4 Blister packaging components

Finished product (FP) consists of medicines in capped bottle or in blister pack, folding box around it and folded patient information leaflet inside the box. Safety label is anti-tampering device, used on both sides of the folded box. The verification of the integrity of the anti-tampering device shows whether the packaging has been opened or altered since it left the manufacturer, thereby ensuring that the content of the packaging is authentic [5].

Packaging materials are divided as primary and secondary. Primary packaging materials are bottle, cap, and foil – those that are in direct contact with the medicines. Secondary components are labels, patient information leaflet, and folding box – components that are not in direct physical contact with the medications. Types of raw materials used in packaging are cardboard for boxes, paper for leaflets and labels, glass for bottles, plastic for caps and bottles. Materials used in a production process are ordered and received only from suppliers who are approved by the quality department.

1.2 Production volumes

Acino's portfolio, besides blistered products has changed over the last five years. In 2017, main product produced was painkiller, while last year mainly antidepressants were packed. Produced bottle and blister products, also finished products volumes evolution in years 2017 until 2021 shown in Figure 1.5. Due to confidential info, volumes are multiplied with a random coefficient. For reasons of comparability, 2022 volumes are excluded.

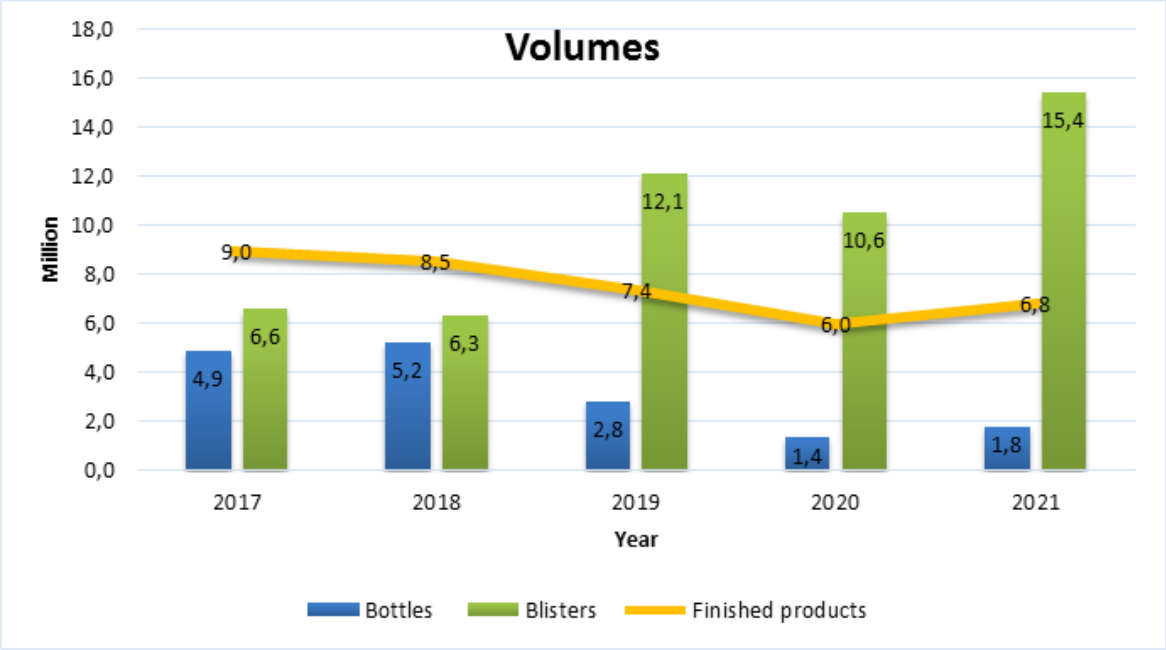


Figure 1.5 Acino's production volumes over the last 5 years

Bottled products volumes are descending, even though medicines packed in blisters are growing steadily. Packaging type depends on the customer demand. Bottled medicines are packed as one bottle in folded box. Blisters are packed from 1 blister up

to 20 blisters in one folded box. In 2017 and 2018 blisters were packed mainly singly, since 2019 blisters are packed mostly doubled or more. Therefore finished products numbers have declined, while produced blisters have increased.

Within 5 years, approximately 76% of produced products are medicines packed in blisters. Blister line number two started producing blister products in July 2021. Blister products packaging units will increase henceforth, as third blister line was added to the production area in March 2022. In sum, 2 bottle and 3 blister packaging lines are in use at the current moment (as of 31.03.2022). Secondary packaging for blisters on carton line 1 was done on the first floor until April 2020. Blisters and bottles were produced on the second floor and cartooning was done on the first floor.

Produced batches per production line listed in Table 1.3. Due to confidential data, numbers are multiplied with a random coefficient. Third blister line data is not brought out as only full year numbers are presented. Batch is a defined quantity of starting material, packaging material or product processed in one process or series of processes so that it could be expected to be homogeneous [6].

Table 1.3 Produced batches per production line

Year	Carton line	Bottle line 1 (T1)	Bottle line 3 (T3)	Blister line 1 (B1)	Blister line 2 (B2)
2017	144	186	261	70	-
2018	101	226	151	89	-
2019	343	89	176	255	-
2020	46	14	207	216	-
2021	-	24	219	359	72

1.3 Pharmaceutical quality system

Quality of pharmaceutical products is the most important aspect, being base for all other activities. Pharmaceutical quality system is defined as a management system to direct and control a pharmaceutical company by regard to quality [7]. Packaging of pharmaceutical products is strictly regulated and it is important to comply with applicable laws, rules, regulations, guidelines to produce safe and pure products keeping in mind that the main duty is not do place patients at risk. It is important to highlight that pharmaceutical industry focus is on compliance.

Requirements for manufacturing medicinal products specified in the Good Manufacturing Practice (GMP), which is applicable for production and quality control. Safeguarding a high level of product quality and regulatory compliance is a

fundamental objective of Acino and its operations [1]. The five principles of GMP in pharmaceutical industry are presented in Figure 1.6.

Figure 1.6 Five principles of Good Manufacturing Practice [8]

People are the most important asset, personnel must know clearly their responsibilities and they must be trained sufficiently [8]. GMP guideline state that the correct manufacture of medicinal products relies upon people [10]. Products must have high quality and must be safe. Premises and equipment must be design to avoid cross contamination and mix up. Also, rooms and equipment must be easily cleanable and maintained. Procedures and processes must be in place. Crucial part in manufacturing pharmaceuticals is documentation as it is base of complying GMP requirements. Procedures, processes, instructions must be written down and signed by authorised persons. Moreover, all indirect or directly connected activities to the production must be documented at the time action is taken.

EudraGMDP database affirms that Acino Estonia has GMP certificate no IN-2-14/21/1 (H-Mf) [9]. GMP certificate proves manufacturer complies with quality standards. The basic concepts of Quality Management, Good Manufacturing Practice and Quality Risk Management are inter-related and they are described in EudraLex Volume 4 Chapter 1 [10]. In addition, Acino has Estonian Agriculture and Food Board licence to pack food supplements.

Acino Estonia packages, stores, performs quality control of medicinal products and food supplements and provides contract manufacturing and distribution service

according to the Manufacturing Authorization no 419 issued by the Estonian State Agency of Medicines. Authorized activities are [11]:

- Manufacturing operations;
- Wholesale;
- Batch certification;
- Handling of narcotic and psychotropic substances;
- Importation of medicinal products from MRA countries;
- Manufacturing of Human Investigational Medicinal Products.

All operations are done in accordance with written standard operation procedures (SOP). Quality department is responsible for implementation and management of SOP system. Self-inspections and reviews of all operations ensure quality oversight of product quality, processes and the performance of the quality management system itself. All personnel ensure quality and everyone acts with fairness and honesty and in the highest ethical manner in company business and activities [12].

Pharmaceutical quality system elements are [7]:

- Change management system;
- Corrective and preventive action system;
- Process performance and product quality monitoring system;
- Management review of process performance and product quality.

Change management system stands for continuous improvement of products, processes, procedures, equipment within the organization. Corrective and preventive actions also named as CAPA system is an investigation process of finding root cause. Process performance is measured and examples of metrics are recall rate, rejected lots, audit inspections, quality complaints. Product quality should be monitored to assure or even exceed expected product quality. In addition to systems, periodic management review of process performance and product quality is required.

1.4 Premises and technical systems

Total net area of the facility is 4001 m^2 [13]. The building is a three-storey building, which consists of different sections: office, production zone warehouse and utility systems. Premises displayed in Figure 1.7.

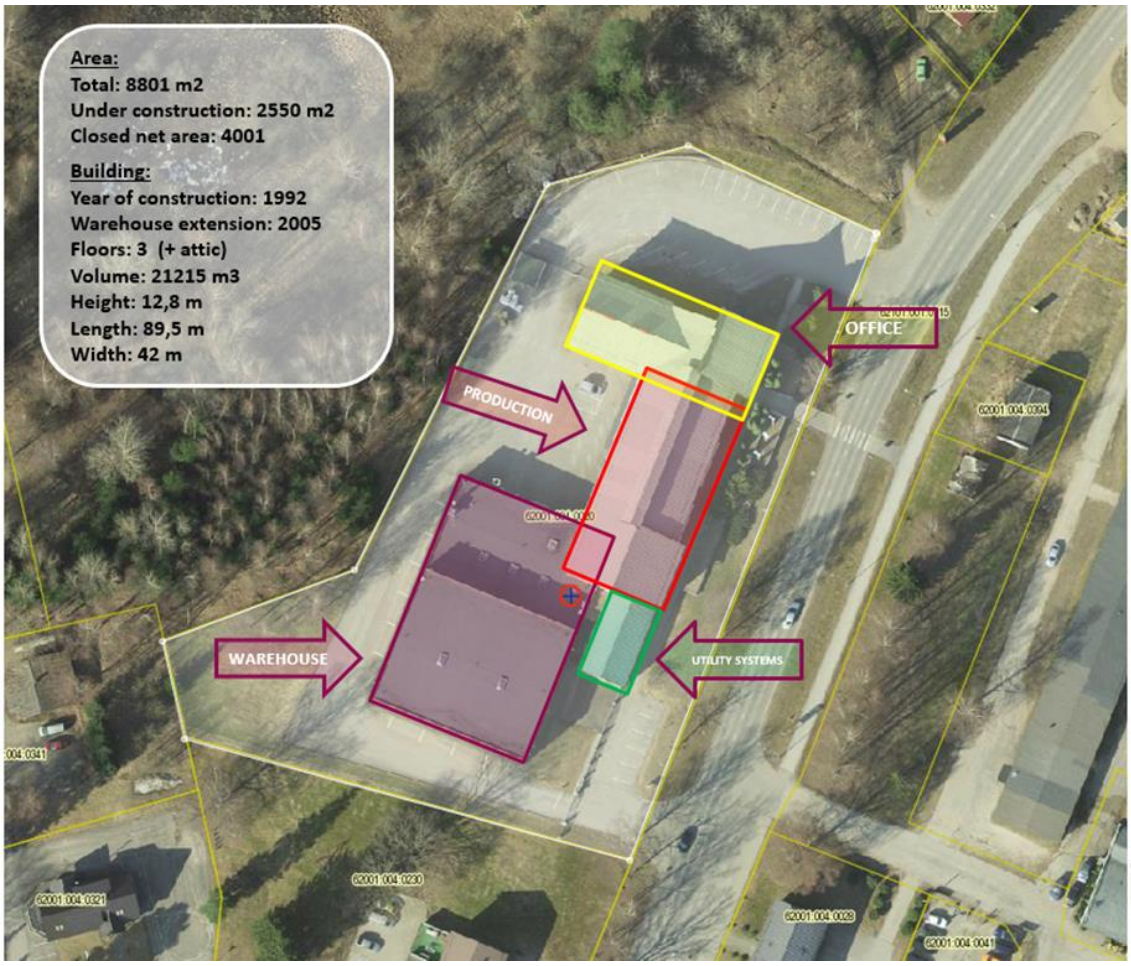


Figure 1.7 Overview of the building sections

Office rooms are mainly on the right section of the building, on the ground, first and second floor. Production rooms are located on the first and second floor. Technical section is on the ground and third floor. Warehouse is connected to the main building and goods are being transported between warehouse and production area via lift. Lift with dimensions 1.8x1.3 meters shown in Figure 1.8.

Figure 1.8 Lift for materials transport

HVAC system in the pharmaceutical industry is key equipment, which maintains required environmental conditions during manufacturing process. Each production floor have their own air-handling unit (AHU) equipped with filtration (EU5 and EU9 filters), heating, cooling, humidifying, and dehumidifying systems. In order to secure product quality, production rooms are pressurized against surrounding areas so the air movement is always outwards.

Humidity and temperature values are constantly monitored throughout all packaging and storage areas. Each room inside storage and production area is equipped with a sensor, which is connected to a Building Management System (BMS). BMS system's main purpose is to control AHU so that the conditions inside production and storage area will remain inside defined limits. BMS is also responsible for logging of temperature and humidity values due to GMP requirements.

Cleanroom environmental requirements and guidelines are provided in ISO 14644-15. Primary zone E corresponds to ISO 8 cleanroom and secondary zone F is equivalent to ISO 9. Requirements for environmental conditions are listed in Table 1.4. Important cleanroom design parameter is an air changes per hour (ACH), mathematically expressed as follows:

$$ACH = \frac{Q}{V} \text{ [14]}$$

To calculate ACH volume of air filtered (Q) has to be divided by the room volume (V).

Table 1.4 Environmental monitoring requirements for production rooms and storage

Parameter	**Zone E**	**Zone F**	**Zone G**
Room class by ISO 14644	ISO 8	ISO 9	n/a
Temperature ºC	+15... +25	+15... +25	+15... +25
Humidity %RH	≤ 60	≤ 60	≤ 60
Filters	EU5 and EU9 for 100% fresh supply air, in addition H14 filters if recirculated supply air	EU5 and EU9 for 100% fresh supply air	EU3 and EU5 for 100% fresh supply air
Air change rate	≥10 x per hour	≥ 3 x per hour	n/a
Differential pressure	Δ Pa ≥10 (against corridors) Δ Pa ≥3 (against sec pack)	Δ Pa ≥ 3 (against corridors)	n/a
Airborne particle concentration	ISO 8	ISO 9	n/a
Microbiology	Grade D (GMP)	Grade D (GMP)	n/a

1.5 Production zone and manufacturing lines

Production rooms are classified as zones to minimize the risk of particulate and microbiological contamination of the product and materials being handled. Entering to the production zone is only permitted to the personnel directly related with production activities, personalized chip cards are in use to control admission.

Controlled zones in Põlva pharmaceutical plant are [13]:

- Zone E for primary packaging;
- Zone F for secondary packaging, auxiliary rooms;
- Zone G for storage areas.

Zones are differentiated with colors, zone E uses red, zone F is marked with green and zone G is colored blue. Drawings of production zones will follow on the next pages named as Figure 1.10, Figure 1.11 and Figure 1.14. Also, personnel and material movement path is shown on the plans.

Different zones have certain apparel requirements to protect the product and personnel. Zone E and F insist hair cover, lab coat, shoes, and beard cover. Additionally, facemask and gloves are mandatory in zone E. Zone G do not have specific requirements for apparel, but safety shoes are worn where required. Personnel hygiene topic is critical and special rooms are in use for hand washing and disinfection.

Airlocks (AL) are between rooms with different cleanliness levels used by people and goods, bubble type airlock shown in Figure 1.9. Airlock is an enclosed space with two or more doors which are between two or more rooms, e.g. of differing class of cleanliness, for the purpose of controlling the air-flow between those rooms when they need to be entered [6]. Airlock main purpose is to avoid cross-contamination. Airlock between zone E and F is for personnel and materials, airlock between zone F and G is only used by goods. Airlocks are marked on the drawings as MAL (material airlock) and PAL (personnel airlock).

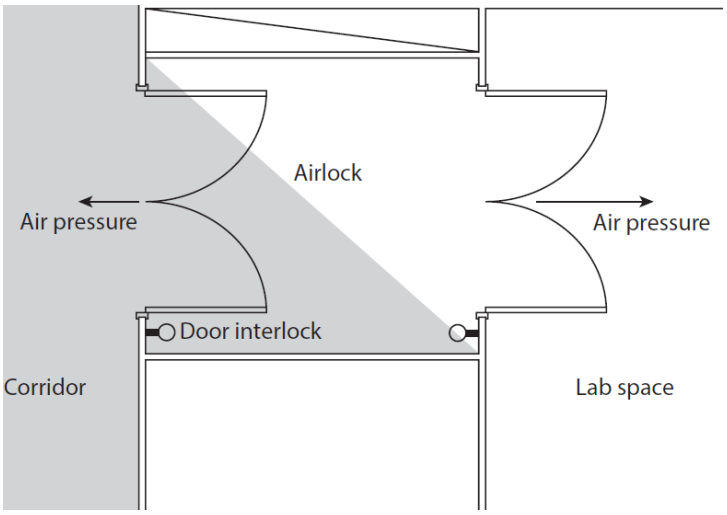


Figure 1.9 Bubble type airlock [15]

Warehouse, office, archive and auxiliary rooms are on the ground floor. The production and warehouse are located in different controlled zones accordingly zone E and zone G. Lift is in use to transport packaging materials to the production floor airlock and finished products down to the warehouse. Separate warehouse areas are on the ground floor. Main area for bulk, packaging materials and finished products, area 1 for narcotic drugs and area 2 for finished products reference samples. Ground floor layout, material and personnel movement is shown in Figure 1.10 and room sizes are listed in Table 1.5.

Table 1.5 Ground floor room sizes (As Is)

No	**Area name**	**Size (m^2)**
1	Warehouse	1322,5
2	Warehouse 1	44,8
3	Warehouse 2	15,7
4	Laundry room	35,1
5	Workshop	36,4

Not all facility rooms are marked and brought out, only areas that are production rooms or related with production activities. As reusable protective clothing is used in production zone, laundry room is needed for clothes washing and it is used daily. Workshop includes machines used for repair work, 3D printing and for overall engineering purposes.

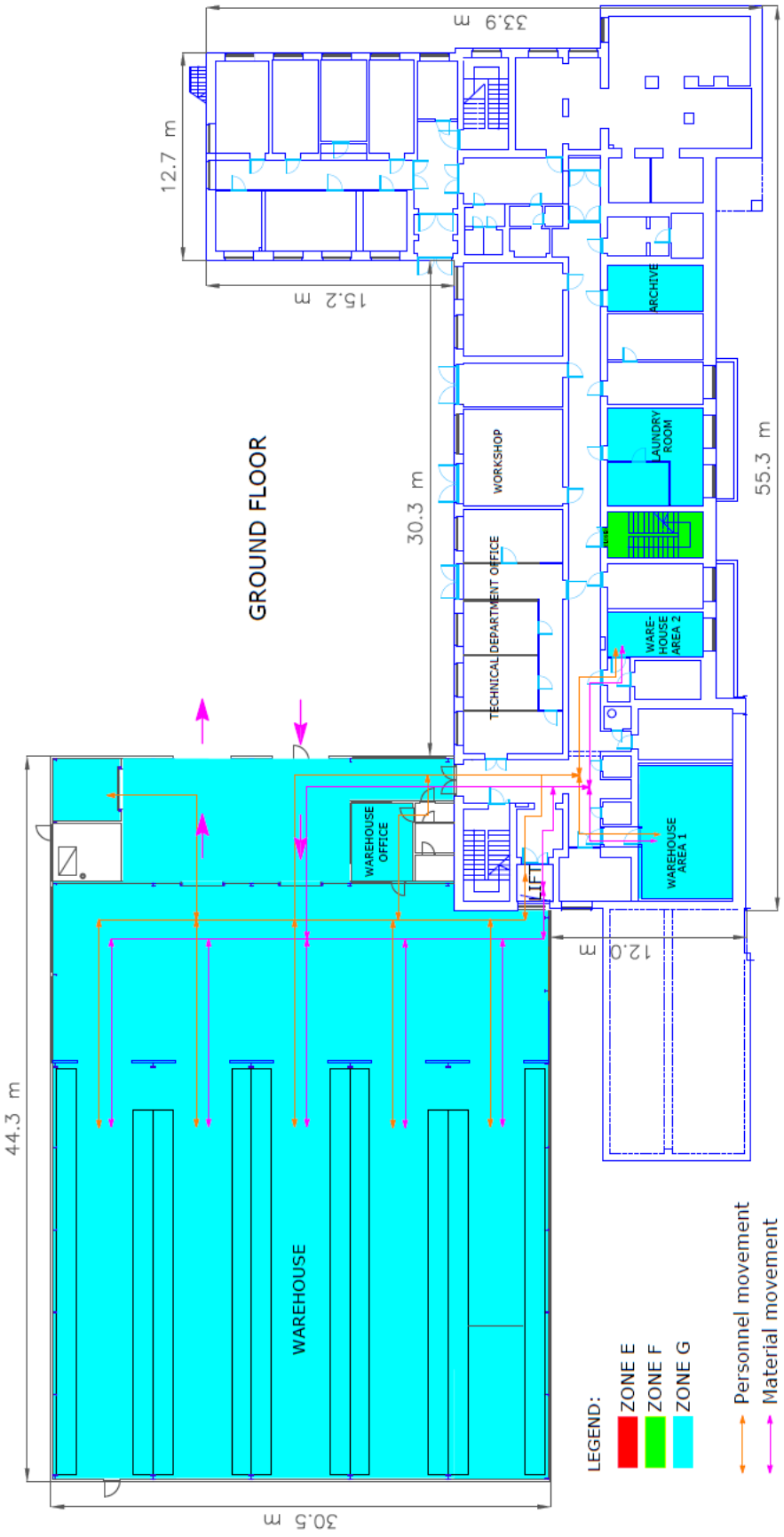


Figure 1.10 Ground floor zone concept and movement of personnel and material

Two automated blister packaging lines named as B2 ja B3 are located on the first floor, B2 line layout shown in Figure 1.12. As blister packaged products demand has been higher than bottle packaged products, further analyse will focus on blister packaging lines and products. As lines B2 and B3 are similar, only B2 layout with measures and workstations are brought out. Workstations are marked with colour red and can be seen Figure 1.13. In addition, office and auxiliary rooms are on the first floor. First floor layout and movements shown in Figure 1.11 and room sizes are listed in Table 1.6.

Table 1.6 First floor room sizes (As Is)

No	**Area name**	**Size (m^2)**
1	MAL (warehouse)	5,4
2	Wash area	24,5
3	B3 MAL/PAL	5,2
4	B3 primary	31,2
5	B3 secondary	90,6
6	B2 MAL/PAL	3,3
7	B2 primary	34,6
8	B2 secondary	69,6
9	Production office	36,8
10	Format parts	13,0
11	Clothes change room W	10,7
12	Clothes change room M	14,8

Format parts are cleaned manually by using tap and pure water (Type 2) operation is performed in wash area. Type 2 pure water is distributed from a tap water source and it is composed of three different sections: water purification, storage tank and point of dispense [16].

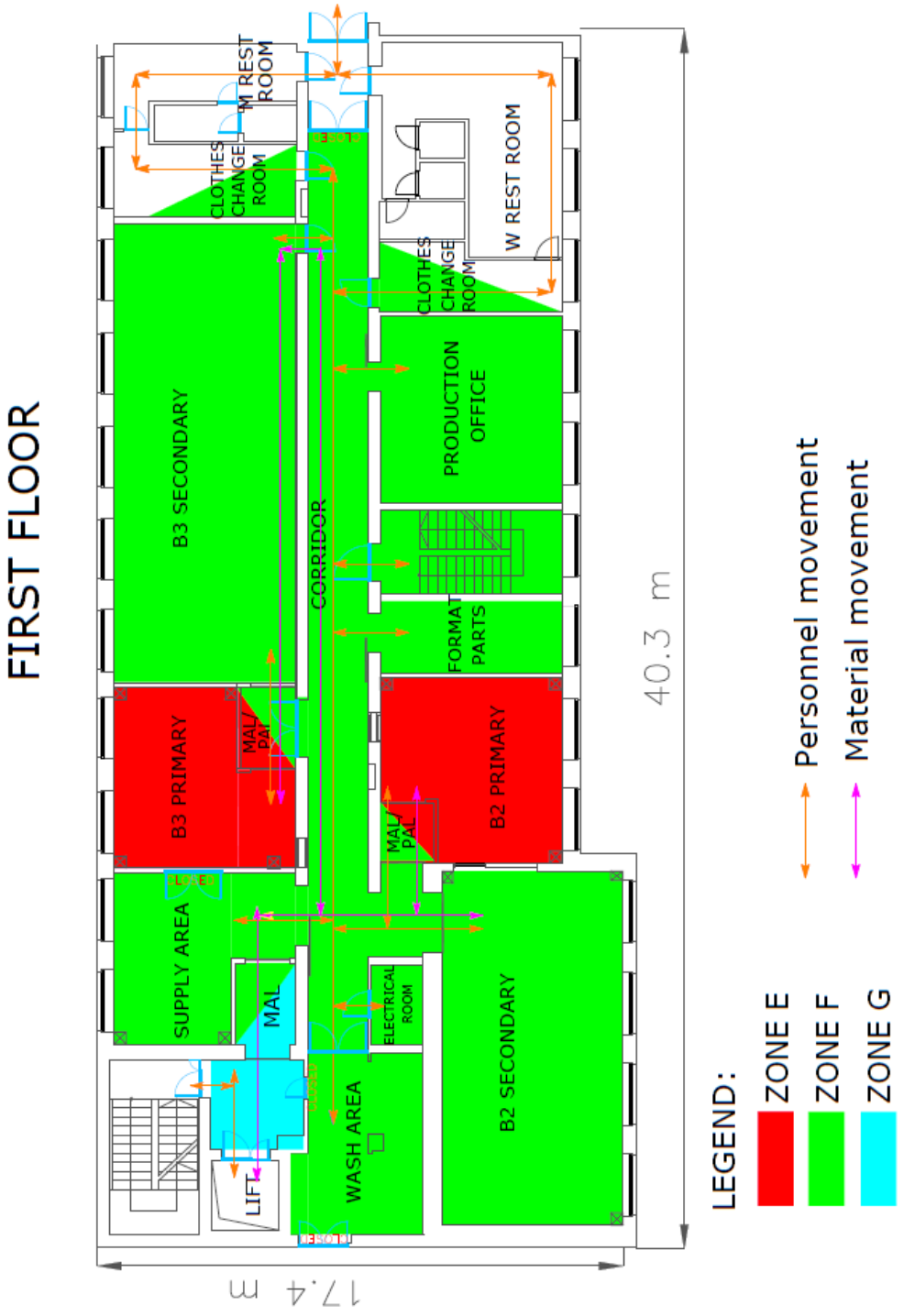


Figure 1.11 First floor zone concept and movement of personnel and material

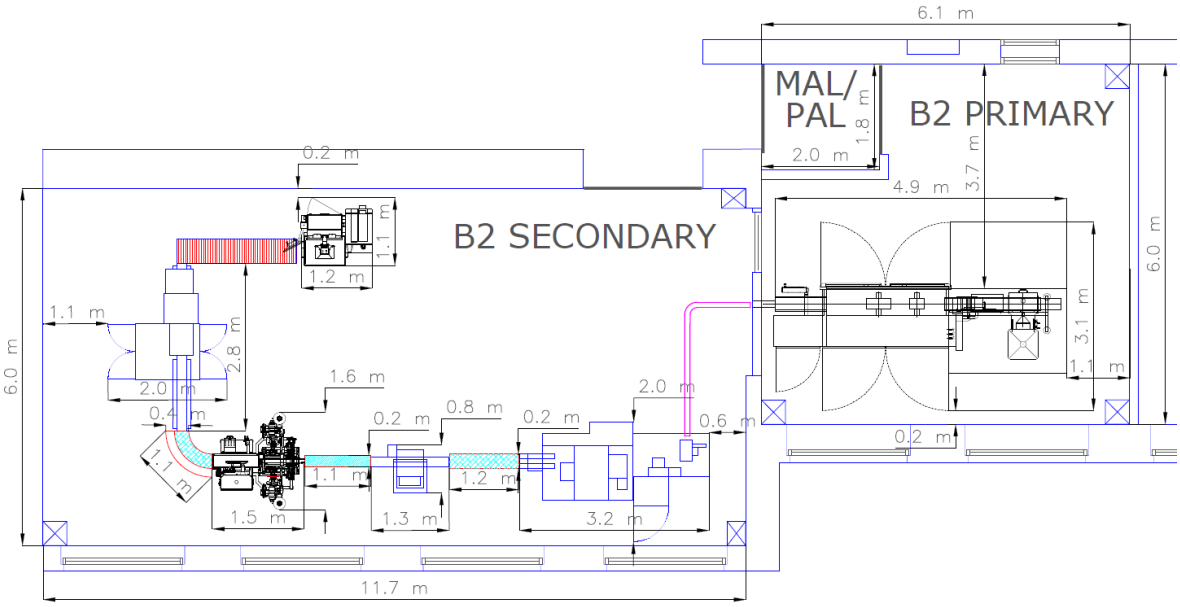


Figure 1.12 Blister packaging line B2 layout

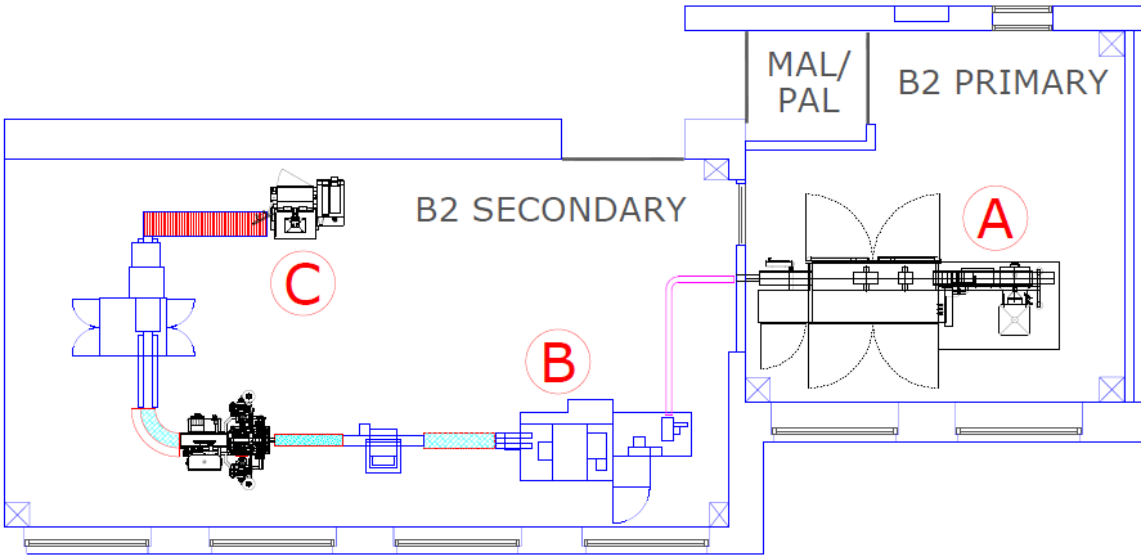


Figure 1.13 Blister packaging line B2 workstations

One production line is typically operated by one technician in primary zone position marked with A and by two operators in secondary zone marked as B and C. May occur, depending on workstation B speed, that only 1 operator is needed in secondary area.

Second floor zone concept and personnel, material flow is shown in Figure 1.14 and room sizes are listed in Table 1.7. Two automated bottle-filling lines named as T1 and T3, one automated blister packaging line B1, office rooms and warehouse areas are located on second floor. As well, quality department and quality control (QC) room is located on the same floor.

Table 1.7 Second floor room sizes (As Is)

No	**Area name**	**Size (m^2)**
1	Warehouse 3	69,9
2	Warehouse 4	24,5
3	Workshop	12,5
4	B1 secondary	64,0
5	B1 primary	37,6
6	B1 MAL/PAL	6,5
7	T1 secondary	52,7
8	T1 primary	52,0
9	T1 MAL/PAL	11,4
10	Format parts total	24,6
11	Wash area	34,1
12	T3 secondary	89,9
13	T3 MAL/PAL	5,5
14	T3 primary	35,6
15	MAL (warehouse)	4,9
16	QC	33,7

Figure 1.14 Second floor zone concept and movement of personnel and material

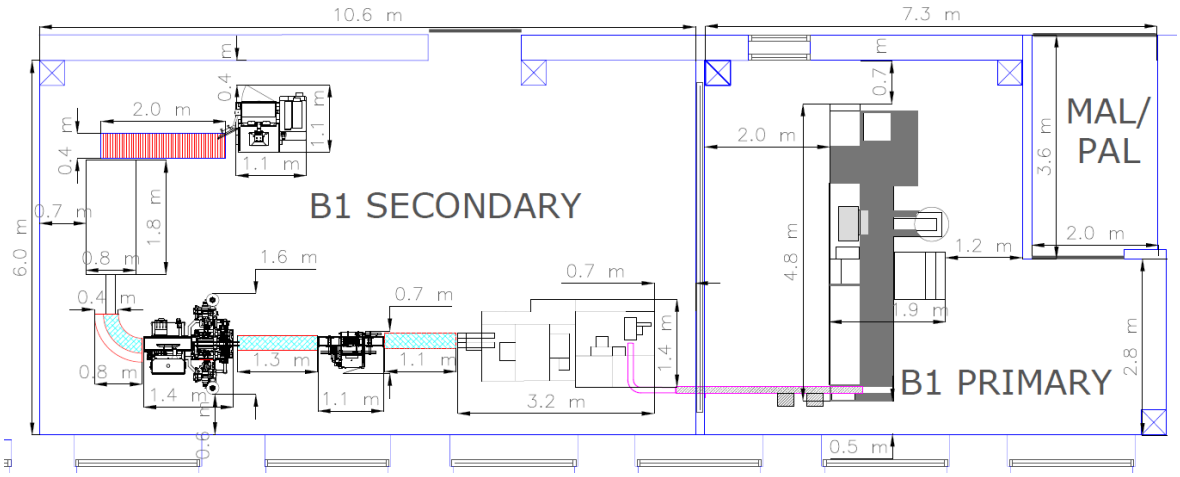


Figure 1.15 Blister packaging line B1 layout

Figure 1.15 presents blister packaging line B1 layout with machines and conveyors measures and Figure 1.16 shows same line layout with workstations marked as A, B and C.

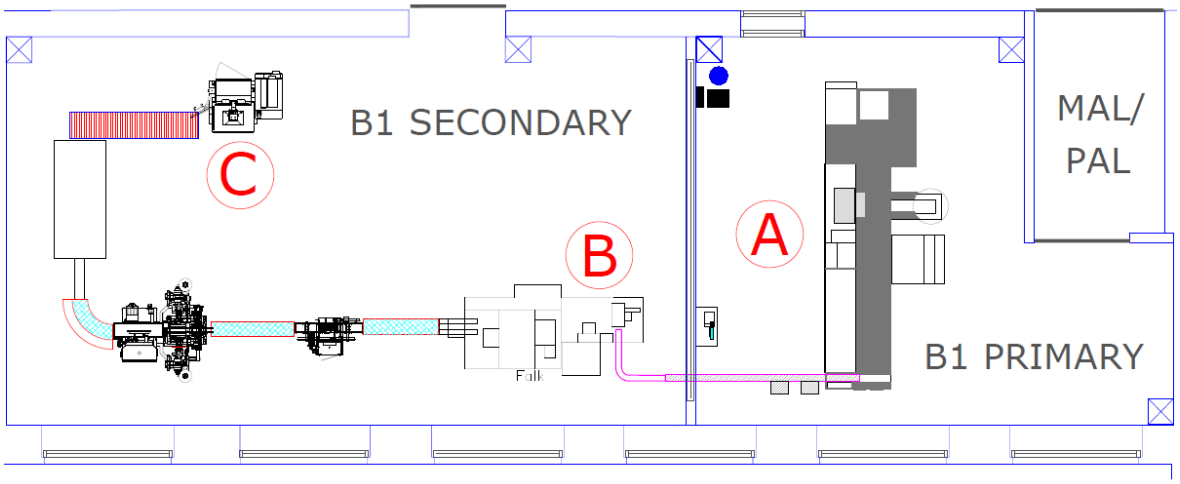


Figure 1.16 Blister packaging line B1 workstations

1.6 Manufacturing operations

Manufacturing operations are primary and secondary packaging. Primary packaging is critical to maintain safety, efficacy, potency, and purity of the drug product [15]. Secondary packaging follows primary packaging. Both operations are held in separate rooms, but are connected with transfer conveyor. Manufacturing areas are on the first and second floor where plant layout is considered as product layout and on the manufacturing lines flow principle is applied. Medicines are packed on an assembly

line, where every machine has certain task to process. Blister packaging operations sequence in primary and secondary room is shown in Figure 1.17 and Figure 1.19.

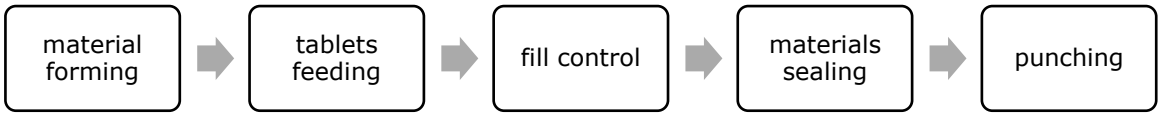


Figure 1.17 Blister packaging operations sequence in zone E

Overall purpose of all pharmaceutical packaging is to protect the product, and in a wider sense to preserve and collate dosage units [17]. Blister packaging machine is located in the primary zone E, machine picture with materials and medicines moving flow is shown in Figure 1.18. Blister packaging machine is the workstation A in the Figure 1.13. First step with this machine is forming aluminium foil. After the sockets are formed, tablets are fed. Next step is camera fill control and after that forming and lid materials are sealed. Aluminium or PVC foil is used as a lid material. Punching is the last step with the blister packaging machine.

Figure 1.18 Blister packaging machine

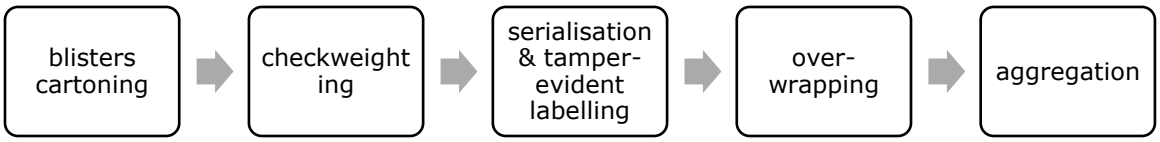


Figure 1.19 Blister packaging operations sequence in zone F

Blister packaging secondary zone F consists of 5 machines: cortoner, checkweighter, serialisation station, overwrapper and aggregation station. An intermittent motion cartoner packages blisters to the folded box and adds leaflet. Carton serialisation, tamper-evident labeller and aggregation unit machines are needed to meet the legal specifications. Cartoner is marked as working place B in Figure 1.13 and picture of the cartoner can be seen in Figure 1.20. Medicinal product packages are serialised, having unique code on the folding box to prevent falsified medicines reaching to the patient. The package not only protects the product but also provides a method for tracking its use or compliance [18]. For patient protection, prescription medicine folding boxes must have serial number and anti-tampering labels. Serialisation unit is with inkjet printer and VisioRead inspection system. Tamper evident labeller enables double-sided sealed labelling of pharmaceutical boxes. Bundling machine has heat sealing banding station which provides product bundling flexibility. In addition, products are aggregated for tracing purpose. Aggregation unit is with camera scanning individual packs and picture of the machine is shown in Figure 1.21 and it is marked as workplace C in Figure 1.13.

Figure 1.20 Cartoner [19]

Figure 1.21 Aggregation unit [20]

2 THEORETICAL OVERVIEW

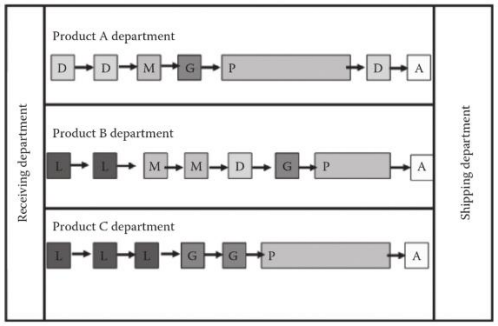
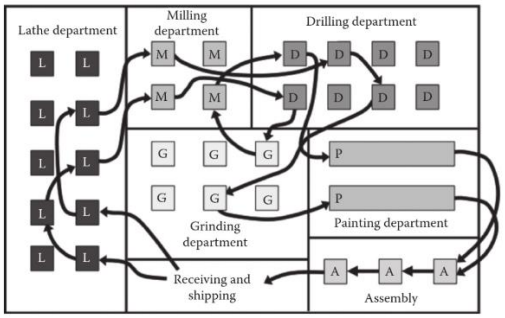
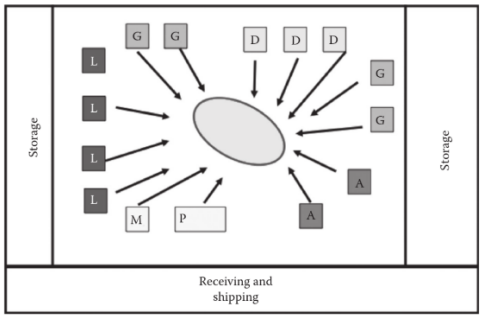
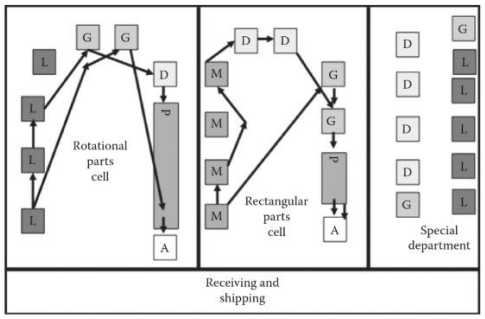
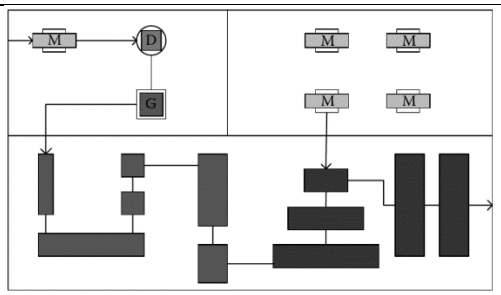
2.1 Manufacturing facility layouts

To start designing manufacturing facility, it is important to have an overview of general manufacturing layouts. Manufacturing facilities design is the organization of company's physical assets to promote the efficient use of resources such as people, material, equipment, and energy [17]. Right layout will give many benefits for the company. The quality and cost of the product and supply ratio are directly affected by the facility design [17]. To start with, facility layouts are studied, general layout types according to literature are [21], [22], [23]:

- Product layout;
- Process layout;
- Fixed-Position layout;
- Functional layout;
- Hybrid layout.

In product layout, material flow is usually one-directional, output of one machine is input to the next machine. Machines are set along the product route in a sequence of operations the product goes [21]. The product layout is also named as flow layout, assembly layout or line layout. In a process layout workstations are arranged based on the operations performed [21]. Process layout flow pattern is typically indirect according to machines locations. Fixed-position layout means operations with the product are done in one place. Mainly used for manufacturing large and heavy objects such as ships and planes. Functional layout indicates that similar resources are located together [22]. Hybrid layout type or also named as combined layout refers to the manufacturing where two or more layouts as described above are in use. Layout schemes shown in Table 2.1.

Table 2.1 Facility layout [21]

Layout type	**Layout scheme**
Product	
Process	
Fixed-position	
Functional	
Hybrid	

Movements through the facility are one of the major topics to analyse while designing the plant as smooth flow of operations will increase the efficiency. The shorter the flow of material is through the plant, the better the reduction costs are [22].

2.2 GMP facility

GMP is a worldwide pharmaceutical manufacturing standard [24]. Good manufacturing practice guidelines have in total four parts providing guidance for medicinal products for human and veterinary use. It is a system of processes, procedures, and documentation to ensure products are produced and controlled according to quality standards [25]. Designing GMP facility main purposes are to protect the medicinal product, prevent contamination and to comply with safety, health and environmental requirements. GMP facility must satisfy demanding regulatory conditions.

Production, storage, quality control and ancillary areas must meet the requirements as described in GMP premises and equipment chapter. Facilities and the flow of material and personnel through the facilities shall be designed to ensure that different substances and materials are kept separate and do not contaminate each other [26]. Manufacturing medicines insists high level of cleanliness in production. Premises and equipment layout and design must aim to minimise the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt and, in general, any adverse effect on the quality of products [27].

One important part of GMP requirements is avoiding contamination and confusion of materials and products [28]. The design has to take into account the guidelines of different regulatory authorities of countries to which the product will be delivered [28].

Operations in manufacturing facility need their own exact area. Specific areas demarcated for [29]:

- Holding rejected components, drug product containers, closures, and labelling before disposition;
- Storage of released components, drug product containers, closures, and labelling;
- Storage of in-process materials;
- Manufacturing and processing operations;
- Packaging operations;
- Quarantine storage;
- Control and laboratory operations;
- Aseptic processing:

- Floors, walls, ceilings with smooth, hard surfaces to be easily cleanable;
- Temperature and humidity controls;
- Air supply filtered through high-efficient particulate air filters under positive pressure;
- System for monitoring environmental conditions;
- System for cleaning.

One main idea is that space for listed areas must be allocated in the facility to avoid cross-contamination and mix-ups. What is more, good facility design is necessary in order to ensure that processes can be validated and that they will continue to perform reliability and consistently, including facility layout, equipment, environment, and critical utilities [30].

The ground floor should be considered premium space and such should be reserved for functions that cannot be located elsewhere [17].

2.2.1 Clean area

Clean area is located in the production zone, it is a room with a controlled environment. Cleanroom designed, maintained, and controlled to prevent particle and microbiological contamination of the products [31]. Clean areas are classified as shown in Table 2.2.

Table 2.2 ISO and GMP cleanroom classifications [32]

ISO classification	**EU GMP**
ISO 4.8	Grade A
ISO 5/7	Grade B
ISO 7/8	Grade C
ISO 8	Grade D

Designing ISO class 8 cleanroom include requirements for [33]:

- HEPA filtration,
- Air pressure;
- Temperature and humidity control;
- Number of personnel working in the area;
- Static control requirements;
- Maximum contaminant levels;
- Sanitation requirements;
- Number and type of windows and doorways;
- Lighting and electrical needs.

2.3 The Lean philosophy

Lean is identifying and eliminating the waste. Lean manufacturing is a generic process management philosophy derived mostly from the Toyota Production system [34]. Wastes that do not add value to the customer and should be eliminated are [34], [35]:

1. Overproduction;
2. Waiting;
3. Inventory;
4. Transportation;
5. Over-processing;
6. Motion;
7. Defects.

Overproduction is manufacturing product before it is needed, being costly to the manufacturer [34]. When good are not moving or being process is defined as waiting, waste of waiting is quite easy to identify [35]. Inventory represents items waiting for actions, holding costs increase with the size of the inventory size costing more to hold more [35]. Transportation including material handling is moving items from one location to another, distance for moving items are determined by the layout of the facility and the routing sequence of operations [35]. Next, over-processing is taking extra steps that are not feasible, for example adding additional parts for improving visual look, but what is not expected by a customer. Unnecessary motion is also consider as waste, referring to the producer, equipment, worker movement, which could cause damage, fatigue, and safety issues [34]. Major source of waste is defects in any product or service [35].

It is efficient to eliminate the tasks that do not add the value to the product [36]. Lean definition by David Rizzardo is said as lean is a strategy designed to embed a culture of continuous improvement where everyone strives to eliminate waste in company process by utilizing the appropriate tools to add ever-increasing value for customer [37]. Another explanation by Darina Lepadatu and Thomas Janoski is lean, long-term and loyal [38].

Implementing lean production system (LPS) greatly relays on employees knowledge. The most important success factors revolve around leadership and aspects related to the qualification of employees. If these are not taken into account sufficiently, they might act as barriers [39]. To start with a lean project, qualified members from the company and consultants outside the company are preferably needed. To decide on

the scope of the LPS implementation and which methods and tools need to be used, a systematic evaluation of the company is essential [39].

Development of lean production is a mix of management and industrial engineering principles [38]. Summarizing Lean production from a management and industrial engineering perspective according to literature are [38]:

- Long-term philosophy;
- Standardization;
- JIT inventory;
- Relations with suppliers;
- Teamwork;
- Buffering permanent employees;
- Design of the workspace.

Following gives brief explanation for lean production approaches. To understand work content and company philosophy, company decisions should be based on a long-term philosophy [38]. Assembly-line tasks have to be standardized for a visual control by using technologies [38]. Just-in-time (JIT) means producing necessary units in the necessary quantities at the necessary time [40]. By relations with suppliers is meant creating a trusted network of suppliers including JIT [38]. Teamwork is essential for every company to have good cooperation both for developing and problem solving. Buffering permanent employees is replacing employees who are absent from work for a short time. Design of the workspace is connected with JIT, using pull system based on orders that operates on the basis of continuous flow [38].

As mentioned before in pharmaceutical quality system paragraph - it is important to highlight that pharmaceutical industry focus is on compliance. GMP focus is to manufacture safe medicines for the patient, while lean focus is improvement and value creation from a customer's perspective [41]. Lean and GMP cab be associated by knowing well different regulations and expectations for pharmaceutical company. Human medicines packaging is highly complex and regulated, need to comply authorities, business partners, and shareholders requirements. Lean manufacturing and GMP in pharmaceutical manufacturing features are compared in Table 2.3.

Table 2.3 Lean and GMP comparison [41]

No	Area	Lean	GMP
1	Objectives	Waste reduction Value creation	Ensure product effectiveness Harm prevention
2	Focus	Value stream	Product development Quality assurance
3	Approach to manufacturing	Quality and productivity	Quality first
4	Improvement	Continuous	Regulated
5	Main goals	Cost reduction Quality improvement Reduce cycle time Reduce inventory Improve delivery	Follow validated processes Prevent deviation
6	Main tools	Value stream mapping Kaizen Training	Documentation Personal qualifications and training Cleanliness Validation and qualification Audits

3 CURRENT PRODUCTION LAYOUT ANALYSIS (As Is)

Current manufacturing plant is three-storey building and materials are moved from warehouse to the production via lift. Manufacturing activities take place on the first and second floor of the building. Pharmaceutical packaging facility requires separated areas for different operations such as storage, quality control, manufacturing operation, maintenance workshops and other ancillary areas. Figure 3.1 shows concise overview of the main operations from raw materials (RM) receiving until finished products (FP) shipping.

Figure 3.1 Overview of operations sequence in Acino Estonia OÜ

At the beginning of the process, raw materials as tablets, capsules and packaging materials are received and stored in the warehouse (WH) having specified areas for quarantined , rejected and released components. Before storage, containers including medicines are cleaned. Requirements for these activities are stated in chapter 5 of Good Distribution Practice (GDP) of medicinal products for human use. Materials are moved inside the warehouse by using manual pallet trolley and a forklift. Receiving process aim is to ensure that goods are as ordered and have not been damaged during transport.

Next step is a quality control (QC), this area with applicable equipment is use for a primary and secondary packaging components controlling. QC worker gets the raw material samples from the warehouse, which means route from ground floor to the first floor and back has to be taken. No lift is in use for transporting QC samples between floors, stairs has to be taken. What is more, controlled items need utilization, it means checked materials are transported back to the ground floor. In sum, samples are moved along same route 3 times. GMP chapter 6 determines quality control guidelines. QC control purpose is to ensure that received materials comply with specifications.

After the QC has released the necessary materials for the production process, warehouse workers are allowed to bring the materials to the production material

airlock (MAL). This step is done by using lift and manual pallet trolley. As mentioned before, production area is laid on two separate floors. It is import to bring out that only plastic pallets are in use to have an aseptic manufacturing.

Next operation after QC control is manufacturing. Production worker will bring the materials with a manual pallet trolley from the warehouse MAL according to the material class to the primary MAL or to the secondary production room. Production supervisors, also workers control materials correctness and completeness before starting batch production and packaging the pharmaceuticals can begin when correct materials are positioned on production line machines. Production operations are based on written procedures as defined in GMP chapter 5. Finished products are sent back to the warehouse using warehouse MAL and products will stay in the warehouse until QP has finished its operations.

A qualified person (QP) in a quality department room located on the second floor does a batch release. QP receives the batch documentation from the production pharmacist who places the documents to the document airlock (DAL) which is located on the second floor. Batch release detailed guidelines can be found in GMP annex 16. QP role is to check every finished product batch and give out a signed certificate confirming that the batch complies GMP and the requirements of marketing authorisation.

FP are held and sent out from the warehouse. Shipping is done according to GDP chapter 5 guidelines.

All described operations are done in sequence and rooms for these operations should be located as close as possible to minimise the material and personnel movements and to avoid cross-contamination and mix-ups.

Manufacturing flows through facility are categorized as material, personnel, equipment, and waste flow. In this thesis material movements in a production zone are in focus and analysed. Specifically, tablets, capsules, packaging components and finished products movements are inspected. Movements in the production zone simulated using software Siemens Tecnomatix Plant Simulation version 16.0. Siemens Tecnomatix was chosen since student had used it during master's programme and it was the most suitable material flow visualizing software. Current plant first and second floor materials flow rate is shown in Figure 3.2 and Figure 3.3. Tecnomatix tool SankeyDiagram visualizes materials flow rate in purple colour.

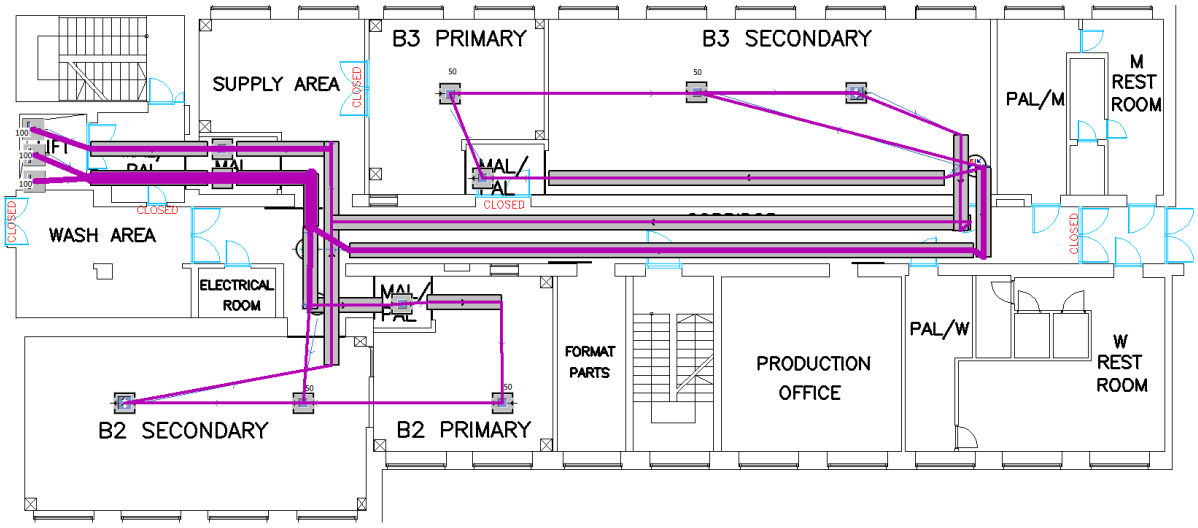


Figure 3.2 First production floor with a Sankey diagram

In 2021 first production floor was reconstructed and built for two blister packaging lines, named as B2 and B3. As aforesaid one manufacturing line passes two production rooms since different environmental conditions are required. Materials movement start on the ground floor, where warehouse worker with the packaging components travel to the first floor by using lift. Lift has an important role in moving materials, as there are no other possibilities to transport pallets between floors. Lift is from the year 1997. Warehouse worker places pallets to the MAL and informs production about it by a phone call.

Figure 3.2 indicates that the heaviest traffic on the first production floor is from the lift until at the beginning of production corridor. This route is used for transporting packaging components for the production process. Important to point out that primary and secondary materials pass the same route and use same airlocks with personnel. Simulation was done with random number to visualize materials moving routes. In the simulation every production line input is 2 sources and output one finished product. As it seen in production zone figure, some doors are marked as closed. These doors are only in use while production does not work, usually on summer and winter holidays for moving machines or other repair work if needed. Distances in meters between these rooms are listed in Table 3.1.

Table 3.1 First production floor distances (As Is)

No	Movement	Distance (m)
1	Lift → MAL	6,2
2	MAL → B2 MAL/PAL	11,2
3	MAL → B2 secondary	13,5
4	MAL → B3 MAL/PAL	47,3
5	MAL → B3 secondary	45,6

In sum, longest distance 47,3 meters on the first floor is between MAL and blister packaging line B3 MAL/PAL.

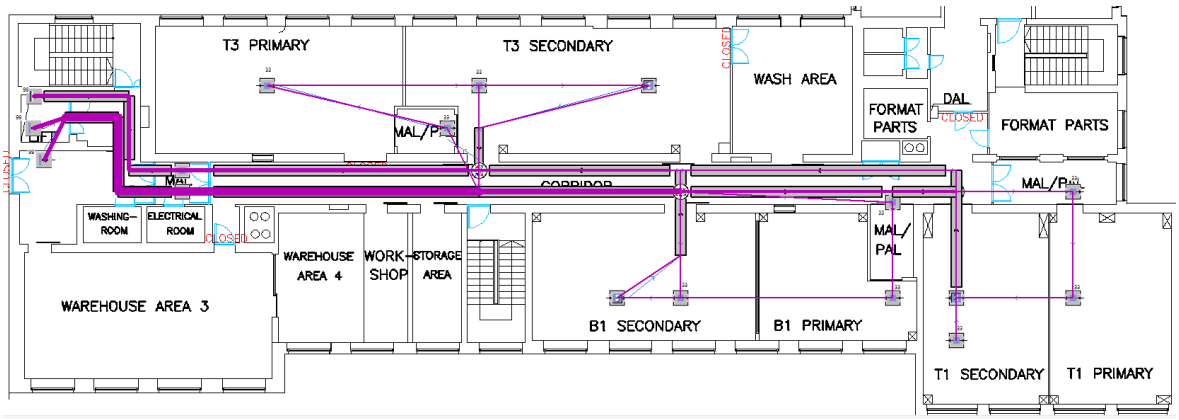


Figure 3.3 Second production floor with a Sankey diagram

Second production floor serves one blister packaging line B1 and two bottle packaging lines T1 and T3. Figure 3.3 indicates that the heaviest traffic on the second production floor is from the lift until T3 production rooms. As on the first floor, primary and secondary materials pass the same route. Second production floor movement distances listed in Table 3.2. Highlighted are the most important movements related to the production process throughout the production area.

Table 3.2 Second production floor distances (As Is)

No	Movement	Distance (m)
1	Lift → MAL	16,2
2	MAL → T1 MAL	42,7
3	MAL → T1 secondary	38,6
4	MAL → B1 MAL	30,2
5	MAL → B1 secondary	23,2
6	MAL → T3 MAL	14,8
7	MAL → T3 secondary	15,5

In sum, longest distance 42,7 meters has to be taken on the second floor from MAL to the blister packaging line T1 MAL/PAL.

4 PRODUCTION LAYOUT DESIGN AND OPTIMIZATION (To Be)

New plant layout designing started with locating all necessary rooms on one ground floor, which are all production rooms and other supporting divisions. Production rooms are primary and secondary packaging areas including personnel and material airlocks. Production office, wash area, format parts, clothes change rooms, laundry, workshop are also essential areas used for supporting production activities. Warehouse including separated quality control area with laboratory is located right beside the production rooms. Facility layout was determined by GMP guidelines, operations sequence, previous in-house know-how and decisions were made centred on the production processes. Accordingly to Lean philosophy, transportation is being analysed.

Rooms and departments that must be nearby:

- Primary and secondary packaging areas;
- Packaging area and production office;
- Raw material and finished products warehouses;
- Quality control room and raw material warehouse;
- Clothes change room and laundry room;
- Primary packaging, wash area and format parts;
- Workshop and clothes change room;
- HVAC aggregates and production area.

Listed rooms and departments need to be as close as possible to have a minimum movement flow for materials and personnel to be well managed and to have more effective production. In addition, new production layout has to be safe. Within the framework of this thesis new layout walking and materials transporting paths must have appropriate sizes and moving trajectory has to be safe for personnel.

At first, side by side rooms were identified and drawn on the paper. Paper pieces were cut out and the most suitable layout plan with work operations adjacent to each other was placed on table. Manual plant layout idea is displayed in Appendix 1. After finding the best layout solution, room sizes were detected which are displayed in Table 4.1. Also, new plant layout movement distances are listed in Table 4.2. Multi floor production facility was designed on one floor. New plant layout drawn using computer-aided design software AutoCAD 2020 and it can be seen in Figure 4.1.

Table 4.1 Room sizes (To Be)

No	Area name	Size (m^2)
1	Warehouse	1555,4
2	MAL (warehouse)	16
3	QC total	80
4	MAL (primary)	6
5	PAL (primary)	6
6	Primary	36
7	Secondary	144
8	Production office 1	20
9	Production office 2	64
10	Wash area	50
11	Format parts	55
12	Technical aggregates	70
13	Clothes change room	16
14	Laundry room	40
15	Workshop	80

All warehouse areas are positioned on one floor instead of having warehouse areas on separate floors as in the current factory on ground and second floor. One great change is that quality control has space for laboratory and testing and it is located right beside incoming raw material warehouse. In the current plant QC do not own separated cleanroom area for testing purposes. To support cleanroom operations, separate floor surface is needed for technical aggregates. Technical aggregates such as cooling unit, air compressor, central vacuum system are designed to be as close as possible to the primary production area, to have minimum piping length and convenient access for maintenance. Another difference is that primary areas are having two separate airlocks, one for personnel and another only for materials. In addition, material airlock between warehouse and production area is designed bigger than in the current factory. Bigger airlock may be needed for machines transport between different cleanliness zones.

New production layout is designed to have two production offices, one near to the primary area and another on the opposite side near the secondary production. Production offices are used by pharmacists and supervisors. Wash area is as close as possible to the primary production rooms to have minimum format parts transportation distance inside the clean area.

Corridors are wider than in the current plant for smooth movements both for personnel and personnel with forklift and materials to have high work safety. It can be seen that facility is designed keeping in mind flexibility. It is possible to expand warehouse and also production area after line number 5.

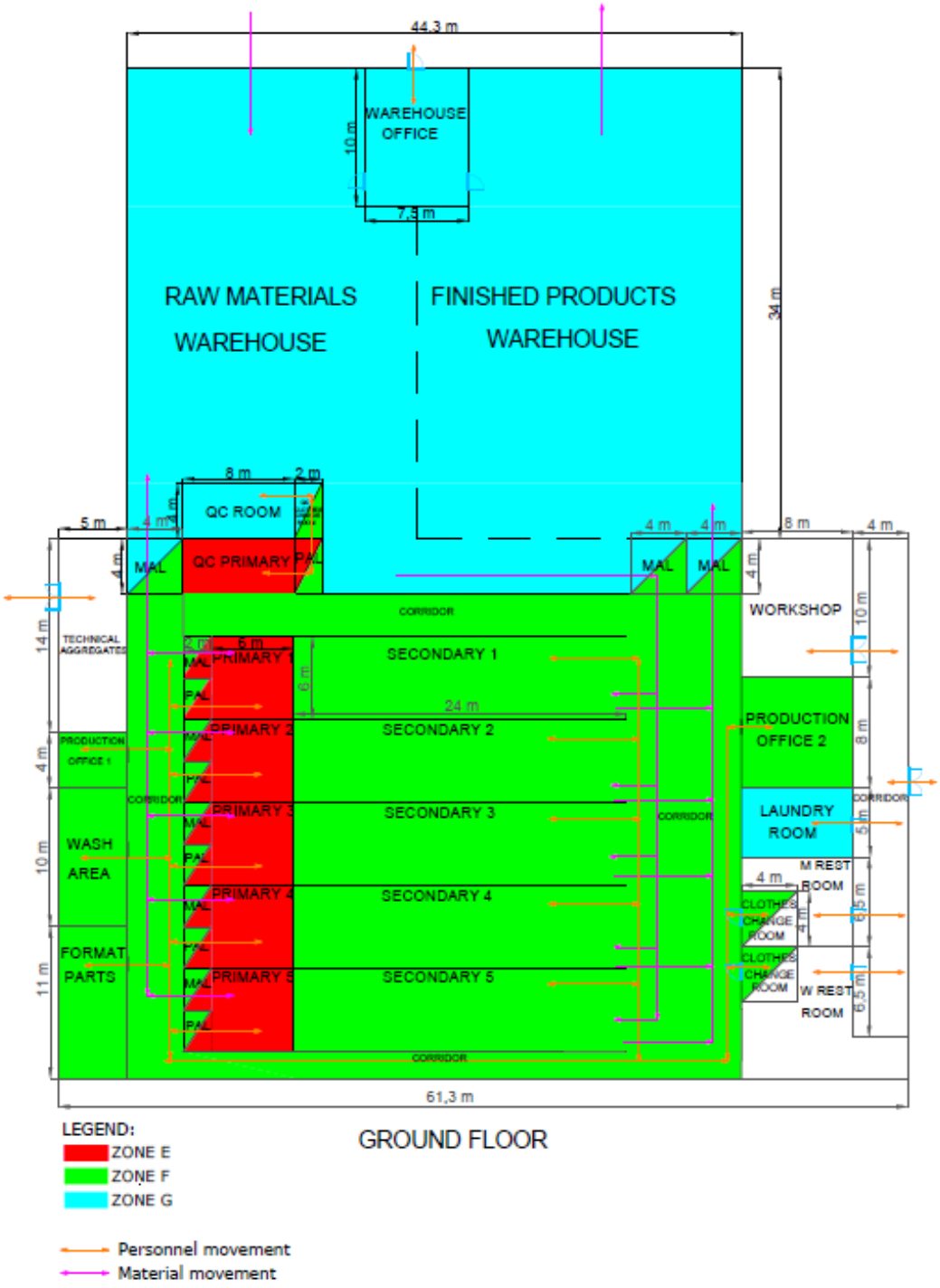


Figure 4.1 New layout with zone concept and movement of personnel and material

First floor is for the office areas. Quality and technical departments are planned to be double-storey areas. Quality office will be on the first floor of the building, while primary sampling room and raw materials control room are on the ground floor. Technical department workshop is located on the ground floor and above the workshop is workplace of engineers. First floor office area exact layout does not affect production process and therefore it is not drawn and presented in this master's thesis.

Manufacturing lines in a new plant are placed in one straight line for a better accessibility for personnel, eliminating curved conveyors as in use in a current plant. Production lines in a new plant are placed as shown in Figure 4.2. Also, workstations are marked with colour red with symbols A, B and C.

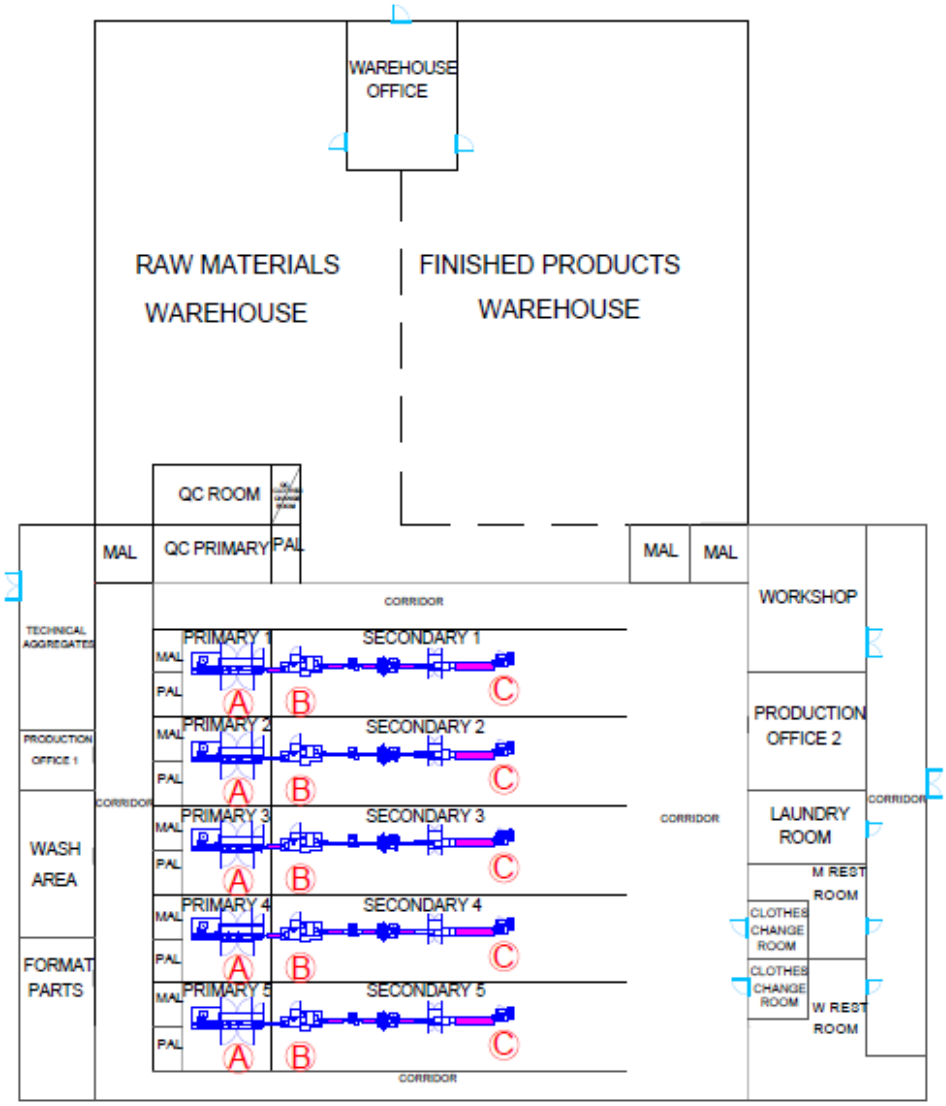


Figure 4.2 Production lines and workplaces in a new plant

Material flow analysis is done in a same way as in the current plant by using Siemens Tecnomatix. New layout materials flow with a Sankey diagram is shown in Figure 4.3.

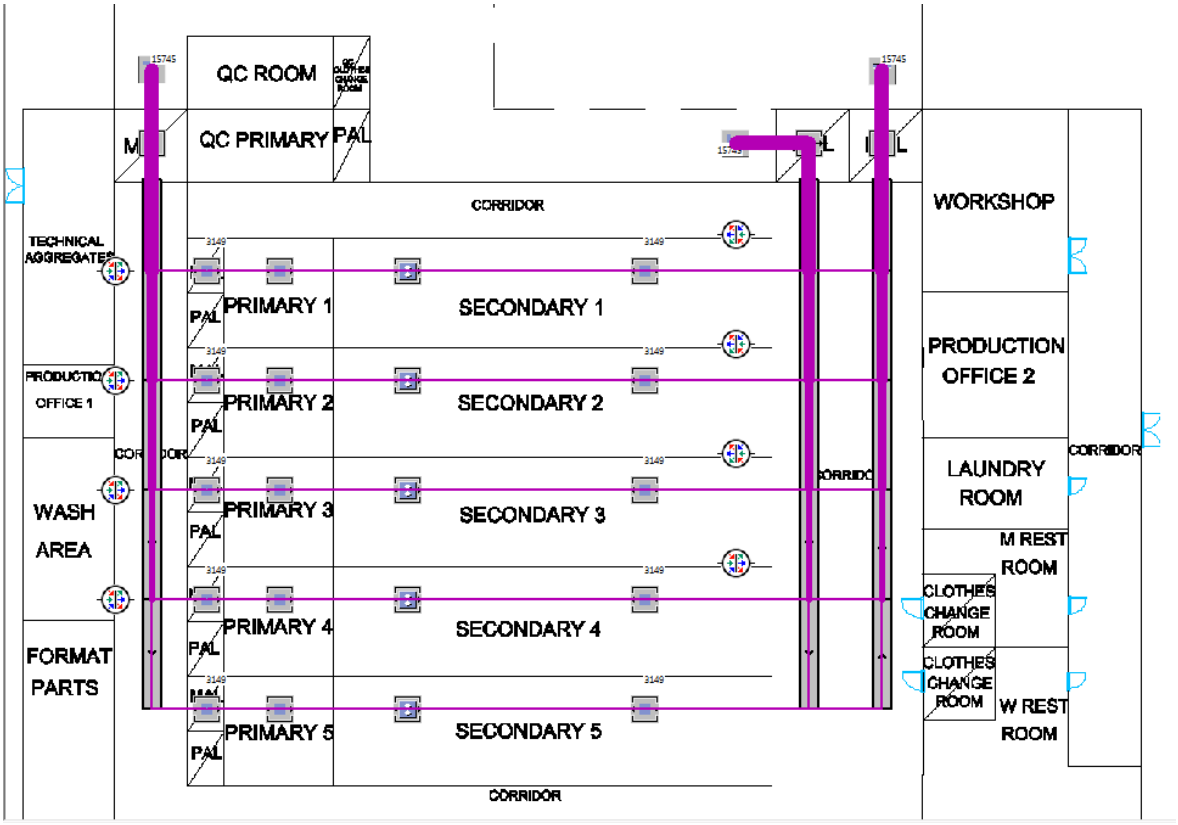


Figure 4.3 New layout with a Sankey diagram

New layout has 3 airlocks, one for raw materials, another for secondary components and last one for finished products. Different airlocks are designed to avoid mix-ups, contamination and to have uninterrupted materials movement. Sankey diagram visualizes that heaviest traffic is near airlocks area, equally crowded before every airlock. Movement distances between production rooms are listed in Table 4.2.

Table 4.2 Movement distances (To Be)

No	Movement	Distance (m)
1	MAL → primary 1 MAL	9
2	Secondary 1 → MAL	15
3	MAL → primary 2 MAL	15
4	Secondary 2 → MAL	21
5	MAL → primary 3 MAL	21
6	Secondary 3 → MAL	27
7	MAL → primary 4 MAL	26
8	Secondary 4 → MAL	32
9	MAL → primary 5 MAL	31
10	Secondary 5 → MAL	39

4.1 As Is and To Be comparison

Almost every room in production area is designed to have same size as in the current facility as shown in Table 4.3. Area sizes are left unchanged that the current and a new layout could be comparable.

Table 4.3 Room sizes in current and new plant

No	Area name	As Is size (m^2)	To Be size (m^2)
1	Warehouse	1477,4	1555,4
2	MAL (warehouse)	5,4	16
3	QC total	33,7	80
4	MAL (primary)	11,4	6
5	PAL (primary)		6
6	Primary	37,6	36
7	Secondary	90,6	144
8	Production office 1	36,8	20
9	Production office 2	28,9	64
10	Wash area	58,6	50
11	Format parts	54,6	55
12	Technical aggregates	70	70
13	Clothes change room	14,8	16
14	Laundry room	35,1	40
15	Workshop	67,8	80

One difference is that QC area is designed more than 2 times bigger because laboratory and testing room is planned to locate in a raw materials warehouse. Currently QC employees can use production room for testing but only while there is no manufacturing ongoing which insists planning. Another instant improvement is that secondary production room is approximately 53 m^2 larger to avoid materials storing in corridors. Other rooms listed are roughly the same size.

As mentioned before, materials movement inside the production zone was simulated by using Tecnomatix Plant Simulation software. Simulations setup is shown in Appendix 2, Appendix 3, Appendix 4 and simulation times are shown in Table 4.4. Every production line in current and in new plant produced 432 pallets finished products, because approximately 2160 pallets were sent out last year. Pallets number that were sent out last year was found by dividing finished products number taken from Figure 1.5 by average finished products pieces on one pallet. Average pieces on one pallet are 3149.

Current plant operates in two different floors hence production material flow simulation times are summarised. It must be pointed out that both layout machines and conveyors work with same speed. One big difference is that current plant uses lift for materials transport, new plant does not need lift because of being single storey

production. Lift travel times were measured and are counted in to the current plant simulations.

Table 4.4 Tecnomatix simulation times

Floor	Current plant (DDD:HH:MM:SS.XXXX)	New plant (DDD:HH:MM:SS.XXXX)
Ground	-	00:18:01:26.4000
1st	03:12:31:44.4000	-
2nd	08:21:11:32.4000	-

Texcnomatix simulations times are converted into hours, 297,7 h in a current plant and 18,01 h in a new plant, time difference is 279,7 hours. Result is that materials movement in a new one storey plant is 94% faster than in the current plant. Next, movement distances are compared and farthest distances are shown in Table 4.5. As stated earlier, last year 2160 pallets were sent out. Based on this number total distances for both layout were found, 5243,6 km in current plant and 2397,6 km in a new plant. Outcome is that material movement distance for producing 2160 pallets per year is reduced in a new plant 54%.

Table 4.5 Farthest distances comparison

Movement	As Is (m)	To Be (m)	Difference (%)
warehouse → farthest primary MAL	58,9	31	-47
warehouse → farthest secondary room	54,8	39	-29

Material flow is analysed using software and discussed hereinbefore. As employees movement all the way through the plant supporting production is also considered imperative thus personnel movements are compared briefly and info can be seen in Table 4.6.

Table 4.6 As Is versus To Be personnel movement comparison

Movement	As Is (m)	To Be (m)	Change (m)
QC room ↔ warehouse	179	2	-177
warehouse lift → MAL	16,2	0	-16,2
secondary → production office	45,3	26	-19,3
Production office → DAL	43,8	3,5	-40,3
Clothes change room → primary PAL	51,7	72,3	+20,6
Clothes change room → secondary	47,1	32,5	-14,6
Laundry room → clothes change room	56,2	12,4	-43,8
Workshop→laundry room→clothes change room	58,7	29,5	-29,2

At first, longest way for personnel from quality control room to the warehouse and back is eliminated as QC area is right next to the raw materials warehouse. Next, as no lift is needed there are any movement necessities for warehouse worker between floors. Movement between secondary and production office was measured until the furthest secondary rooms T1 in current plant and secondary 5 in a new plant. From the secondary room, all documentation and finished product samples are taken to the production office. In current plant document airlock (DAL) is on the second floor positioned between production and office area, it means pharmacist or supervisor who is working in production office one floor below the DAL has to move carrying production samples and document between floors every day.

Production workers move from clothes change room to the primary or to the secondary production area, again the farthest distances are counted in for both layouts. It can be seen that worker heading to the primary room has to take longer distance that it is in the current plant, but primary room is operated only by one technician. Protective clothing used in production is washed daily, transporting of these clothes is needed between clothes change and laundry room. Route from workshop until clothes change room is brought out, as technical department workers who are supporting production activities, use this way on a daily basis.

5 CALCULATIONS

With a new layout, time which takes for material movement is 279,7 hours less than it is in current layout. This time can be converted into personnel cost based on the assumption that on average there is 160 working hours in one month. Following formula (5.1) converts total time savings into saving in months:

$$Time\ saving\ in\ months = \frac{total\ time\ of\ material\ movement\ in\ current\ layout\ [h] - total\ time\ of\ material\ movement\ in\ new\ layout[h]}{average\ working\ hours\ in\ one\ month\ [h]} = \frac{279{,}7\ h}{160\ h} = 1{,}86 \quad (5.1)$$

Acino Estonia OÜ average salary in first quarter of 2021 was 2140 € [42]. Company's actual cost for employer is bigger because of social tax and it is in total 2863,32 €. Company's saving per person is calculated according to calculation (5.2)

$$Employer\ salary\ saving = total\ cost\ for\ epmloyer\ [€] \times time\ saving\ in\ months =$$

$$2863{,}32\ € \times 1{,}86 = 5325{,}78\ € \quad (5.2)$$

Next, lift energy cost is calculated. In 2021 lift was in use for materials transport in total of 196,2 hours. Taking account that the power rating of current lift in Acino Estonia OÜ is 17,3 kW and the average electricity price (incl. taxes) of Acino Estonia OÜ is 0,10819 €/kWh, we can calculate lift's energy cost in euros for one year with the following formula (5.3):

$$Lift\ energy\ cost\ = lift\ usage\ time\ in\ one\ year\ [h] \times lift\ power[kW] \times electricity\ price\left[\frac{€}{kWh}\right] =$$

$$196{,}2\ h\ \times 17{,}3\ kW\ \times 0{,}10819\ \frac{€}{kWh} = 367{,}2\ € \quad (5.3)$$

As current lift has been in use already 25 years in a row and do not meet the needs anymore, price offering for a new lift was received at a price 78 000 € and maintenance cost for one year 900 €. Lift depreciation period is counted as 15 years, depreciation cost for one year would be 5000 €. Total saving for a new proposed layout without having lift according to calculation (5.4) is 11 593 € per year.

$$Toal\ saving = employer\ salary\ saving + lift\ energy\ cost + lift\ maitenance + lift\ depreciation =$$

$$5325{,}78\ € + 367{,}2\ € + 900€ + 5000€ = 11\,593€ \quad (5.4)$$

SUMMARY

Master thesis is titled as "Material flow analysis and optimization in Acino Estonia OÜ". In this thesis pharmaceutical packaging company's material flow in production zone was analysed and suggestion for optimization was proposed. Main objectives were to determine the most effective plant layout by optimizing material movements while keeping in mind the possibility to expand the production area to support growth perspective. Current facility was built 30 years ago having three floors in total, warehouse is on the ground floor while production area is on the first and second floor. Readiness for enlargement has already started as company recently acquired adjacent land plot about 1,8 ha in size for expansion purposes.

During optimization a layout was designed bearing in mind GMP guidelines, operations sequence, previous in-house know-how and decisions were made centred on the production processes. New production layout, designed based on product flow layout, is proposed to be single storey, eliminating the need for a lift and placing rooms according to necessity. Quality control rooms with laboratory and testing room is placed right adjacent to raw materials warehouse enabling fast and on-spot sampling of raw materials. Additionally, cleanrooms are located next to each other making it easier to support them with HVAC, compressed air and other supportive systems located in technical aggregate area. Cleanroom airlock was divided into two for personnel and materials to avoid cross contamination and to have safe and convenient entrance for personnel.

Current production layout and new proposed layout material movements were compared using Siemens Tecnomatix Plant Simulation software. Due to confidentiality, different production related data is multiplied with a random coefficient. Based on a result of comparison, material movement in one storey facility is up to 94% faster and the material movement distance is reduced by 54% than compared with a current three storey building. This was mainly achieved by using multiple airlocks for materials, optimizing production area layout and eliminating lift. In conclusion, for a pharmaceutical company Acino Estonia OÜ one storey facility is more efficient than three storey building.

KOKKUVÕTE

Käesolevas magistritöös analüüsiti ja optimeeriti Acino Estonia OÜ tootmistsooni liikumisvooge. Eesmärgiks oli leida uus ja tõhus tootmishoone planeering, pidades seejuures silmas võimalust hilisemaks tootmishoone laiendamiseks, et toetada ettevõtte kasvuplaani. Hetkel kasutuses olev kolmekorruseline tootmishoone on ehitatud 30 aastat tagasi ning korruste jaotus on järgnev: esimesel korrusel on ladu, teisel ja kolmandal korrusel asuvad toomisruumid. Eelmisel aastal omandas ettevõte kõrvaloleva krundi suurusega 1,8 ha, eesmärgiga laiendada tootmispinda.

Tootmisala planeeringut optimeeriti lähtudes GMP suunistest, operatsioonide järjekorrast, ettevõttesisesest oskusteabest ning kõik valikud tehti tootmisprotsessidele tuginedes. Uus tootmisplaneering on kujundatud ühekorruselisena, eemaldades lifti ning paigutades toomisruumid ja neid toetavad üksused vastavalt protsesside loogilisele järjekorrale. Hetkel kolmandal korrusel asuv kvaliteediüksus on paigutatud sissetuleva kauba alale elimineerides korrustevahelise liikumise ning tagades kohese ligipääsu materjalide kontrollimiseks ja testimiseks GMP-le vastavates ruumides. Kõik 5 tootmisruumi on asetatud kõrvuti, et oleks võimalikult lihtne neid varustada erisuguste tugisüsteemidega: suruõhuga, kesktolmuimemissüsteemiga ning adekvaatse kliimakeskkonna tagamiseks ventilatsioonisüsteemiga. Õhulüüs puhtaruumi ees on planeeritud eraldi nii personalile kui materjalidele, et vältida materjalide segunemist ning tagada personalile ohutu liikumine kahe ruumi vahel.

Praeguse ja ideetehase tootmisplaneeringute analüüsiks kasutati Siemensi tarkvara Tecnomatic Plant Simulation. Tulenevalt konfidentsiaalsusest on Acino Estonia OÜ tegelikud lähteandmed korrutatud läbi koefitsiendiga. Analüüsi tulemusena selgus, et uues tehases on võrreldes praegusega materjalide liikumisele kuluv aeg 94% lühem ning materjalide koguteekonna pikkus väheneb 54% võrra. Ajakulu ja teekonnapikkuse vähendamise saavutamiseks planeeriti sissetulevale ja väljaminevale kaubale eraldi õhulüüsid, tootmisala ja –seadmed paigutati optimaalselt ning hoone planeeriti ühekorruseliseks, et ei oleks tarvidust lifti järele. Käesolevate tulemuste põhjal saab järeldada, et Acino Estonia OÜ näitel sobib ravimitööstusele paremini ühekorrusline kui mitmekorruseline tootmishoone.

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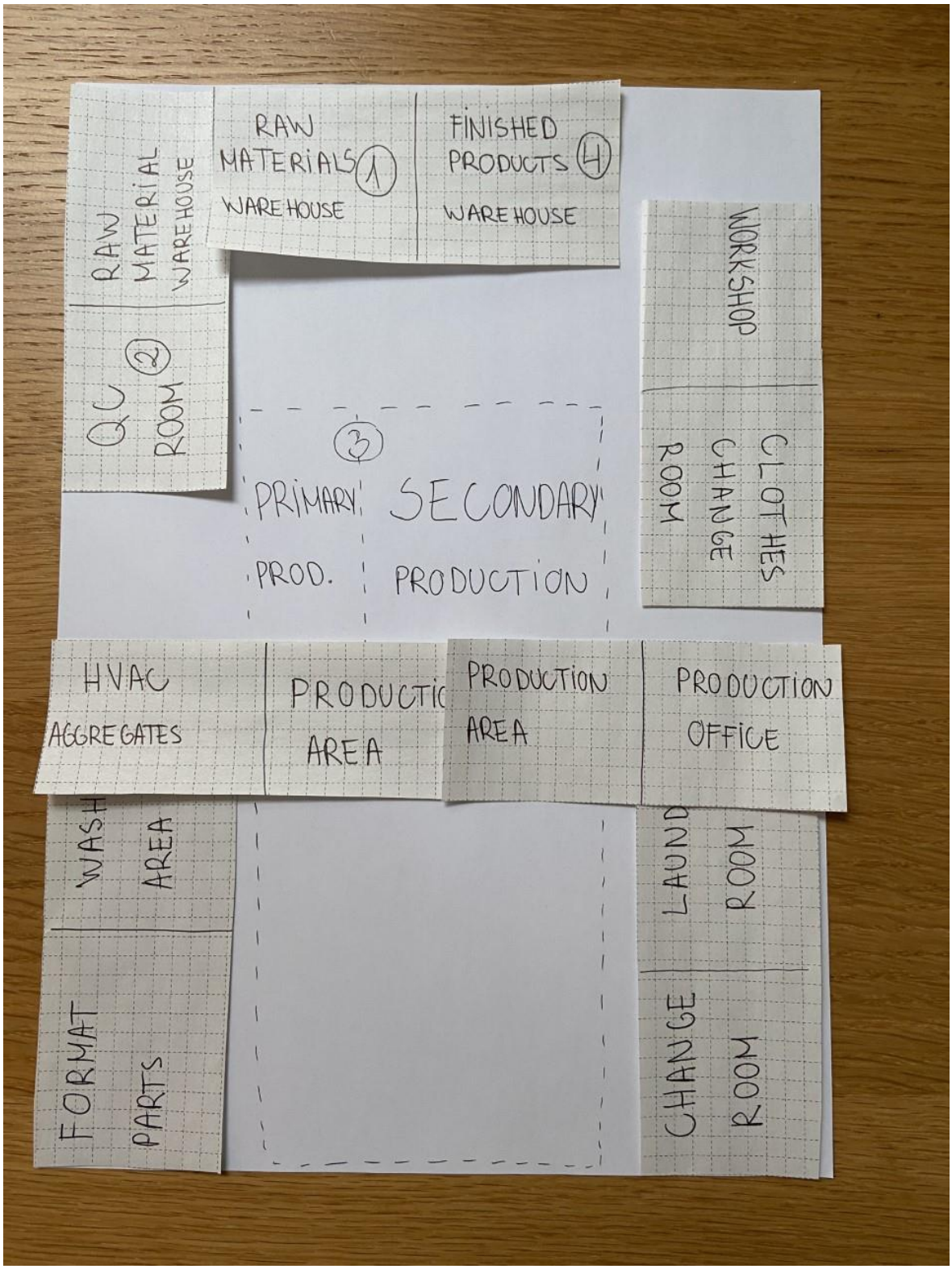
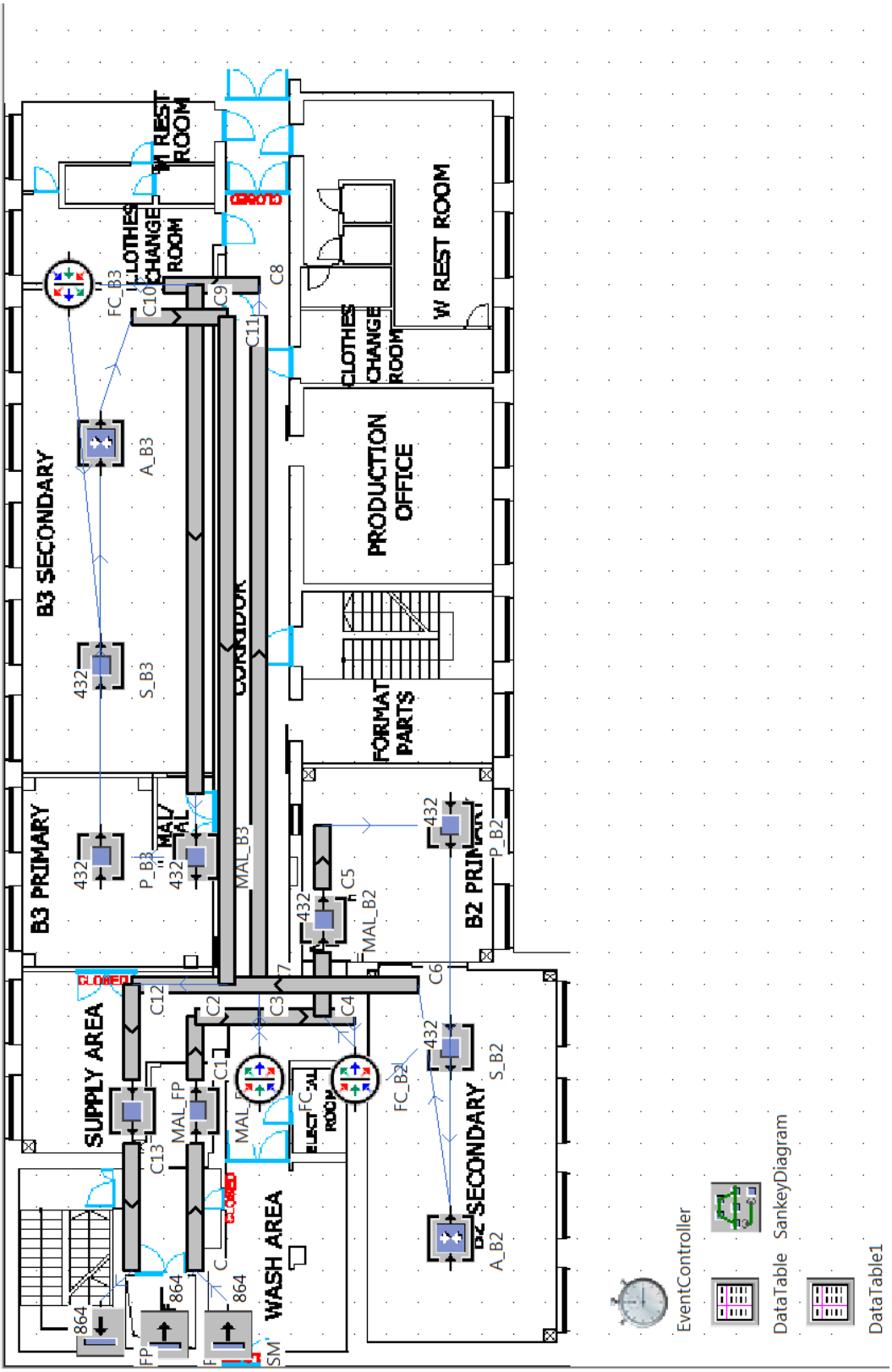
APPENDICES

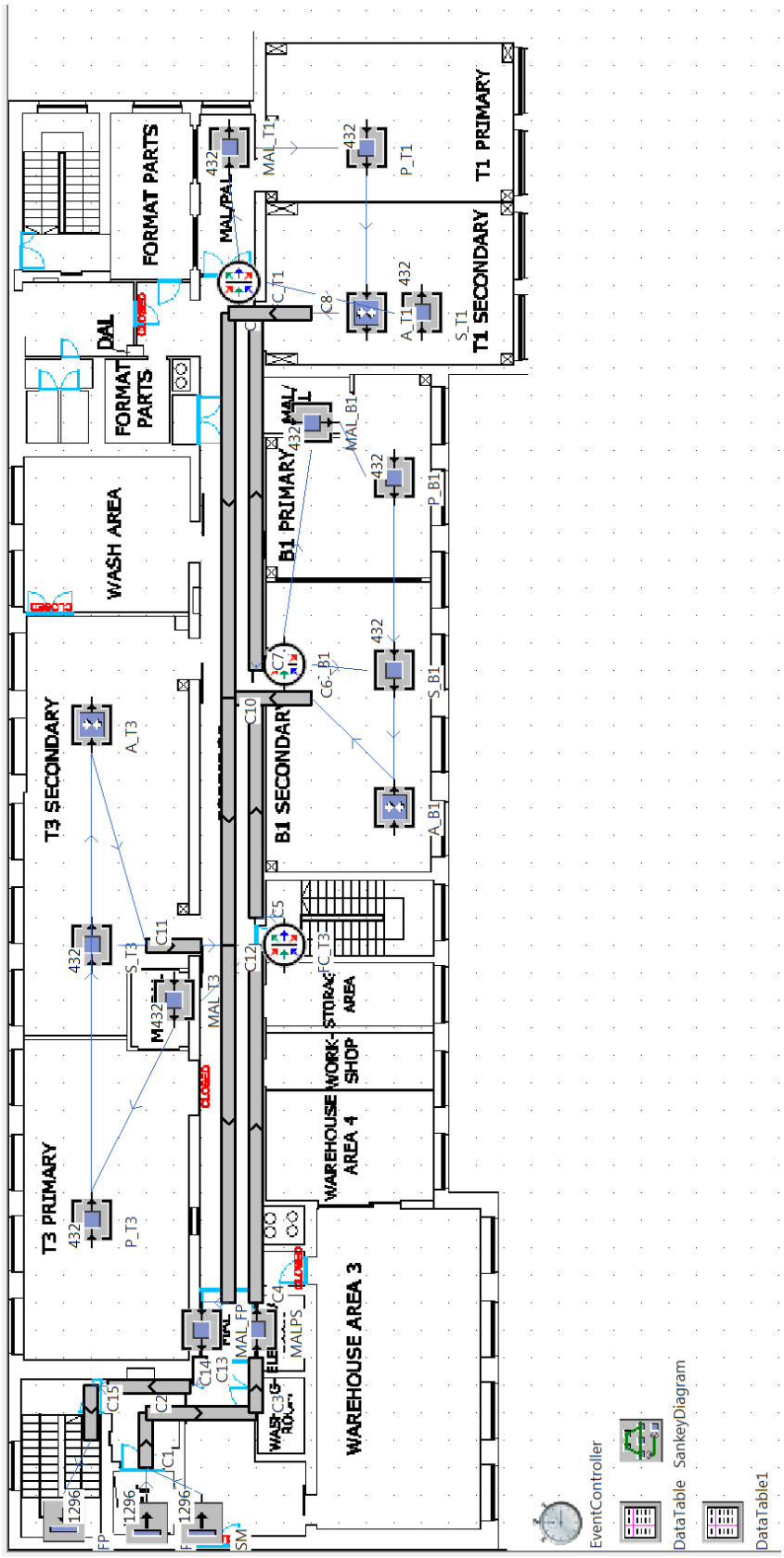
Appendix 1: Plant layout miniature model



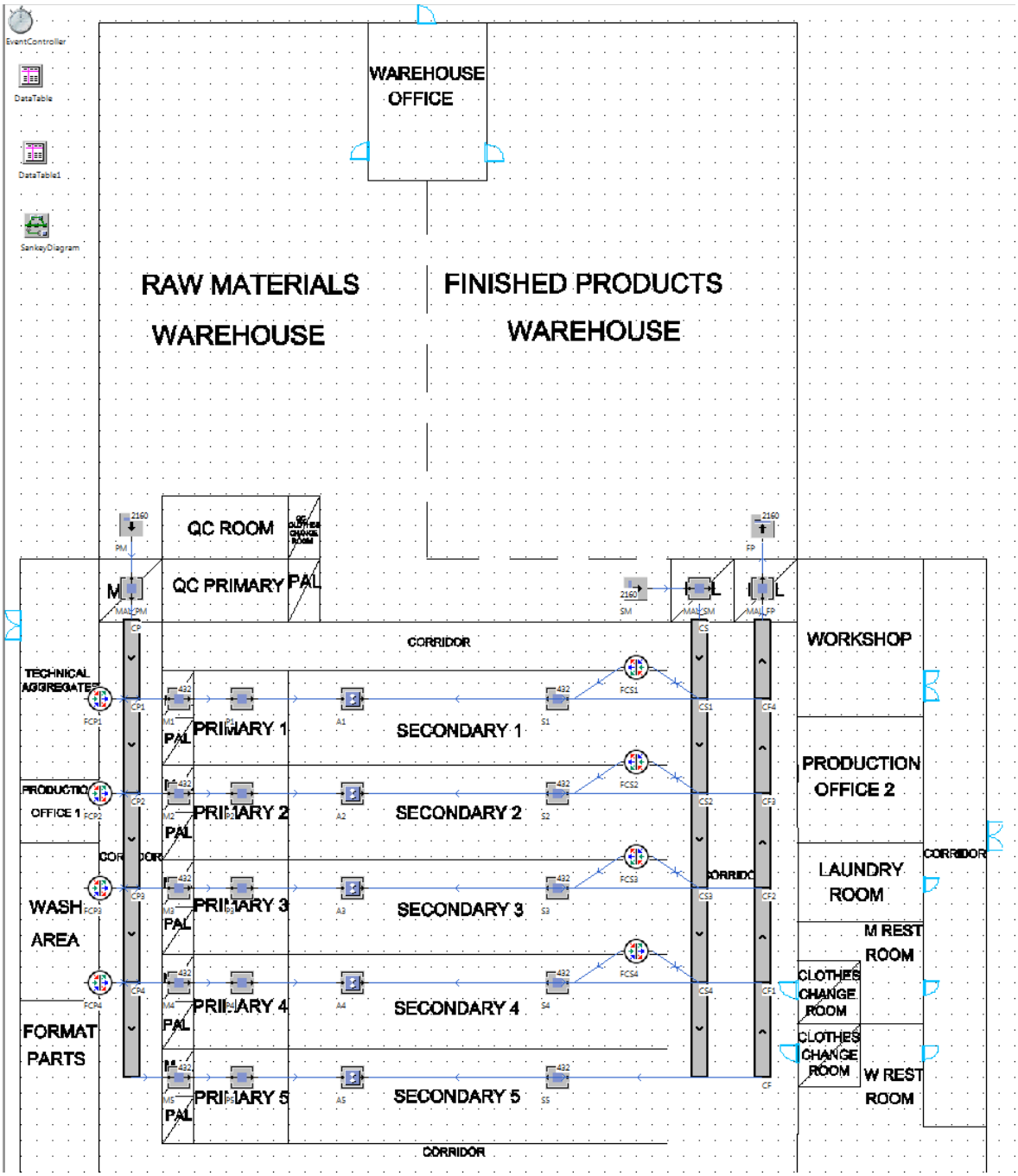
Appendix 2: First producion floor material flow simulation



Appendix 3: Second production floor material flow simulation



Appendix 4: New production layout material flow simulation



GRAPHICAL MATERIAL

Graphical material 1: New production layout