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Master Thesis

Title:

"Unlocking Potential: Financial and Operational Impact of Air Transport on Nuclear Medicine for Diagnostic Business"

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Abstract

This thesis focuses on evaluating the financial feasibility of utilizing air transport as a pivotal strategy for expanding the nuclear medicine industry. The study involves a comparative analysis between this innovative approach and the traditional method of establishing new production facilities to cover new regions.

To meet the defined goals, the author of this thesis focuses on examining a medium-sized company operating in the radiotracer production sector, which operates across multiple countries. This company serves as a representative case study to showcase the concepts discussed. For the sake of this study's scope, the analysis is specifically centred on evaluating France as the sole target country for the proposed strategies.

The research methodology involves gathering secondary data from diverse sources, including financial reports, industry publications, and academic literature. These sources provide insights into the company's operations, financial standing, prevailing market conditions, and regulatory landscape in France. The core evaluation metric utilized is the Net Present Value (NPV) method, which guides the assessment of the financial viability of both strategies.

The research objectives encompass several facets, such as examining the practicality of leveraging air transportation as a pivotal element for expand the company's footprint. Moreover, the study compares the advantages and risks inherent in both suggested scenarios, one considering Air Transportation and one scenario with additional production sites, seeking to identify the investment pathway that aligns with the company's long-term aspirations and growth trajectory.

The study's outcomes contribute to an enhanced comprehension of effective expansion strategies applicable to the nuclear medicine sector. Furthermore, the research underscores the significance of ethical research conduct, safeguarding the confidentiality and integrity of the studied company. The findings could potentially trigger further investigations and subsequently improve access to medical services for underserved patients, particularly those grappling with severe ailments like cancer.

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1. Introduction

1.1 Background Information

As per the findings of Kahl-Scholz & Vockelmann in the year 2023, nuclear medicine stands as a specialized domain within medical imaging. This field employs minute quantities of radioactive substances, referred to as radiotracers, to both identify and manage an extensive array of illnesses and medical states. Nuclear medicine has a rich history and has undergone significant advances in technology since its inception. This specialty focuses on functional imaging, providing information about the physiological and metabolic activity of tissues and organs. It examines how the body functions at a molecular level. In contrast, MRI (Magnetic Resonance Imaging) and US (ultrasound) primarily provide anatomical images, showing the structure and morphology of organs and tissues. Techniques, like Positron Emission Tomography, offer high sensitivity in detecting molecular and cellular processes. They can detect subtle changes in metabolism and function at an early stage, even before structural changes occur. MRI and ultrasound have their own sensitivity limitations, often requiring substantial structural changes before abnormalities become apparent.

It can be stated that the application of nuclear medicine has evolved into two interconnected yet distinct branches, namely diagnostic and theragnostic. These dimensions serve specific purposes while maintaining a symbiotic relationship. Thus, in diagnostic nuclear medicine, radiotracers are used to visualize and assess the functioning of organs, tissues, and physiological processes within the body.

Through the utilization of distinct radiotracers, nuclear medicine imaging methodologies like Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT), alongside gamma imaging, have the capability to furnish significant insights into aspects such as metabolic processes, circulatory dynamics, receptor manifestation, and the pinpointing of pathological sites. This helps in diagnosing diseases, staging cancers, evaluating organ function, and identifying abnormalities. Diagnostic nuclear medicine is primarily focused on providing accurate and detailed diagnostic information. While Theragnostic nuclear medicine combines both diagnostic and therapeutic aspects. It involves the use of radiopharmaceuticals that contain both a diagnostic radionuclide and a therapeutic radionuclide. This approach allows for personalized medicine by using diagnostic imaging to select patients who are likely to respond to specific targeted therapies. This thesis primarily focuses on the diagnostic dimension of nuclear medicine while leaving the theragnostic aspect for future research.

Kahl-Scholz & Vockelmann (2023) define the Radioactivity as a phenomenon resulted of spontaneous nuclear transformations, where certain radionuclides undergo changes from an unstable state to a more stable configuration. As part of this process, energy is released in the form of radiation. The emitted radiation can take various forms, including particles or electromagnetic waves, depending on the specific decay mechanism involved. The measurement unit used to quantify radioactivity is the Becquerel (Bq). Notably, it was Antoine-Henri Becquerel who made the significant discovery of uranium during the late 19th century, laying the foundation for further exploration into radioactive substances.

In the analysis conducted by Hansen, B.S., and Bender, D. (2021), the origins of nuclear medicine trace their roots to the initial decades of the 1900s, a time when scientific explorations uncovered the principles of radioactive disintegration. During the 1930s, researchers embarked on trials involving radioactive isotopes for medicinal objectives. It was during the 1940s that the inaugural radiotracer, iodine-131, made its debut, primarily utilized for addressing cases of thyroid cancer.

Radiotracers are typically produced using cyclotrons, which are large particle accelerators that generate high-energy beams of protons or ions. These beams are used to bombard stable atoms, causing them to become radioactive isotopes. Technetium-99m, Fluorine-18, and gallium-67 stand out as among the frequently employed isotopes within the realm of nuclear medicine imaging.

The earliest recorded development of a particle accelerator can be traced back to the year 1928, when Leo Szilard patented a device for this purpose. However, it was only four years later in 1932 that Ernest Laurence definitively patented the first cyclotron. In conjunction with the discovery of artificial radioactivity by Irene and Frederic Joliot-Curie in 1934, research efforts and programs shifted towards the production of radionuclides. This allowed George

de Hevesy to begin using Phosphorus-32 to study rat metabolism, and Martin D. Kamen to explore plant physiology using Carbon-11. The field of nuclear medicine was truly born in 1941, when Saul Hertz and Arthur Roberts started using Iodine-130 and Iodine-131 in a preliminary treatment of Hyperthyroidism.

Interestingly, the underlying technology of cyclotrons has remained unchanged since 1932, despite significant advancements in process automation, space optimization, availability of isotopes and targets (both liquid and solid), among others. As a result, the cyclotrons available in the market today possess a high energy production capacity at significantly lower costs.

The International Atomic Energy Agency (IAEA) administrates a directory of cyclotrons used for radionuclide production. The data base includes cyclotrons currently in operation or under testing and includes a significant number of cyclotrons worldwide involved in radionuclide production. The directory can be sorted by Member State and location, and it contains over 1300 entries, indicating a 42% increase compared to the 2013 data. Developed countries, particularly the United States, Japan, and Germany, have a notable concentration of cyclotrons, while East Asia, specifically China and Japan, has the largest collective number of cyclotrons used for medical radionuclide production. The growing demand for radiopharmaceuticals, driven by advancements in medical imaging techniques such as Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT), and Positron Emission Tomography-Computed Tomography (PET–CT), has contributed to the expansion of cyclotron numbers in the last decade.

Although the artificial production of radioisotopes is primarily carried out in particle accelerators or cyclotrons, there is also the possibility of utilizing a Generator, which is a remarkably simple and cost-effective device. However, it is important to note that only certain isotopes can be created using this method. Indeed, when discussing the production of radionuclides, it generally refers to cyclotrons as the primary method. This is why in general terms; the production of radionuclides is associated with cyclotrons. The Table 1 illustrates the types of isotopes that can be produced using each method, these radionuclides are chosen based on their specific decay characteristics and their ability to provide accurate information about various biological processes and diseases.

The radioactive decay of these isotopes produces gamma rays, which are detected by special cameras called gamma cameras or PET (Positron Emission Tomography) scanners. PET scanners were first introduced in the 1970s and revolutionized the field of nuclear medicine by allowing for three-dimensional imaging of the body. Nuclear medicine is rapidly emerging as an indispensable diagnostic tool within modern healthcare. In particular, PET scanners has showcased remarkable advancements, surpassing single photon emission tomography (SPECT) in terms of imaging capabilities. The most striking difference lies in the approximately two orders of magnitude higher sensitivity of PET, enabling the detection of nuclear decay within a patient's body with exceptional precision. Moreover, modern whole-body PET scanners achieve an impressive spatial resolution of 4-5 mm, far exceeding the comparatively inferior resolution range of 8-10 mm typically observed in SPECT systems. Another noteworthy advantage of PET is its superior accuracy and straightforwardness in correcting for photon attenuation. As a result, PET images faithfully capture the absolute radiotracer concentration within the body, providing highly reliable and clinically relevant insights.

Nuclide	Symbol	Half-Life	Max Positron Energy (MeV - Mega-Electron Volts)	Production
11-Carbon	11C	20.4 min	0.960	Cyclotron
13-Nitrogen	13N	9.96 min	1.190	Cyclotron
15-Oxygen	15O	2.04 min	1.720	Cyclotron
18-Fluorine	18F	110 min	0.635	Cyclotron
68-Galium	68Ga	67.7 min	1.900	Cyclotron/Generator
64-Copper	64Cu	12.7 h	0.653	Cyclotron
89-Zirconium	89Zr	78.4 h	0.902	Cyclotron

Table 1: Most common isotopes used in Nuclear Medicine Imaging

The importance of nuclear medicine imaging is growing because it offers a distinct way to understand how organs and tissues work and process energy. Unlike other methods used for diagnosis, nuclear medicine imaging doesn't require any invasive procedures, and it lets us see the body's internal processes in real-time. This quality has made

it more and more valuable in identifying and treating a wide range of illnesses, such as cancer, heart problems, and disorders affecting the brain.

1.2 European Business Landscape:

When discussing nuclear medicine, the very terminology suggests a highly complex reality that may not be easily comprehensible to the general public. Understanding the dynamics of the nuclear medicine industry is not exempt from this assumption. Therefore, to grasp how this business operates, it is crucial to comprehend a natural phenomenon that governs the operationalization of this industry: the decay of isotopes, commonly known as half-life. Without delving into the scientific depth that this topic deserves, the following will attempt to shed light on this phenomenon in order to understand the dynamics of the business.

Decay of radiotracers is an important concept in nuclear medicine, as it is the process by which the radioactive material in the radiotracer emits radiation that can be detected by imaging equipment. In simpler terms, it is a natural random process by which an isotope tends to become a stable particle, consequently emitting decreasing levels of radioactivity over time.

Radiotracers are composed of a radioactive isotope and a molecule that is designed to target a specific biological process or structure in the body. When the radiotracer is injected into the body or swallowed, it travels to the target area and accumulates there. As the radioactive isotope in the radiotracer decays, it emits radiation in the form of gamma rays, positrons, or other particles, depending on the type of isotope. The radiation can be detected by special imaging equipment, such as gamma cameras or PET scanners, which use sensors to detect the emitted radiation.

As shown in the previously presented Table 1, the half-life of each isotope is determined by its nature. It can be understood that as each half-life period elapses, the isotope loses half of its previous emission capacity of radioactivity. The decay process of radioactive isotopes is a critical aspect of the nuclear medicine business. The decay process determines the duration of time that a radiotracer can be used for imaging, as well as the amount of radiation that is emitted during the imaging process. As I mentioned earlier, the half-life of a radioactive isotope determines the length of time that it can be used for imaging.

Beyond the fact that this characteristic of radionuclides may initially appear as a serious issue or limitation, in fact, it is a desirable feature when selecting an isotope for use in nuclear medicine. The gradual loss of radioactive potential in the administered radiotracer ensures the safety of the patient, avoiding prolonged exposure to energy that could lead to undesired reactions. In summary, patient safety is prioritized in nuclear medicine, leading to the utilization of isotopes with reasonable half-lives that allow for versatility in their application and provide sufficient time for the diagnostic procedure to be conducted.

Given this natural phenomenon, the general approach adopted by all the European Market participants was to develop a network of production facilities spread across a certain region to reach as many patients as possible. These facilities require skilled personnel, sophisticated equipment, and adherence to strict safety protocols. The number and capacity of these production sites depend on the demand for nuclear medicine diagnostics in a given region. These centers act as hubs from which the radiopharmaceuticals are further distributed to various healthcare facilities, including hospitals, clinics, and imaging centers.

Consequently, this production network landscape has made this industry require an intensive capital investment and posed a great challenge for new competitors. The production of radiopharmaceuticals involves complex processes, regulatory compliance, and specialized expertise. Additionally, existing businesses may have established relationships with healthcare providers, making it difficult for new competitors to enter the market. The industry is subject to stringent regulatory requirements, and maintaining safety and quality standards requires ongoing investment. While advancements and increasing demand may create opportunities, the barriers to entry remain significant.

However, it is important to note that this business dynamic is not universally applicable but rather a system adopted in Europe, in particular. In other markets such as the United States and Australia, a distribution system has been

developed that focuses more on optimizing logistics rather than establishing a strict network of production facilities.

1.3 Dual Perspective: Capacity Constrain or Overcapacity

In line with the prior section, the diagnostic radiotracer production industry has opted to develop an extensive network of cyclotrons. This means that there are currently a significant number of production facilities equipped with cyclotrons throughout Europe.

The natural phenomenon described in the previous section, referring to the decay or half-life of an isotope, presents a formidable challenge for diagnostic radiopharmaceutical companies. These companies are faced with a significant limitation, as they can only supply radiotracers within a limited distance radius. Consequently, potential patients residing beyond this accessible perimeter are left without the necessary diagnostic solutions.

To reach to these underserved individuals, the company must take proactive steps to expand its scope. According to European companies, the most viable approach involves the establishment of additional production plants strategically located to cover a broader geographical area. In essence, by increasing the number of cyclotrons, the company can enhance its capacity to diagnose patients located far beyond its current technical range.

However, this constraint on the geographical reach of patients is primarily due to the transportation modality used in Europe (via land) rather than a technological issue. According to an expert from a medium-to-large company in this industry (personal communication, 2023), the cyclotrons currently operational in the market have a capacity to generate activity that far exceeds the daily demand for reachable patients. This expert explains that with each production batch, a substantial amount of energy is generated, which could be utilized and incorporated into multiple doses, allowing for the simultaneous procedures of hundreds of patients. Nevertheless, a significant portion of this capacity goes unused since the company's geographical range may lack sufficient infrastructure to accommodate a higher number of patients at the same time.

In this manner, all companies in this sector have been consistently expanding their network of factories in order to serve a larger number of patients. However, it is a common challenge that each added plant often struggles or hardly ever reaches its full potential.

It is crucial to highlight that the production of a batch must be carried out with extreme mathematical precision to ensure that the dose reaches the patient with the required activity. Depending on the specific radiotracer, currently, between 5 and 60 patients are served per batch. According to a Subject Matter Expert (SME) of medium-sized company in the nuclear medicine industry (Personal Communication, 2023), it could be possible to produce approximately 130 doses without significant effort.

The question arises as to why there are capacity constraints when cyclotrons have the technical capability to produce larger quantities of doses per batch. The answer may have been explained previously. This limitation occurs primarily due to the distance between the diagnostic centers where patients are treated. Nearly all distribution is carried out via land transportation, creating a significant bottleneck for the industry.

The transportation process poses logistical challenges and time constraints, affecting the timely delivery of radiotracers to the diagnostic centers. This, in turn, impacts the overall production capacity. Additionally, factors such as regulatory requirements, quality control, and scheduling of patient appointments further contribute to the limitations in capacity.

In summary, while cyclotrons have the technical capability to produce larger quantities of doses, the distribution process and the distances involved create significant challenges and bottlenecks, thereby constraining the overall capacity of the industry. Thus, the production of radiotracers has become a capital-intensive business in which significant investments in strategic locations are required to increase revenue or gain access to new patients. Expanding the production capacity involves substantial Capital Expenditures (CAPEX) for the establishment of new cyclotrons or the enhancement of existing facilities. These investments are necessary to meet the growing demand for radiotracers and to ensure efficient supply to diagnostic centres. Strategic placement of production

facilities in proximity to high-demand regions or healthcare hubs becomes crucial to optimize access and minimize transportation bottlenecks.

1.4 Problem Statement:

Building upon the previous sections, in Europe, companies dedicated to the manufacturing of radiotracers for diagnostics have developed an extensive network of production sites aimed at reaching end patients. These production facilities are strategically located in areas with high population density and availability of diagnostic scanner devices. While the woven network of cyclotrons is already significantly large, there are still extensive areas that remain underserved. This suggests that considerable investments are needed to address the potential unmet demand in those regions.

While the installed technical capacity of the currently operational sites is being underutilized, meaning that the utilization of each batch is well below its actual capacity, companies are faced with a significant challenge: is it possible to reach customers located further away with the existing production facilities and utilizing the same logistics systems?

Expanding the reach to customers located farther away poses logistical challenges and requires careful consideration. It would involve optimizing the existing logistics systems, improving transportation efficiency, and potentially establishing additional distribution channels. Companies may need to evaluate the feasibility of extending their delivery networks, collaborating with third-party logistics providers, or exploring alternative transportation methods to ensure timely and cost-effective delivery of radiotracers to distant customers.

Efficient utilization of existing production capacity and the exploration of innovative logistics solutions will be critical in meeting the demand in underserved regions without the need for significant infrastructure investments. However, it is essential to carefully assess the feasibility, costs, and potential risks associated with expanding the reach to distant customers while maintaining the required product quality and timely delivery.

1.5 Thesis Statement:

The master's thesis focuses on the financial viability analysis of developing an improvement in the efficiency of the logistics and distribution system of a radiotracer manufacturing company. The thesis statement is as follows:

Is it possible to expand a company's footprint by reaching customers located in underserved areas through the utilization of air transportation without the need for significant CAPEX investment, while sacrificing only a reasonable portion of the margin.

The thesis aims to investigate the feasibility and potential benefits of utilizing air transportation to extend the company's reach to underserved regions. The focus will be on assessing the financial impact of this approach, considering the costs associated with air transportation, potential margin reduction, and the overall profitability of the company. The analysis will provide insights into whether this strategy can be a viable solution for expanding the company's customer base without incurring significant capital expenditures.

1.6 Thesis Questions and Objectives:

Considering the context and intended focus of the research investigation, the central inquiry driving the primary research question is:

Is it financially advantageous to transport radiotracers by air compared to constructing a new production site to reach new customers?

The primary research question can be broken down into several sub-questions, each requiring investigation to ultimately address the main inquiry.

- Are the current regulations in Europe conducive to air transportation?
- What is the cost associated with establishing a new radiopharmaceutical production facility in Europe?
- To what extent can a radiotracer be distributed while ensuring the required quality conditions for the diagnostic procedure?
- What is the financial implication of air transportation, if it is feasible?

The main goal of this research endeavour is to evaluate the feasibility of utilizing air transportation for PET radiotracers. The assessment involves analysing the economic viability of this logistical methodology compared to ground transportation, quantifying the potential increase in the number of patients reached, and determining the required capital expenditure.

1.7 Methodology

1.7.1 Introduction

The main purpose of this thesis is to assess the financial viability of using air transport as the primary pillar for the expansion strategy (hereafter Air Transportation Scenario). Additionally, it aims to compare this innovative approach with the traditional proposal that companies in this industry have been following over the last few decades: expansion through the construction of new factories in target regions (hereinafter referred to as the +2Sites Scenario). To conduct the analysis, a specific real medium-sized company operating in Europe, with a presence in multiple countries, will serve as the object of study. However, for the sake of reducing complexity and maintaining the thesis's focus, only one country will be considered for the outlined objectives.

It is essential to highlight that in order to carry out a reliable and accurate analysis of the proposed cases, information intricately related to technical, financial, commercial, and administrative aspects of the real company has been utilized. Necessary precautions have been taken to ensure that sensitive data that could affect the company is not revealed or exposed, in accordance with confidentiality and limited disclosure agreements signed by the author. Furthermore, disclosure of employee names, positions, locations, offices, cities, brands, or any other data that could lead to inferring the company's identity is strictly prohibited. Therefore, throughout this thesis, the term "the company" will be used to refer specifically to the firm taken as an example. This approach ensures that the focus remains on the case study and facilitates a clear understanding of the analysis presented.

By adhering to these confidentiality measures, the thesis ensures ethical research practices and maintains the privacy and integrity of the company being studied. The focus remains on the evaluation of the air transport-based expansion strategy's financial feasibility compared to the traditional factory construction approach. The insights gained from this analysis will contribute to a better understanding of effective expansion methods within the industry and may provide valuable guidance to companies seeking to grow and optimize their operations.

1.7.2 Research Objectives

The main objectives of this study are:

- To assess the feasibility of deploy air transportation as a key driver for footprint expansion.
- To compare the potential benefits and risks of Air Transportation and +2Sites Scenarios.
- To utilize the NPV method as the key metric to evaluate the financial viability of each strategy.
- To validate the thesis statement by determining which investment option aligns with the company's long-term objectives and growth strategy.

1.7.3 Research Methodology

1.7.3.1 Data Collection

The research will rely on secondary data obtained from various sources, such as financial reports, industry publications, and academic literature. Data pertaining to the Company's operations, financials, market conditions, and relevant regulatory information in France will be gathered.

It is crucial to highlight that information related to business specifics, such as sales volumes, prices, capital requirements, among others, is not publicly available. To gain access to this information, the only viable approach is through direct engagement with these companies within the business sphere. This limitation arises from the fact that companies in this particular market are not publicly traded and, therefore, are not obligated to submit their financial reports. Consequently, for the primary analysis of this thesis, company information from the sector has been utilized without revealing the identities of the specific firms involved, in accordance with confidentiality and limited disclosure agreements. Moreover, this thesis avoid disclosing sensitive data that could negatively impact the strategic, financial, and overall health of the concerned firm.

Each dimension of the relevant information gathered for the analysis and evaluation of the proposed cases to address the questions in this thesis has been validated by Subject Matter Experts (SMEs) and aligns with the actual dynamics of the business under study. The data collected from various sources has undergone rigorous scrutiny and verification by experts who possess in-depth knowledge and expertise in the field. This validation process ensures the accuracy and reliability of the information used in the research.

Moreover, to maintain the integrity and credibility of the study, the information has been cross-referenced with real-world scenarios and practices within the radiopharmaceutical industry. By grounding the analysis in the actual dynamics of the subject business, the thesis aims to provide valuable and actionable insights that reflect the challenges and opportunities faced by companies in this sector.

1.7.3.2 Data Analysis

The collected data will be analysed to understand the Company's financial position, market trends, and competitive landscape in France. The NPV assessment will be conducted for both investment options using the financial data to quantify the potential cash flows, costs, and risks associated with each project.

1.7.3.3 Feasibility Assessment

To assess and test the thesis statement and address the research problem, an analysis of two hypothetical expansion strategies for the Company into western France was conducted. The first strategy aligned with the overall dynamics of the nuclear medicine industry in Europe, involving territorial expansion through the construction of additional production plants. On the other hand, the second alternative proposed a hypothetical scenario wherein new plants would not be built, and instead, air transportation would be adopted to reach the target regions, eliminating the need for significant capital investment.

For the weighting and evaluation of the feasibility of the two proposed strategies, the Net Present Value (NPV) method was employed. This objective of this analysis was to determine which of the two alternatives generates greater value and, more importantly, to ascertain whether the strategy of transporting radiopharmaceuticals by air is a realistic and sustainable possibility for implementation. Additionally, sensitivity analyses of key variables were conducted, and risks and opportunities suggested by the thesis statement for the development of the potential distribution modality were carefully considered.

1.7.3.4 Scope and Limitations

The analysis conducted for verifying the hypotheses in this thesis has been developed through desk research instead of a field study. The main assumptions made are that, if the legal and regulatory viability of transporting radioactive products for medical purposes by airplanes is confirmed, there will be market providers offering this service without limitations. Additionally, the evaluation of the two proposed alternatives (air transportation and +2Sites

options) is done independently, considering them mutually exclusive. It is also assumed that the company has sufficient financial resources to undertake either of the projects. Furthermore, the analysis focuses on a single country, assuming there are no constraints that would allow for a combination of multiple countries.

The limitations of a desk study include:

- Non empirical Research: A desk study relies on existing information and data, which may not cover all aspects and intricacies of the actual situation. The absence of firsthand data from real-world scenarios could limit the accuracy and depth of the analysis.
- Limited representation: The focus on a single country for analysis may not capture the full diversity of regulatory environments, market conditions, and potential opportunities in other countries. This could reduce the generalizability of the findings to a broader global context.
- Simplification of complexities: The assumption of independent evaluation and mutual exclusivity of the proposed alternatives might oversimplify the reality. In practice, these options could be interrelated, and synergies might exist between them, which could impact the overall conclusions.
- Uncertain feasibility of market providers: While assuming that market providers offer the service without limitations, the actual availability and capability of these providers in the industry may vary. The real-world market dynamics and the complexities of transporting radioactive products could present practical challenges that were not fully considered in the desk study. Similarly, it is assumed that the company has the capability to develop all the necessary processes and workflows to implement air transportation as the main means of transportation.
- Limited exploration of combinations: Restricting the analysis to a single country might overlook potential benefits or synergies that could arise from considering multiple countries in the expansion strategy. The complexities of cross-border operations and regulations could play a significant role in shaping the feasibility of such combinations.

In summary, while a desk study offers valuable insights into the viability of the proposed hypotheses, it has limitations that should be acknowledged when interpreting the results. To gain a more comprehensive understanding and validate the findings, further research involving field studies, real-world data collection, and considerations of multiple countries and their interactions would be beneficial. Such an approach would provide a more robust foundation for making informed decisions and recommendations in the context of the radiopharmaceutical industry.

1.7.3.5 Conclusion

The Master Thesis will conclude with a comprehensive evaluation of the feasibility of the two strategic alternatives for market expansion. The NPV analysis will provide valuable insights into the potential financial benefits and risks associated with each investment option.

The findings of this research will not only validate the thesis statement but also provide valuable insights to recommend the most advantageous investment path for the Company's growth. Beyond its financial implications, this study holds significant potential from a social responsibility standpoint. The research's outcomes have the power to inspire further investigations and contribute to the enhancement of access rates for underserved patients, particularly those grappling with serious diseases such as cancer. By addressing the accessibility challenges in healthcare, the research's impact can extend far beyond the business realm and make a meaningful difference in saving lives and alleviating the substantial burdens that these diseases impose on society.

2. Literature Review

2.1 Introduction

The purpose of this chapter is to delve into a deeper understanding of key concepts relevant to comprehending the dynamics of the industry under analysis, which are essential for the proposed thesis. To optimize the comprehension of these important concepts, the following segmentation of information is proposed:

- Radiopharmaceuticals production
- Regulations and regulatory framework for the transportation of radioactive materials
- Successful Cases
- Market Analysis
- Theoretical Fundamentals

In the section titled "Production of Radiopharmaceuticals," a comprehensive explanation is provided regarding all the intervening variables in the production and application of a radiopharmaceutical. The objective of this section is to comprehend the complex reality associated with this industry.

Next, the regulatory framework is provided to assess the possibility of expanding the distribution of radioactive products by deploying air transportation in Europe.

The section "Registry of Successful Cases" summarizes and presents the results of the collection and documentation of specific cases that support the comparative feasibility of providing radiotracers over long distances and using air transportation.

The main objective of the Market Analysis section is to present and analyse future projections and trends in the nuclear medicine market for diagnostics, specifically in Europe.

Finally, the theoretical and conceptual underpinning of the intervening variables in the selected methodology for addressing the issue of this thesis is developed. The aim is to provide a clear theoretical framework for comprehending the research findings.

2.2 Radiopharmaceutical Production

Hansen and Bender (2021) explain that artificial radionuclides are typically generated through a nuclear reaction where a specific nucleus is bombarded by a smaller particle. This collision leads to the nucleus breaking into two smaller fragments, with the heavier fragment being the desired outcome. Different types of particles, such as protons or neutrons, can be used depending on the desired result (Figure 1). For the reaction to occur, the colliding particle needs to possess sufficient energy to overcome the repulsion between itself and the nucleus. The required energy depends on the size of the nucleus.

Additionally, Hansen and Bender (2021) describe that radionuclides for PET imaging are commonly produced using a medical cyclotron, mentioning the importance of the physical half-life of a radionuclide, which limits the time available for production and imaging, determining how long a study can be carry out screening biological processes. The positron branching ratio affects image quality and patient dose.

If the ratio is low, it is needed to increase the injected activity, leading to higher doses and potential image noise. Higher positron energy increases radiation dose and slightly reduces image sharpness. Some radionuclides emit additional gamma rays, which can complicate image interpretation and contribute to the radiation dose.

Figure 1: Nuclear reaction where target nucleus A is bombarded with beam particle a, resulting in the product nucleus B.

2.2.1 Cyclotrons

Cyclotrons are defined perfectly by Powsner and Palmer (2022) as round machines where charged particles, such as protons and alpha particles, get faster while moving in a spiral inside a vacuum. An electrical supply applies a rapidly changing voltage between the two halves of the circle, known as dees. This creates a back-and-forth electric field that speeds up the particles, giving them high energies in a short time. The particles then move outward in a spiral due to the magnetic field until they reach a certain speed and are guided into a target using a deflector. The deflector directs the particles out of the cyclotron through an opening and towards the target. Some of these particles transfer their energy to the atoms in the target. In the target, the atoms become excited and unstable due to the transferred energy. Figure 2 provides a simplified diagram illustrating the overall operation of a cyclotron, and gives a visual representation of how an actual cyclotron device looks like. The presented cyclotron model is the GE Healthcare PETtrace 800 cyclotron series, is a compact and automated system used for producing PET tracers. It is designed to be efficient and flexible, allowing for fast and easy production. The cyclotron can accelerate both protons and deuterons, making it versatile and cost-effective (www.gehealthcare.com).

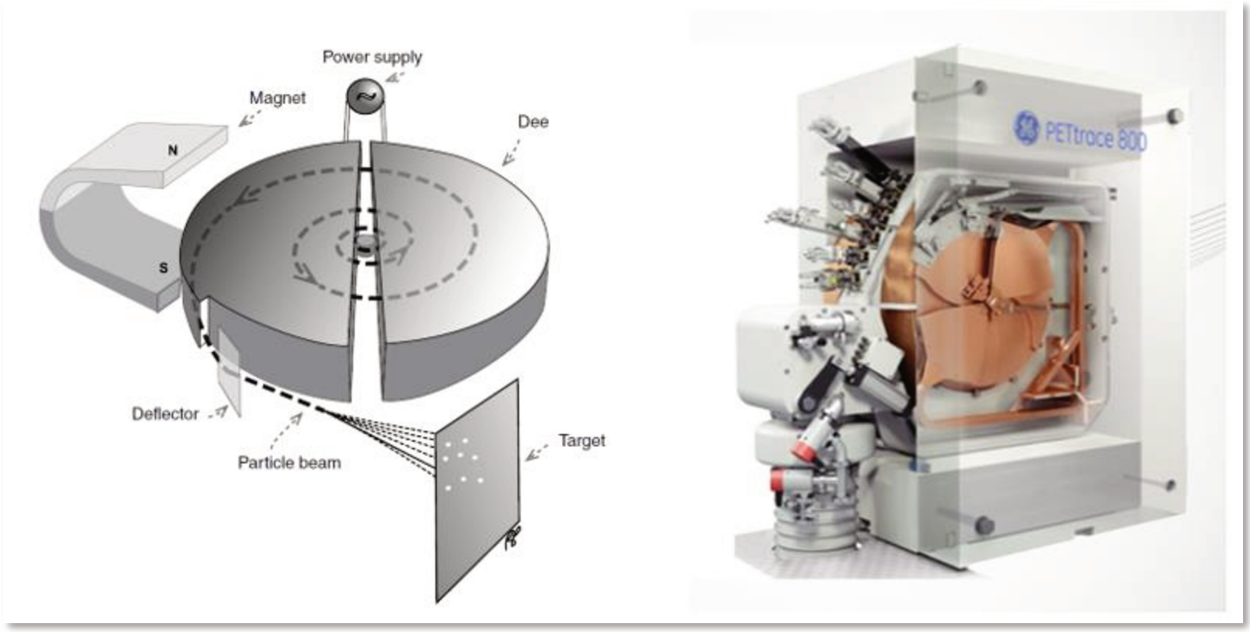

Figure 2: General operating diagram of a cyclotron and a 3D view of the PETtrace 800 model produced by GE Healthcare Company. Source: Powsner, Palmer, and Powsner (2022) and www.gehealthcare.com, equipment prospectus.

2.2.2 PET Tracer Production Workflow

Like any productive process, the manufacturing of radiopharmaceuticals for diagnostic purposes in PET scanners consists of standardized stages. Rensch, Jackson, and others (2013) provide a clear overview applicable to any radiotracer produced using a cyclotron, based on 18F-fluorodeoxyglucose (FDG), this work flow is presented in Figure 3.

Rensch, Jackson, and others (2013) summarize the process breaking it down in 4 simplified steps, as follows:

STEP 1 (Cyclotron): During the initial phase, the creation of Radioisotope Fluoride-18 (18F) takes place by subjecting enriched water to proton bombardment, utilizing the 18O(p, n)18F nuclear reaction. Following this, the resulting 18F content is either partially or entirely conveyed to the synthesizer for PET (Positron Emission Tomography) tracer production.

The transfer of 18F can be achieved through two distinct methods: the first involves direct tubing linking the cyclotron (where 18F is generated) and the synthesizer, while the second entails utilizing an intermediary transport container that can be transported from the cyclotron facility to the synthesizer's location.

Moreover, specific medical radionuclides can be produced utilizing an activity generator. This generator employs a long-lasting parent isotope that undergoes decay to yield the desired medical isotope. In such cases, the requirement for a cyclotron is eliminated. As an example, the production of Gallium 68 Isotope (Ga-68) relies on Germanium-68 (Ge-68) as the parent isotope.

STEP 2 (Synthesizer): In this phase, the radioisotope acquired in the initial step undergoes a direct interaction with the precursor, either directly or through intermediate stages. This interaction results in the creation of the PET tracer, commonly combined with a saline buffer solution, leading to a final volume within the range of 6 to 14 mL.

The quantity of radioactive isotopes utilized during the synthesis dictates the eventual dosage of the PET tracer. This dosage can be customized to suit the needs of a single patient (individual dose) or multiple patients (batch mode), depending on the specific amount of tracer required.

STEP 3 (Dispenser & Quality Control): In this stage, the PET tracer solution produced in batch mode is divided into smaller aliquots to serve multiple patients. However, apart from the patient-specific aliquots, additional samples are reserved for the purpose of quality control.

The PET tracer is subjected to a thorough validation process to establish its appropriateness for administration to human patients. This validation procedure encompasses a series of assessments that scrutinize a range of parameters, including pH levels, chemical purity, residual solvent content, radionuclide purity, radiochemical purity, concentration of radioactivity, specific activity, sterility, bacterial endotoxin levels, and the integrity of the filtration membranes.

These evaluations for quality control are conventionally carried out within a specialized laboratory dedicated to quality control (QC). The principal objective is to ensure that the PET tracer adheres to all required standards and is safe for subsequent administration to patients.

STEP 4 & 5 (Transfer to patient & PET scan): This stage involves the logistics of delivering each PET tracer dose to the patient in preparation for the PET scan. When the PET tracer production facility and the patient's location are within the same institution (in-house), the transfer process is generally efficient and rapid.

As it is highlighted by Rensch, Jackson, and others (2013), for centralized PET tracer production at a radiopharmaceutical facility, with subsequent shipping to hospitals located at a distance, typically within a two-hour driving distance, several technical, economic, and practical challenges emerge. These challenges mainly relate to potential activity loss and a decrease in specific activity of the PET tracer due to the transfer time. The geographical distance between the PET tracer production facility and customer hospitals, particularly in low-density versus high-density populated areas, needs to be considered. Additionally, the scheduling of patients at the point of use further complicates the logistics.

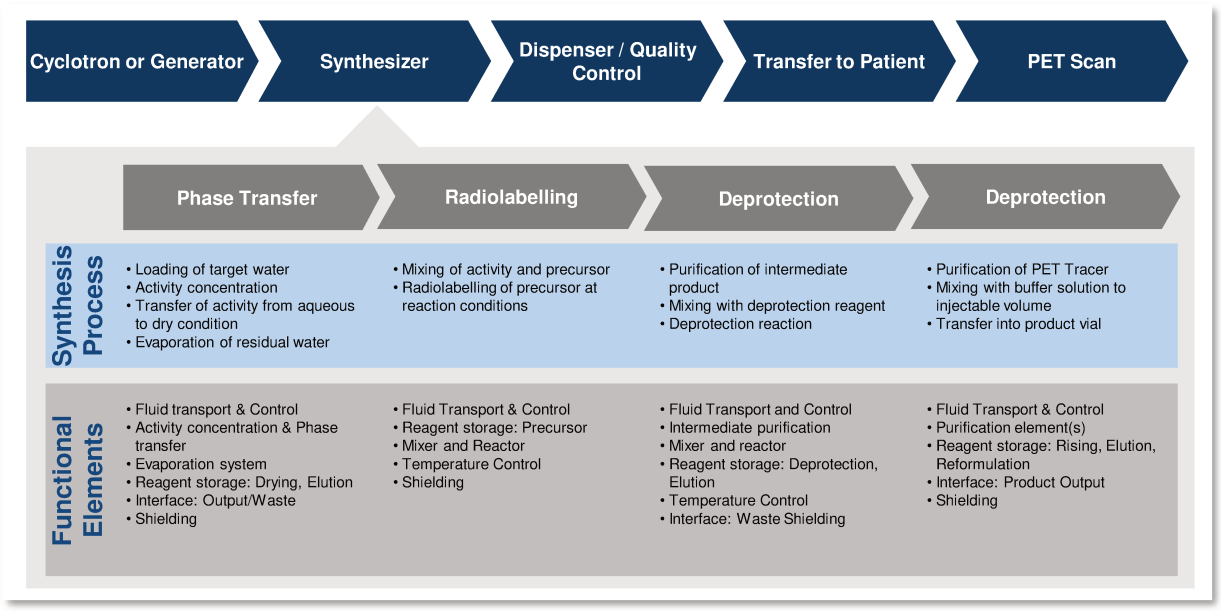

Figure 3: Radiotracer production workflow based on FDG. Source: Rensch, Jackson, and others (2013).

2.2.3 Scanners: SPECT vs PET

As is stated by Siikanen, J. (2015) in the field of nuclear medicine diagnostics, a typical procedure entails the introduction of a compound into the body that is tagged with a radioactive nuclide. Following the injection, specialized external cameras equipped with sensitive detectors are utilized to detect and capture the emitted photons originating from the radioactive material within the body. These cameras serve the vital function of recording and monitoring the distribution of the radioactive nuclide over time. By employing sophisticated mathematical algorithms, the temporal data on the distribution of the radioactive nuclide can be transformed into functional images.

In 1958 was introduced an innovative imaging device known as the scintillation camera, revolutionizing medical imaging. This imaging technique, is known as Single Photon Emission Tomography (SPECT), is typically performed using two camera heads positioned opposite each other, Siikanen, J. (2015). This camera was equipped with a collimator that selectively detects photons arriving at the camera perpendicular to its surface. Specifically designed for detecting photons emitted by single-photon-emitting radioactive materials like 99mTc, it provided planar images that visualize the spatial distribution of radioactivity within the body from a single viewpoint. However, these planar images lack critical depth information regarding the precise location of radioactivity in the projection. To overcome this limitation, the camera head could be rotated, enabling data collection from multiple angles to reconstruct cross-sectional images of the patient.

Siikanen, J. (2015) states that, Positron Emission Tomography (PET) relies on the use of radionuclides that possess an excess of protons, allowing them to capture an external electron or emit a positively charged electron known as a positron. This emission leads to the annihilation (is when a particle and its opposite partner collide and disappear. In PET imaging, annihilation happens when a positively charged particle called a positron collides with a negatively charged particle called an electron.

Additionally, Siikanen, J. (2015) mentions that, when these particles collide, they both disappear and release energy in the form of two photons, or particles of light, that move away in opposite directions) of the positron when it encounters an electron in close proximity to the decay site. As a result, the combined mass of the electron and positron is converted into two photons that move in nearly opposite directions. These emitted photons can be detected by a PET camera within a narrow time window, forming Lines of Response (LOR).

Finally, according to Siikanen, J. (2015), by analysing a multitude of these lines, mathematical algorithms are employed to calculate the distribution of radioactivity within the subject. PET and Single Photon Emission Computed Tomography (SPECT) are functional imaging techniques often complemented by anatomical imaging

methods like Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) to accurately correlate the functional activity observed in PET and SPECT with the precise anatomical location within the object or subject being examined. Figure 4 depicts a simplified diagram that facilitates the differentiation between the two scanning techniques.

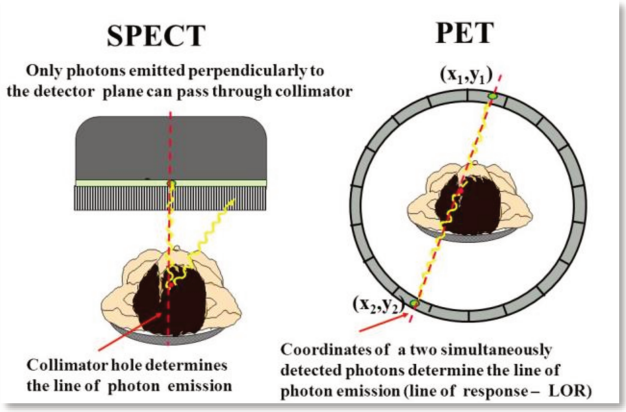

Figure 4: Comparative Illustration of the Operation of SPECT and PET Scanners. Source: Nuclear Medicine Systems: PET Instrumentation.

In concordance with earlier assertions, the work of Rong J., Haider A., and other researchers (2023) emphasizes that once a patient receives the tracer injection, they are positioned within a circular scanner. This apparatus gauges the radioactive signal in order to pinpoint the tracer's location across various organs. The positron emitted by the tracer travels a specific distance and collides with an electron, resulting in a mutual annihilation. This annihilation process transforms their combined mass into electromagnetic energy, particularly two gamma rays that emanate in opposing directions. The PET camera detects these photon coincidences and reconstructs the points of annihilation. The PET data can be processed to generate an image that depicts the distribution of the tracer in space, facilitated by specialized algorithms.

Overcoming challenges in PET image reconstruction encompasses compensating for issues like scattering, random coincidental occurrences, and signal weakening as it traverses diverse bodily tissues. Often, PET imaging is combined with computed tomography to offer anatomical context and address signal attenuation.

Rong J., Haider A., and others (2023) also present a very intuitive diagram that allow a comprehensive understanding of the whole procedure. The Figure 5 replicate this operational flow graph which includes 1) Radionuclide generation. 2) Tracer synthesis. 3) Quality control (QC). 4) Intravenous tracer injection. 5) PET scan: positron decay, annihilation, and coincidence detection. 6) Image analysis and data quantification.

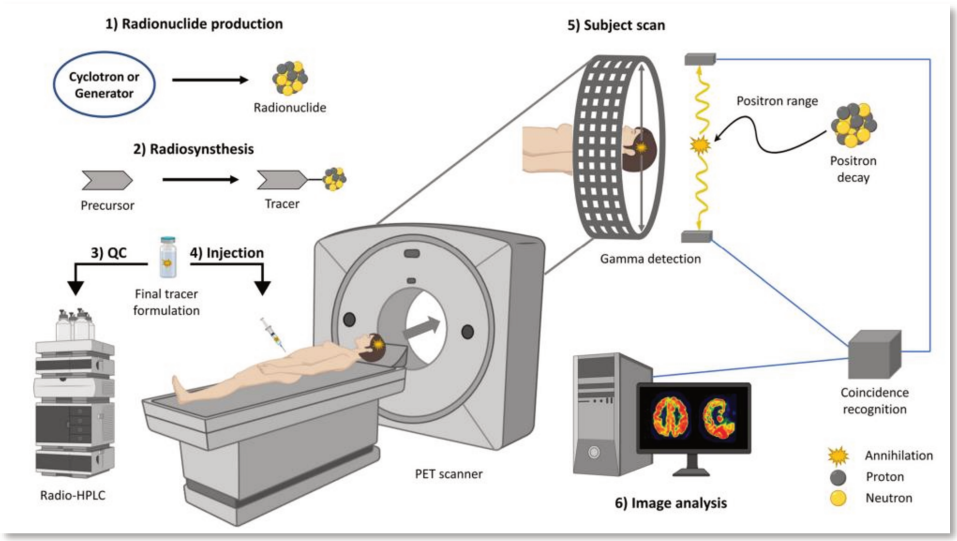

Figure 5: Diagnostic Procedure Using Radiotracers with PET Camera. Source: Rong J., Haider A., and others (2023)

2.2.4 Radiotracers

According to the National Institute of Biomedical Imaging and Bioengineering (NIBIB) of the United State, a radioactive tracers consist of carrier molecules tightly bound to radioactive atoms, and their composition varies depending on the intended purpose of the scan. These tracers can interact with specific proteins, sugars, or even the patient's own cells. For instance, in cases where the source of intestinal bleeding needs to be identified, red blood cells from the patient are labelled with radioactive atoms and reinjected. A SPECT or PET scan is then performed to track the movement of the blood within the patient, revealing any accumulation of radioactivity in the intestines that indicates the location of the problem. In nuclear medicine diagnostic studies, the radioactive tracer is typically administered through intravenous injection, although other methods such as inhalation, oral ingestion, or direct organ injection may be used depending on the specific disease being investigated. The mode of tracer administration is chosen based on the particular disease process under examination.

The following provides a comprehensive overview of the key radiotracers presently employed, delineating their importance, reliability, and indications.

2.2.4.1 Fludeoxyglucose F18 (FDG)

Ashraf, M and Goyal, A (2022) clearly explain that Fludeoxyglucose F18 (FDG) is a radioactive tracer that mimics glucose and is utilized in conjunction with positron-emission tomography (PET) for diagnostic purposes. Its primary role is to identify tissues exhibiting altered glucose metabolism. It does not possess therapeutic properties. Abnormal glucose metabolism is relevant in conditions such as cancer, epilepsy, myocardial ischemia, inflammation, and Alzheimer's disease. PET scans involve the injection of radiotracers into the patient before imaging, enabling visualization of blood flow, as well as metabolic and biochemical activities in both diseased and healthy tissues. FDG, being an analog of glucose, has a tendency to accumulate in tissues with heightened glucose demand, such as tumours and inflammatory cells.

As per the work of Ashraf and Goyal (2022), while traditional imaging techniques like X-ray, CT, and MRI provide detailed images of healthy and diseased tissue, they may not detect certain diseases or early-stage abnormalities. PET scans complement these structural imaging methods by visualizing blood flow and metabolic activities in tissues. FDG, a glucose analog, accumulates in tissues with high glucose demand, such as tumours and inflammatory cells. In neurology, FDG helps identify abnormal glucose metabolism associated with epileptic seizures and aids in diagnosing conditions like Alzheimer's disease and brain trauma. In oncology, it is used for evaluating and monitoring treatment in cancers like lung cancer, lymphomas, and breast cancer. In cardiology, FDG assists in identifying myocardial dysfunction and visualizing atherosclerosis and myocardial ischemia. It is also applied in inflammatory conditions such as orthopedic infections and rheumatologic disorders.

In summary, FDG works by mimicking glucose, a type of sugar that our bodies use for energy. When FDG is injected into the body, it is taken up by cells that have a high demand for glucose, such as cancer cells and cells involved in inflammation. The FDG emits positrons, which are tiny particles, and when these positrons encounter electrons in the body, they annihilate each other, releasing energy in the form of gamma rays. The PET scanner detects these gamma rays and creates images that show areas with high FDG uptake, indicating areas of increased glucose metabolism. This helps doctors identify and monitor conditions like cancer, inflammation, and certain neurological disorders.

Figure 6: FDG Vial example. Source: www.r2ibf.com.br

FDG is presently the most commonly employed radiopharmaceutical in the industry for diagnostic purposes across various applications. Physicians often opt to use FDG beyond the previously mentioned indications due to its proven reliability and cost-effectiveness in comparison to other available alternatives. Although there are currently no companies holding exclusive intellectual property rights for this radiopharmaceutical, most manufacturers have registered their own trademarks. Figure 6 provides an example of the appearance of an FDG vial.

2.2.4.2 Fluorocholine (FCH)

Fluorocholine, a radiolabelled form of choline, is a positron emission tomography (PET) tracer utilized for oncologic imaging. It surpasses certain limitations of FDG (fluorodeoxyglucose), making it preferable for specific cases. FDG fails to visualize small tumours, brain tumours, intrapelvic tumours, and to differentiate between malignancy and chronic inflammation. In contrast, fluorocholine exhibits promise in visualizing these tumours types and distinguishing between malignancy and inflammation. Fluorocholine finds application across multiple indications in oncology. It has proven successful in visualizing brain tumours, lung cancer, oesophageal cancer, colon cancer, bladder cancer, prostate cancer, and other malignancies. Moreover, it aids in assessing therapeutic response in head and neck cancer and detecting lymph node metastases in lung cancer. Hara, T. (2003).

In summary, fluorocholine represents a valuable PET tracer for oncologic imaging, particularly in cases where FDG has limitations. Its potential lies in visualizing diverse tumours types and evaluating therapeutic response. Hara, T. (2003).

FCH is a radiopharmaceutical that has been on the market for over 20 years. Unlike FDG, it is expected that procedures will decrease in the coming years with the introduction of more specific radiotracers and improved performance for detecting certain types of diseases. For instance, this is the case with the imminent approval of FPSMA, a fluor-based radiotracer associated with the prostate-specific membrane antigen, which is specifically prescribed for the diagnosis of prostate cancer. It is anticipated that FCH will only be utilized to a limited extent for certain special indications.

2.2.4.3 Fluoro-DOPA (FDOPA)

Fluoro-DOPA is a radiotracer employed in positron emission tomography (PET) imaging to investigate the dopaminergic system within the brain. It is a modified version of L-DOPA, a precursor to dopamine, a neurotransmitter crucial for various brain functions. The primary application of Fluoro-DOPA is in diagnosing and monitoring Parkinson's disease and other movement disorders. By enabling the visualization and quantification of dopamine synthesis and metabolism, it provides valuable insights into the integrity of the dopaminergic system (Pretze, M., Wängler, C., & Wängler, B., 2014).

One notable advantage of Fluoro-DOPA is its high specificity for the dopaminergic system, as it is selectively taken up by dopaminergic neurons and converted into fluorodopamine, which can be detected through PET imaging. This specificity allows for precise evaluation of dopamine function in the brain. Nonetheless, the use of Fluoro-DOPA does have certain limitations. One limitation is its short half-life, as it is a radioactive tracer. This restricts the available imaging time and necessitates on-site production of the radiotracer. Additionally, Fluoro-DOPA lacks specificity for Parkinson's disease and can accumulate in other tissues, leading to potential false-positive results (Pretze, M., Wängler, C., & Wängler, B., 2014).

2.2.4.4 Flutemetamol F 18

According to the prospectus published online for this radioactive tracer, Flutemetamol (18F), marketed as Vizamyl by GE Healthcare, is a radiopharmaceutical utilized in positron emission tomography (PET) scanning. It incorporates the radionuclide fluorine-18 and serves as a diagnostic agent for Alzheimer's disease.

Beta-Amyloid plaque estimation is a diagnostic procedure that uses a radioactive substance in PET brain imaging to measure the density of amyloid plaques. These plaques are associated with conditions like Alzheimer's disease. A negative scan indicates few or no plaques, while a positive scan indicates moderate-to-frequent plaques. During the procedure, a small amount of the radioactive substance is injected into the patient's vein, and images are taken

90 minutes later. The images show the distribution of the radioactive substance in the brain. The presence of amyloid plaques can be determined by comparing the activity in different areas of the brain. (GE Healthcare, Vizamyl Prospect)

It's important to note that the procedure has some side effects like flushing, increased blood pressure, headache, nausea, and dizziness. It also carries a small risk of radiation exposure. The procedure is contraindicated in patients with a history of allergic reactions to certain ingredients. Overall, the procedure helps doctors assess the presence of amyloid plaques in the brain, aiding in the diagnosis and evaluation of conditions like Alzheimer's disease. (GE Healthcare, Vizamyl Prospect)

2.2.4.5 The new generation of radiotracers

In the last decade, nuclear medicine has been evolving at an unprecedented pace. In both the scientific and market environments, a revolutionary concept that is now part of the current reality has gained solid ground and are considered as part of the new generation of radiopharmaceuticals, known as "radioligands". That concept refers to radiopharmaceuticals that contain a radioactive substance and are used for diagnostic or therapeutic purposes. Radioligands, specifically, are a type of radiopharmaceutical that consist of a ligand (a molecule that binds to a specific target) labelled with a radioactive atom. Radioligands offer several advantages over traditional radiopharmaceuticals. They are designed to selectively bind to specific receptors or molecules of interest, allowing for more targeted imaging or therapy. This specificity enhances the accuracy and sensitivity of diagnostic procedures and enables the visualization of specific biological processes in the body. (www.pointbiopharma.com)

A radioligand works by binding to specific molecules or receptors in the body. It is a molecule that has a radioactive atom attached to it, allowing it to be detected and visualized using imaging techniques like positron emission tomography (PET) or single-photon emission computed tomography (SPECT). The radioligand is designed to selectively target certain molecules or receptors that are involved in various biological processes. (www.pointbiopharma.com)

When the radioligand is injected into the body, it travels through the bloodstream and binds to its specific target in the tissues or organs of interest. The radioactive atom attached to the radioligand emits signals in the form of gamma rays or positrons, which can be detected by the imaging equipment. By measuring the distribution and intensity of these signals, images can be generated that reflect the concentration and activity of the target molecules or receptors in the body. (www.pointbiopharma.com)

Radioligands are valuable tools in medical research and clinical practice as they provide a way to study and visualize specific biological processes, such as receptor binding, neurotransmitter activity, or disease-related changes in the body. They help researchers and healthcare professionals gain insights into the functioning of various organs and tissues, diagnose diseases, monitor treatment responses, and develop new therapies.

The following section presents the currently most significant radioligands under development, anticipated to be imminently accessible in the market. It is crucial to comprehend that these radioligands incorporate a radioactive isotope chosen according to whether they are intended for diagnostic applications (e.g., Fluorine, Gallium, Copper, etc.) or therapeutic interventions (e.g., Lutetium):

- **PSMA (Prostate-Specific Membrane Antigen)** is a protein found on the surface of prostate cancer cells. Ligands targeting PSMA, such as PSMA-617, are used in molecular imaging and targeted therapy of prostate cancer. They bind specifically to PSMA-expressing cells, allowing for the detection and localization of prostate cancer lesions.
- **DOTA (DOTATATE, DOTA-octreotate, oxodotreotide, DOTA-(Tyr3)-octreotate, and DOTA-0-Tyr3-Octreotate)** is a chelating agent that forms stable complexes with radioactive isotopes. It is commonly used to label peptides and other targeting molecules in radiopharmaceuticals. By attaching DOTA to a ligand, such as a peptide or antibody, it enables the binding of specific radioactive isotopes, such as Gallium-68 or Lutetium-177, for imaging or therapy.
- **FAPI** is a ligand that targets fibroblast activation protein, which is overexpressed in the stroma of various solid tumours, including pancreatic, lung, and breast cancers. FAPI ligands, such as FAPI-04 or FAPI-46,

can be labelled with radioactive isotopes for imaging purposes, aiding in the detection and characterization of tumours.

2.2.5 Good Manufacturing Practice (GMP)

Good Manufacturing Practice (GMP) comprises a comprehensive set of guidelines and rules that have been established to uphold the quality, safety, and uniformity of pharmaceutical, biotechnological, and medicinal products throughout their manufacturing process. The primary purpose of GMP standards is to mitigate the potential risks associated with pharmaceutical production and to guarantee that the end products adhere to stringent criteria for efficacy, safety, and purity. Pharmaceutical and medicinal product manufacturers who adhere to GMP principles can effectively ensure a superior level of quality control and produce products that are secure and efficacious for consumers. Regulatory authorities in each respective country or region oversee the enforcement of GMP standards through regular inspections. Non-compliance with GMP regulations can lead to severe consequences, including penalties, product recalls, or even the suspension of manufacturing operations.

As highlighted by Lis, Horowitz, and their colleagues (2023), the European Commission introduced significant revisions to Annex 1 of the Good Manufacturing Practice (GMP) guidelines in August 2022, specifically focusing on "Manufacture of Sterile Medicinal Products." These updates are poised to exert a substantial influence on manufacturers intending to bring aseptically prepared products to the EU market. It's noteworthy that these regulatory modifications are applicable to all sterile drug products destined for the EU market, irrespective of their origin. To comply with the newly outlined expectations, manufacturers must adapt their practices by August 2023, leaving them with a limited window to strategize and implement essential alterations before the enforcement phase commences.

One notable aspect of the updated Annex 1 is the infusion of quality risk management principles throughout the document. Additionally, the concept of a Containment Control Strategy (CCS) is introduced, addressing contamination control concerning sterility assurance. This strategy mandates the establishment of comprehensive and meticulously documented measures to curb contamination. Importantly, certain changes mandated by these revisions might necessitate considerable capital investments, which, in turn, could lead to potential disruptions in supply.

The revised guidelines include several significant adjustments. Facilities, for instance, are now required to employ Restricted Access Barrier Systems (RABS) or isolators as the baseline approach to aseptic processing. Moreover, the criteria for aseptic processing have been rendered more rigorous, with "no growth" microbial contamination stipulated in Grade A areas, and stricter success criteria for Aseptic Process Simulations (APSs) introduced.

The updated Annex 1 is slated to come into effect on August 25, 2023, with the exception of lyophilizer sterilization, which will be enacted a year later. It's of paramount importance for manufacturers to be fully cognizant of these changes and ensure compliance to align with EU GMP guidelines. This alignment is crucial not only for regulatory compliance but also to facilitate the successful market placement of their products within the EU market.

2.3 Regulations and regulatory framework for the transportation of radioactive materials

As indicated by the title of this section, the subsequent discussion is dedicated to an exhaustive exploration of the applicable legal and regulatory framework that provides the foundation for the transportation of radioactive materials. This chapter adopts a holistic approach, gradually transitioning towards more specific themes that hold particular relevance in addressing the central thesis statement and its associated complexities. To fulfill the objectives of this section, it is paramount to commence by introducing a pivotal regulatory and oversight entity within this domain, namely the International Atomic Energy Agency (IAEA).

According to its official website, the International Atomic Energy Agency (IAEA) is an international organization established on July 29, 1957. It was founded in response to the "Atoms for Peace" initiative proposed by US President Dwight D. Eisenhower to promote the peaceful use of nuclear energy while ensuring its safe and secure implementation.

The IAEA currently consists of 173 member states, including virtually all countries with an interest in nuclear energy. Its membership includes both nuclear-armed states and non-nuclear-armed states, with the goal of fostering cooperation and promoting the peaceful use of nuclear technology.

The primary objective of the International Atomic Energy Agency (IAEA) centers on advancing the constructive use of nuclear energy. This encompasses its application in generating electricity, facilitating medical and industrial endeavors, and contributing to agricultural practices. Integral to this mission is the agency's commitment to heightening nuclear safety and security measures. It also undertakes the crucial role of verifying the non-military nature of nuclear initiatives, extending technical aid and expertise in domains related to nuclear energy, radiation, and nuclear applications. Additionally, the IAEA plays a pivotal role in curbing the proliferation of nuclear weapons.

Regarding regulations, the IAEA plays a crucial role in establishing and promoting international standards and safety measures in nuclear activities. It develops and sets international guidelines and safety standards through its various publications, such as safety guides, technical documents, and regulations. The IAEA's role is to provide guidance and assistance to member states in implementing these regulations and ensuring the safe and secure use of nuclear technology. It also conducts inspections and safeguards activities to verify compliance with international nuclear non-proliferation obligations and agreements.

Thus, the International Atomic Energy Agency (IAEA) shoulders the critical role of promulgating fundamental principles that govern the safe movement of radioactive materials. In its most recent release of 2019, titled "Regulations for the Safe Transport of Radioactive Material. Specific Safety Requirements (SSR-6) (Rev. 1)," the IAEA furnishes an exhaustive reference delineating requisite safety protocols and directives for the secure transportation of radioactive substances.

The publication stands to furnish both regulations and safety benchmarks to ensure the secure conveyance of radioactive materials. Backed by six accompanying IAEA Safety Guides, these guidelines elucidate and offer practical insights to facilitate the effective application of the stipulated requirements. Importantly, the set of regulations extends to all modes of transportation – whether land, water, or air – and encompasses incidental transportation linked to the handling of radioactive materials. These comprehensive regulations span various aspects, ranging from the design, creation, and maintenance of packaging to the logistics surrounding the preparation, loading, unloading, and reception of both radioactive material and the packages containing them.

The regulations embedded within SSR-6 carry international recognition, rendering them an indispensable compass for governments, regulators, and individuals entwined in the intricate web of radioactive material transportation. Furthermore, a dedicated subsection within the publication serves to present a comprehensive overview of the currently effective principles enshrined in SSR-6.

2.3.1 Regulations for the Safe Transport of Radioactive Material. Specific Safety Requirements. No. SSR-6

The SSR-6 (Section I and II) provides a solid framework for regulations for the transport of radioactive material including several safety standards and measures to ensure the protection of people, property, and the environment. Some of these standards are the following:

- Restriction of Radioactive Release: The process of packaging and transporting radioactive material mandates the incorporation of a suitable containment system to avert the unintended release of radioactive substances.

- Management of External Radiation Exposure: Stringent regulations dictate the management of the radiation dose rate emanating from transported radioactive materials. This encompasses setting precise limits on the radiation dose rate and implementing mechanisms to ensure adherence to these limitations.
- Prevention of Critical Situations: Stringent conditions are imposed on both package design and operational aspects to avert criticality incidents – uncontrolled nuclear chain reactions. These conditions are tailored to the inherent hazards of the radioactive contents and are formulated to ensure the utmost level of criticality safety.
- Thermal Damage Prevention: Comprehensive provisions are established to counteract the potential damage arising from heat generated by radioactive substances during transit. This involves establishing strict limits on the heat output of packages and instating measures to guarantee strict adherence to these parameters.
- Graduated Approach: The regulatory framework employs a graded methodology concerning package and conveyance content limits, along with performance standards for package design. This approach is attuned to the inherent risks of the transported radioactive contents, ensuring that appropriate safety measures are applied based on the severity of transportation conditions.
- Administrative Oversight: Robust administrative controls are mandated, encompassing the necessity for transport activities to receive the approval of competent authorities. These controls are instituted to ensure the meticulous adherence to safety standards and provide an added layer of safeguarding throughout the transportation of radioactive materials.

Section III of the SSR-6 offers a comprehensive delineation of the overarching stipulations pertaining to radiation protection during the transportation of radioactive material. This section underscores the paramount significance of mitigating radiation exposure to individuals, mandating the establishment of robust radiation protection initiatives. Moreover, it emphasizes the implementation of effective emergency response protocols, guaranteeing strict conformity with regulations, and facilitating comprehensive training for personnel engaged in the transport of radioactive materials.

The training required for individuals engaged in the transport of radioactive material includes:

- Foundational Awareness Training: This form of training imparts a comprehensive overview of various radioactive material classifications. It encompasses facets like labeling, marking, placarding, packaging, segregation prerequisites, and acquaints participants with the contents and significance of the radioactive material transport documentation.
- Task-Specific Proficiency Training: This training delves into specific requirements pertinent to the individual's role in radioactive material transport. It delves deeply into areas like handling of packages, appropriate stowage methods, procedures for emergency responses, and the broad spectrum of hazards tied to distinct radioactive material categories.
- Safety Instruction: Tailored to the degree of potential exposure and the individual's responsibilities, this training arms participants with knowledge to counteract possible releases. It encompasses preemptive measures, utilization of personal protective gear, and immediate action protocols in case of accidental radioactive material release.

The provision of training should occur upon employment and undergo periodic validation or enhancement through retraining, as deemed suitable by the competent authority. To ensure comprehensive record-keeping, employers are responsible for maintaining records of all safety training undertaken.

Furthermore, the SSR-6 serves as a resource on the classification and activity thresholds pertaining to radioactive substances. It encompasses tables presenting specific values for individual radionuclides, along with guidelines for the determination of these values for radionuclides not explicitly listed. The document also encompasses selections from the United Nations (UN) list, which feature proper shipping names and descriptions applicable to diverse types of radioactive materials.

The table delineating activity concentration limits for radionuclides furnishes insight into the activity concentration limit for exempt materials, as well as the activity limit for exempt consignments across various radionuclides. These

values are quantified in terms of Becquerel per gram (Bq/g) for activity concentration and Becquerel (Bq) for activity limits.

In line with International Atomic Energy Agency (IAEA) regulations, the classification of radioactive materials hinges upon their specific activities. This is evaluated by comparing the material's specific activity against the activity concentration limits delineated in a dedicated table (Table 2 of the IAEA SSR-6).

Specific activities are calculated by dividing the activity of a radionuclide by the mass or volume of the material. The specific activity is expressed in units such as Bq/g or Bq/cm^3. Based on the specific activity, radioactive materials can be classified into different categories:

- Exempt Material: Radioactive materials with low specific activities that are considered to pose minimal risk.
- Low Specific Activity (LSA) Material: Radioactive materials with higher specific activities than exempt material but still below certain limits. LSA materials are further classified into LSA-I and LSA-II based on their specific activities. LSA-I includes uranium and thorium ores, unirradiated uranium and thorium compounds, and other materials with low specific activities. LSA-II includes materials with slightly higher specific activities.
- Surface Contaminated Objects (SCO): Solid objects that have radioactive contamination on their surfaces. SCO materials are classified based on the level of non-fixed contamination on the accessible surface.
- Special Form Radioactive Material: Radioactive materials that are in a specific form, such as sealed sources or encapsulated materials, which provide a high degree of containment and prevent dispersion of radioactive material.
- Fissile Material: Materials that are capable of sustaining a nuclear chain reaction. Fissile materials are subject to specific regulations and requirements.

The specific activity limits for each classification are specified in the IAEA regulations and may vary depending on the radionuclide and the type of material.

For radioactive materials used for medical purposes, the International Atomic Energy Agency (IAEA) provides specific regulations and guidelines. These guidelines cover the transport, handling, and disposal of radioactive materials in medical applications.

According to the IAEA regulations, radioactive materials used for medical purposes are classified as "Radioactive Material, Excepted Package - Medical Use" (UN 2915). This classification applies to radioactive materials that are used for diagnostic or therapeutic purposes in medicine.

The activity concentration limits and activity limits for exempt consignments for medical radioactive materials are specified in Table 2 of the IAEA regulations. These limits vary depending on the specific radionuclide used in medical applications. For example, the activity concentration limit for exempt material for Technetium-99m (Tc-99m) is 1 TBq/g, and the activity limit for an exempt consignment is 1 TBq.

It is important to note that the use of radioactive materials for medical purposes must comply with additional regulations and guidelines specific to the country or region where the medical procedures are performed. These regulations ensure the safe handling, storage, and disposal of radioactive materials in medical settings.

The IAEA regulations provide specific provisions for the air transportation of radioactive materials for medical purposes. According to the regulations, radioactive materials used for medical purposes can be transported by air under certain conditions.

The specific provisions for air transportation of radioactive materials for medical use are mentioned in paragraph 410 of the IAEA regulations. It states that a single package of non-combustible solid LSA-II or LSA-III material, if carried by air, shall not contain an activity greater than 3000 A1.

This provision ensures that the activity of the radioactive material being transported by air for medical purposes is within the specified limit to maintain safety during air transportation.

For the transport of radioactive materials, including those used for medical purposes and air transportation, the International Atomic Energy Agency (IAEA) regulations classify packages into different types based on their design and characteristics. The conditions and requirements for each type of package are presented in Figure 7 and described as follows:

Type A Package: This type of package is designed to withstand normal conditions of transport and prevent the release of radioactive material under accident conditions. It is suitable for transporting radioactive materials with higher levels of radioactivity.

Type B Package: This type of package is designed to withstand more severe accident conditions than Type A packages. It is used for transporting radioactive materials with higher levels of radioactivity, including those used in medical applications.

Type C Package: This type of package is designed to withstand severe accident conditions, including those involving fire. It is used for transporting large quantities of radioactive materials, including those used in medical applications.

Excepted Packages: These packages are used for transporting small quantities of radioactive materials with low levels of radioactivity. They are exempt from some of the more stringent requirements applicable to Type A, B, and C packages.

It is important to note that the specific design and requirements for packages used in the transport of radioactive materials, including those for medical purposes and air transportation, vary depending on the country or region. Therefore, it is essential to consider that national regulation requirements are applied following the principles provided by the IAEA.

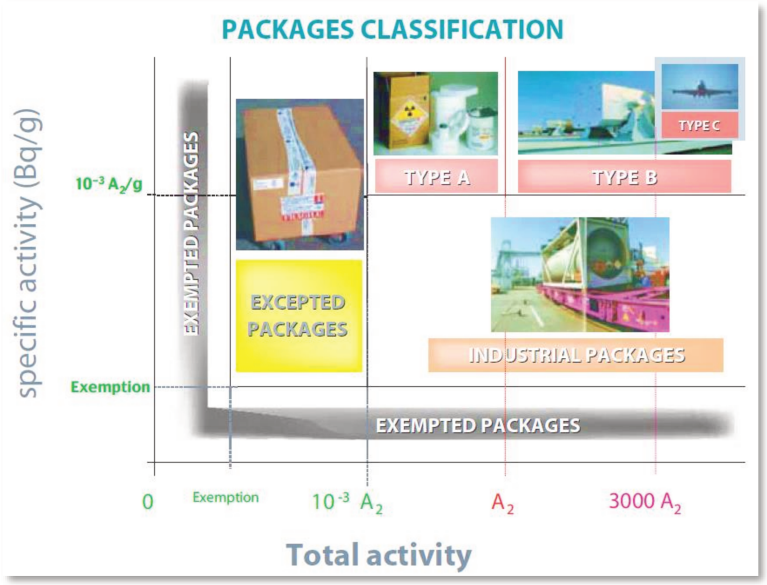

Figure 7: Types of packages depending on total and specific activity. Source: IAEA SSR-6

These principles aim to ensure the safe transport of radioactive materials by verifying compliance with design specifications, containment integrity, criticality safety, proper closure, and prevention of contamination.

It is fair to mention that the principles outlined by SSR-6 document do not specifically mention radioactive materials for medical purposes or air transportation. However, the regulation guidance mentioned in the document apply to the transport of radioactive materials in general, without specifying any particular purpose.

Within the SSR-6, a condensed compilation of the primary principles recommended by the IAEA for the transportation of radioactive materials is presented. The document outlines these principles as follows:

Before the Inaugural Shipment:

- Packaging is to be crafted in strict alignment with design specifications and pertinent regulatory provisions.
- In instances where the containment system's design pressure exceeds 35 kPa, the packaging must exhibit its integrity under this pressure.
- For specific packaging categories and those carrying fissile material, efficacy in terms of shielding, containment, heat transfer traits, and confinement systems must remain within approved thresholds.
- Criticality safety attributes, along with the efficacy of neutron poisons (if applicable), must conform to design requisites.

Before Each Shipment:

- Affirm that the package indeed contains the designated radionuclides and contents in their specified states.
- Fulfill all requisites stipulated in the regulations and relevant certificates of approval.
- Disengage or render ineffectual any lifting attachments not meeting specified criteria.
- For particular package types, demonstrate adherence to temperature and pressure criteria.
- Guarantee the proper closure and sealing of containment system apertures to forestall the escape of radioactive contents.
- Conduct measurements and tests for packages containing fissile material to affirm secure closure.
- Confirm proper maintenance of packaging components and radioactive contents during storage.

Transportation of Other Commodities:

- Packages should solely encompass items essential for the utilization of radioactive materials.
- Containers such as freight containers, Intermediate Bulk Containers (IBCs), tanks, and other forms of packaging, utilized for transportation, should not double as storage units or transport vessels for different goods unless they have been decontaminated to specified levels.

Regarding air transportation, it is important to note that the regulations for the transport of radioactive materials generally apply to all modes of transportation, including that modality. Specific requirements and controls for air transportation may be outlined in other sections or documents not included in the SSR-6.

Administrative Requirements

The SSR-6 provides guidelines for obtaining approval for shipments and outlines the information that needs to be included in the application for approval. It also mentions the requirements for shipments under special arrangements and the issuance of certificates of approval.

Based on the provided document, there is no specific mention of radioactive materials for medical or healthcare purposes. The document primarily focuses on the approval and certification requirements for special form radioactive material, low dispersible radioactive material, and fissile material. It outlines the necessary information and tests required for approval, design specifications, management systems, and pre-shipment actions.

Regarding air transportation, the document does not explicitly mention air transportation requirements. It primarily focuses on the design, approval, and certification aspects of radioactive materials, without specifying any particular mode of transport.

The document underlines that the regulations governing the secure transport of radioactive material extend their jurisdiction to encompass all modes of transportation, including air travel. These regulations span the entire spectrum of activities and circumstances associated with the conveyance of radioactive material. This encapsulates the gamut of actions, ranging from the design, fabrication, maintenance, and restoration of packaging, to the orchestration, dispatching, loading, transit, delivery, unloading, and ultimate reception of both radioactive material and packaging.

These regulations lay down explicit benchmarks for various levels of severity, encompassing typical transport conditions, standard transport conditions, and transport scenarios involving accidents. It is noteworthy, however, that these regulations are not applicable to radioactive material that constitutes an integral part of the transport vehicle itself.

It's imperative to highlight that the document does not offer specific intricacies pertaining to the requisites and procedures governing the air transportation of radioactive materials.

2.3.2 French Local Regulatory framework

On a national scale, the French Nuclear Safety Authority operates under the name "Autorité de Sûreté Nucléaire" (ASN). As an autonomous administrative entity, it assumes responsibility for overseeing and regulating nuclear safety, radiation protection, and the transportation of radioactive materials within France. A fundamental tenet of the ASN's mandate is to safeguard the security and integrity of nuclear operations, materials, and facilities across the nation. To execute this mission, the ASN wields regulatory authority, conducts rigorous inspections, and ensures compliance with safety protocols and standards across the nuclear sector and affiliated industries.

Within France, the ASN plays a pivotal role in monitoring the transportation of radioactive materials. Over the past decade and a half, the ASN has made notable strides in this arena. It has synchronized transportation oversight with the safety framework governing nuclear facilities, introduced regional inspection systems, and expanded the International Nuclear and Radiological Event Scale (INES) classification to encompass transport-related incidents. Collaborative efforts with institutions such as the Institute for Radiation Protection and Nuclear Safety (IRSN) and the International Atomic Energy Agency (IAEA) have been instrumental in shaping regulations and nurturing ongoing collaboration with international counterparts. A significant emphasis has been placed on transparency through initiatives like the dissemination of inspection follow-up letters and endeavors aimed at informing the general public, elected officials, and the media.

The implementation of the standards TSN (Transport Safety Nuclear) Act in 2006 provided a stronger legal framework for ASN's actions. They gained the authority to impose sanctions, enhancing their regulatory role and credibility. Additionally, the adoption of technical regulations for Basic Nuclear Installations (BNI) in 2012 marked a significant step in updating the regulatory pyramid, with further resolutions expected to tighten safety requirements for transport within BNIs. Audits conducted by the IAEA have confirmed that ASN has successfully implemented recommendations and suggestions to improve their oversight.

Additionally, the ASN continuously explores prospective measures to further enhance their oversight of radioactive material transport, considering advancements in technology, changes in international standards, and potential collaborations to ensure the safe and secure transportation of such materials.

The distribution of shipments reveals that around 15% of annual transport movements involve the nuclear power industry, which receives substantial media attention. The remaining 85% of shipments cater to health, non-nuclear industries, and research sectors, with the medical field accounting for about 30% of these shipments.

Specifically, within the fuel cycle of nuclear power plants, various types and quantities of shipments are necessary. These include fresh uranium-based fuel, Mixed Oxide Fuel (MOX fuel), spent fuel destined for reprocessing plants, and shipments of uranium hexafluoride and plutonium oxide. Additionally, approximately 1,000 shipments, involving around 50,000 packages, occur annually between France and foreign countries.

Safety principles play a critical role in mitigating risks associated with transporting radioactive materials. Risks include potential exposure to radioactive particles, external irradiation, environmental contamination, and the risk of uncontrolled nuclear chain reactions. Ensuring package integrity in scenarios such as fire, physical impact, water ingress, chemical interactions, and excessive heat release is crucial to avoid material release or package deterioration.

Regulatory oversight by the ASN is fundamental to maintaining transport safety. ASN conducts safety checks throughout the package's life cycle, encompassing design, manufacture, and maintenance. Compliance with safety regulations during shipment and transportation is rigorously monitored. It is mandatory to notify ASN of any deviations from regulations or incidents related to transport.

The medical sector plays a significant role in the transport of radioactive materials, particularly in the context of radioactive pharmaceutical products. Examples include the transport of technetium generators commonly used in nuclear medicine departments. This highlights the vital role of safe and efficient transport within the healthcare industry.

In summary, the transport of radioactive materials involves a distribution of shipments, including those for the nuclear power industry and various sectors. Safety principles, regulatory oversight by ASN, and the importance of the medical sector are key elements in ensuring the secure and effective transport of these materials.

2.3.3 Enforcement and monitoring authority in France:

The Institute of Radioprotection et de Sûreté Nucléaire (IRSN) serves as the public expert in research and knowledge concerning nuclear and radiological risks. It operates as a public establishment with an industrial and commercial nature, and its responsibilities are defined by the law n°2015-992 of August 17, 2015, related to the energy transition for green growth. The organization and governance of IRSN are specified in the decree n°2016-283 of March 10, 2016. The institution operates under the joint supervision of the Minister of Ecological Transition, the Minister of the Armed Forces, and the Ministers in charge of Energy Transition, Research, and Health.

The core missions of IRSN encompass expertise, research, protection, anticipation, and knowledge sharing, all in service to the public authorities and the population. What sets IRSN apart is its ability to combine researchers and experts to anticipate upcoming questions on the evolution and management of nuclear and radiological risks. The dedicated workers at IRSN are committed to disseminating their work and sharing their knowledge with society. This contributes to improving access to information and fostering dialogue with stakeholders. The Institute actively contributes to public policies concerning nuclear and radiation safety, health, the environment, and crisis management.

According to IRSN data, approximately 940,000 packages of civil-use radioactive materials are transported annually in France (10 million worldwide), accounting for approximately 615,000 shipments. The vast majority of these transports involve radioactive materials used in the medical, pharmaceutical, industrial, or construction sectors. Notably, only 15% of these transports are related to nuclear fuel cycle-related radioactive materials. The packages' weight varies from a few grams (vials) to several hundred tons ("casks"). Radioactive material transportation constitutes less than 3% of all hazardous material shipments.

This organisation also presents an extremely relevant fact, the primary mode of transporting packages containing radioactive substances is by ground transportation, with approximately 96% of packages exclusively transported via this mode. The remaining 4% of packages are subject to combined transport, notably by road and air (3% of packages) and by road, sea, and rail (1% of packages).

2.3.4 Section Conclusion:

After conducting an in-depth analysis of the regulatory framework applicable to the transportation of radioactive substances, beginning with global accepted general principles suggested by the International Atomic Energy Agency, and then examining how these global guidelines are adopted and implemented in France, it is interpreted and concluded that there is no explicit impediment or prohibition for conducting the transport of radioactive substances by air. Furthermore, sufficient evidence has been found throughout the reviewed literature that clearly indicates the regular transportation of radioactive substances in the market.

Moreover, it can be added that due to the extremely low activity concentrations carried by the doses used in nuclear medicine, these packages pose minimal risk to the safety of individuals in direct contact with the transported object and do not represent a significant hazardous to society. In other words, it is concluded that there is a practical possibility of transporting radiopharmaceuticals by air, provided that the strict safety standards established by the current regulations are adhered to.

Additionally, it is essential to acknowledge the importance of continuous monitoring and evaluation of safety protocols and practices during the transportation of radioactive substances by air. While the risks may be deemed low due to the low activity concentrations, safety remains paramount, and any potential risks must be carefully managed and mitigated.

Furthermore, close collaboration between regulatory authorities, transportation companies, and relevant stakeholders is crucial in ensuring effective implementation and enforcement of safety measures. Strict adherence to established safety guidelines, training of personnel involved in the transportation process, and routine inspections of transportation facilities are essential elements in maintaining a high level of safety and security throughout the entire process.

It is also worth noting that technological advancements and research in nuclear medicine and transportation methods are continuously evolving. Therefore, regular updates and improvements to safety regulations should be considered to stay abreast of emerging best practices and enhance safety standards further.

2.4 Successful Cases

Through a thorough research, two highly relevant success cases have been detected, providing robust support for the thesis statement. While these success cases do not originate precisely in France, they shed significant light from a practical perspective. In other words, they positively contribute to the hypothesis that the transportation of radioactive materials for medical purposes can be conducted via air travel over considerably long distances, surpassing what could be achieved through land transportation. Moreover, these cases underscore the adherence to optimal conditions of quality and safety, ensuring the proper execution of the medical diagnostic procedure.

2.4.1 Case 1: Cyclotek Pharmaceuticals Limited

Cyclotek, an Australian-based enterprise specializing in the production of radioactive compounds utilized for diagnostic applications, operates an intricate network of radiotracer production facilities. With an initial installation of the GE PETtrace Cyclotron in 2002, serving as the primary source for the commercial production of FDG (Fludeoxyglucose) for PET Clinical Service Providers in Australia and New Zealand, Cyclotek's expansion has been marked by the establishment of additional cyclotrons, facilitation of research and development endeavors, and establishment of partnerships with healthcare entities.

The significance of this company to this thesis lies in its regular distribution over considerably greater distances compared to the distances covered by firms sitting in Europe. Figure 8 provides a clear visualization of the extensive geographic reach achieved by this firm, with relatively few production sites. The primary mode of transportation is air, even though the final distribution is executed via land routes, consequently aircrafts play a pivotal role in the distribution network.

Notably, Cyclotek's growth has been underscored by its proactive expansion across geographically expansive regions. The company employs air transportation as its primary mode to bridge considerable distances, enabling the efficient supply of radiopharmaceuticals. This methodology has been particularly salient due to the expansive nature of Australia's landmass compared to other regions. As it is reported by the Australian Geoscience Department, Australia has an extension of about 7.7 million square kilometres, compared to France which has q much smaller land area of only 0.64 million square kilometres, according to data from the Wikipedia website. This signifies that Australia surpasses France in geographical size by a factor of 12. A graphical representation of the precise disparity between both countries is depicted in Figure 9, using the freely available algorithm from "The True Size" website. This tool allows for accurate comparisons of real dimensions between countries, mitigating the typical distortions resulting from widely accepted cartographic techniques.

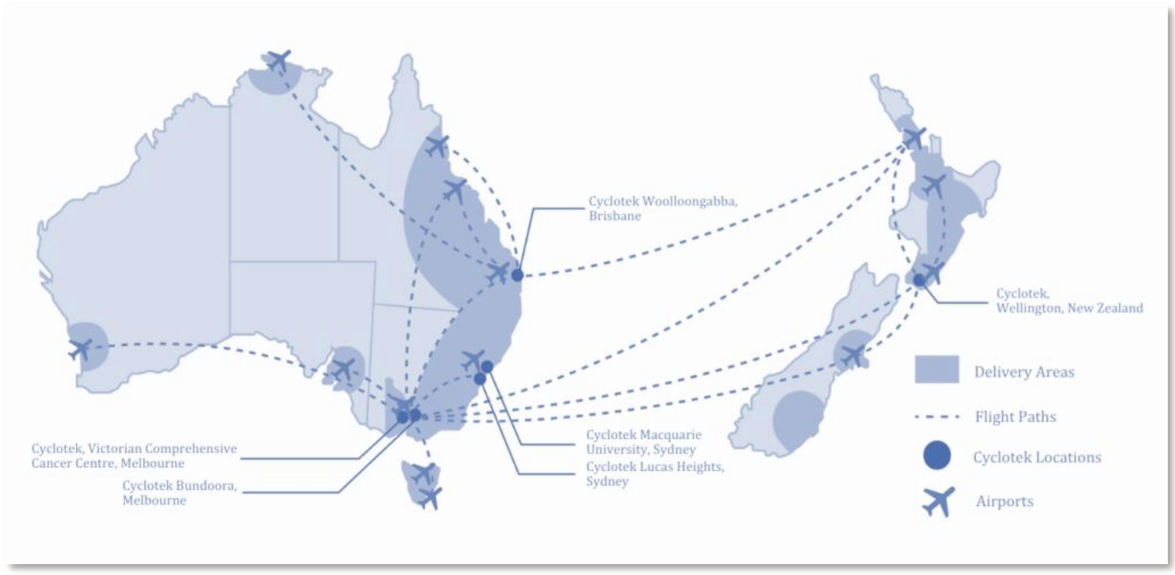

Figure 8: The geographical area covered by Cyclotek through air transportation. Source: www.cyclotek.com/logistics

Additionally, the Australian Government's Department of Infrastructure, Transport, Regional Development, Communications, and the Arts records an approximate monthly count of 50,000 domestic flights, further emphasizing the prominence of air travel within the country. In contrast, France, despite its relatively smaller land area, registers a variable monthly range of domestic flights, underscoring the country's robust air transportation network.

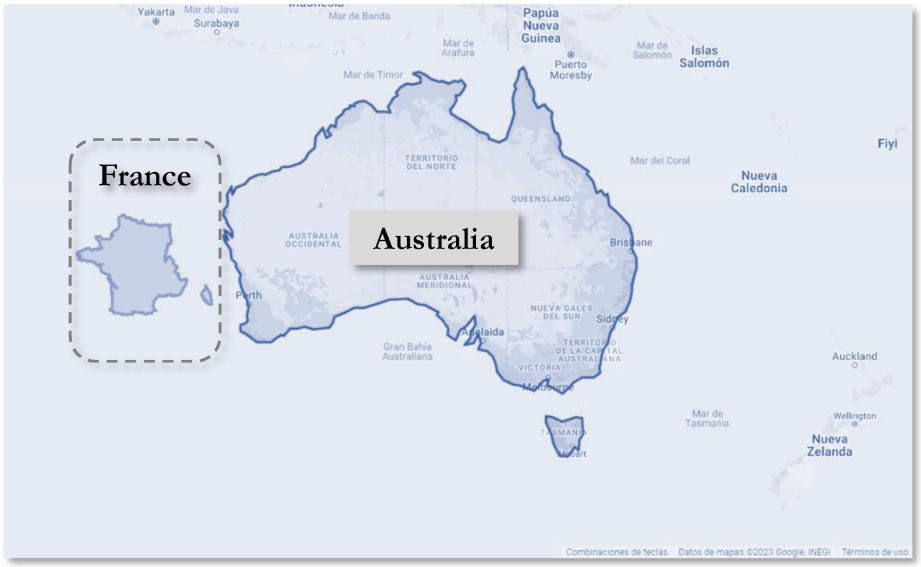

Figure 9: Geographical Comparison between Australia and France. Source: www.thetruesize.com

The case study of Cyclotek clearly illustrates that the transportation of radiotracers over long distances is indeed feasible, underpinned by the company's successful distribution network. This achievement is emblematic of the company's dedication to adhering to quality standards while ensuring the accurate and effective execution of diagnostic procedures for patients. In a landscape characterized by logistical complexities, Cyclotek's utilization of air transportation for extensive distribution underscores the viability of maintaining product quality and regulatory compliance. As a result, the analysis of Cyclotek's operations illuminates the potential for the successful transportation of radiotracers over substantial distances, bolstered by strategic operational choices and stringent adherence to regulatory imperatives.

2.4.2 Case 2: Winnipeg Great-West Life PET/CT Imaging Centre

In contrast to the previously examined Case 1, the present research focuses on a diagnostic center as opposed to a radiopharmaceutical manufacturing establishment. More specifically, the research cores on assessing the practical feasibility of effectively supplying radiotracers across extended geographical distances while adhering to rigorous standards of excellence. The primary objective is to determine whether it is possible to uphold optimal levels of quality control, thereby ensuring the accurate and reliable execution of diagnostic procedures for patients, despite the inherent challenges associated with long-distance transportation.

The study conducted by Ducharme, J., Goertzen, A., and others (2009) focuses on the practical aspects of utilizing PET with 18F-FDG in a PET/CT center. The primary issue addressed in the research revolves around the center's dependence on a distant supplier for 18F-FDG, leading to potential disruptions in patient scheduling and scan cancellations. In simpler terms, the PET/CT center faces a significant challenge in relying on a distant supplier to provide the necessary 18F-FDG. This reliance on long-distance transportation, subject to airline schedules, and the limited shelf life of the product pose risks of delays or cancellations in patient scans, resulting in potential frustration for all involved.

Per the research conducted by Ducharme, J., Goertzen, A., and their collaborators in 2009, the Winnipeg-based Great-West Life PET/CT Imaging Centre in Canada strategically acquires 18F-FDG. This radiopharmaceutical is procured from a production hub situated at a considerable distance of 1,200 kilometers. Additionally, the center maintains a backup supplier located even farther away, spanning a distance of 1,800 kilometers. It is noteworthy that despite the availability of closer vendors in the United States, the procurement protocol is bound by regulatory stipulations. Specifically, these regulations dictate that the center must exclusively source 18F-FDG from suppliers sanctioned by Health Canada. This regulatory requirement finds its roots in the context of ongoing clinical trials, emphasizing the pivotal role of regulatory adherence in the procurement dynamics.

According to the research, the main risks when transporting a radiopharmaceutical by air are related to the distance between the production facility and the imaging center. The transportation of FDG is dependent on commercial airline cargo, which can introduce several challenges and risks. Some of the risks identified in the research include:

- **Reliance on airline schedules:** The production schedule of FDG is closely tied to airline schedules, as there is only one Canadian commercial airline that transports radioactive substances. Delays or disruptions in airline schedules can impact the timely delivery of FDG to the imaging center.
- **Transport failure or delays:** There is a risk of complete transport failure, where FDG is not delivered to the imaging center as planned. Additionally, delays in transport can occur, leading to a longer shipping time and potential expiration of the FDG before it reaches the center.
- **Limited shelf life:** FDG has a limited shelf life, typically around 12 hours from preparation. The transportation time, including clearance by Transport of Dangerous Goods inspectors, adds to the overall shipping time. This limited shelf life poses a risk of FDG expiring before it can be used for patient scans.

These risks associated with air transportation of FDG can result in disruptions to patient scheduling, cancellations of scans, and challenges in maintaining a reliable supply of FDG for imaging procedures.

In the face of considerable challenges inherent in transporting radiotracers across extensive aerial distances, the study demonstrated encouraging outcomes. Through the strategic implementation of contingency strategies and meticulously tailored protocols within our operational framework, a discernible upswing in patient scans was observed. Specifically, the tally of patient scans surged from 659 during the first year to 993 in the third year, translating into a remarkable 51% surge. Worth highlighting is the fact that this increase materialized even though the actual count of scan days merely witnessed a 24% escalation.

Integral to the study are timetables delineating 18F-FDG injection schedules across various scenarios. These encompass typical deliveries, instances involving lower shipped activity, and situations where delivery encountered delays. The meticulous crafting of contingency protocols coupled with the adept management of 18F-FDG shipments not only facilitated enhanced patient throughput but also effectively curtailed disruptions.

In conclusion, the strategic utilization of contingency plans and proficient handling of radiotracer shipments can lead to enhanced patient scan volumes and mitigate potential disruptions in the imaging process.

2.4.3 Section Conclusion

In conclusion, the research highlights two distinct cases involving the transportation of radiopharmaceuticals by air. Case 1 involves Cyclotek Pharmaceuticals Limited, an Australian-based company that successfully distributes radioactive molecules, including 18F-FDG, over considerable distances via air travel. This case demonstrates the feasibility of utilizing air transportation to effectively supply PET radiopharmaceuticals to various locations, thereby surpassing the limitations of land transportation.

Likewise, Case 2 examines the Winnipeg Great-West Life PET/CT Imaging Centre, a diagnostic center in Canada that relies on distant suppliers for 18F-FDG. The study identifies significant challenges in air transportation, primarily related to long distances, reliance on commercial airline schedules, limited shelf life of the radiopharmaceutical, and regulatory constraints. These challenges can lead to disruptions in patient scheduling and scan cancellations, causing potential frustration.

However, despite the challenges, the study demonstrates that implementing contingency plans and tailored protocols can yield positive results. In the case of the Winnipeg Great-West Life PET/CT Imaging Centre, the careful management of 18F-FDG shipments led to a substantial increase in patient scans, optimizing patient throughput and minimizing disruptions.

Overall, while air transportation presents complexities and risks, the research underscores that with careful planning and management, it remains a viable option for supplying radiopharmaceuticals over long distances, facilitating essential diagnostic procedures, and contributing to improved patient care.

2.5 Market Analysis: Understanding Market Trends and Dynamics

The main aim of this section is to present a comprehensive overview of the European nuclear medicine market. This will be accomplished by using thorough market research as the underlying basis, which involves a detailed examination of specialized market reports produced by dedicated consulting firms. The objective is to identify significant trends and key drivers that influence the market, thereby facilitating an enhanced understanding of its current structure and future potential.

The subject of investigation in this thesis pertains to a highly distinctive and intricate industry. Information concerning various aspects such as trade volumes, strategies, financial performance, and more is notably hard to come by and isn't readily accessible within existing literature or books. As a result, the inclusion of a market report prepared by a specialized consulting firm has proven indispensable. This report has provided a crucial avenue for obtaining a holistic understanding of both the current status and the anticipated future trajectory of this industry.

2.5.1 Europe Nuclear Medicine for Diagnostics Market

The research on the Nuclear Medicine Market was conducted by the consulting firm Sky Research Forecast (2022), a team of industry experts specializing in market analysis. They performed a detailed study to gain insights into various aspects of the market, including its structure, segmentation, and competitive landscape. As it is mentioned in the report document, to gather data, the authors conducted interviews with key industry players, such as Chief Executive Officers (CEOs), Marketing Directors, and Business Development Managers, to understand their perspectives and obtain valuable information.

In addition to primary interviews, Sky Research Forecast (2022) also extensively utilized secondary research sources, such as technical journals, trade magazines, government publications, and verified data sources. They collected and validated market data related to distribution channels, market classification, and segmentation. By combining primary and secondary research with professional experience, those experts forecasted future market trends, technological developments, and demand projections for the next seven years.

Throughout the research process, Sky Research Forecast (2022) employed a range of analytical tools and models to supplement their analysis. These tools allowed them to convert qualitative and quantitative indicators into precise market estimates, enabling a more accurate forecast of the market's trajectory and potential opportunities. The comprehensive approach adopted by the consulting firm ensured a thorough understanding of the Nuclear Medicine Market, providing valuable insights for both present and future market dynamics.

2.5.1.1 Value Chain Analysis

Porter, M. (1998), introduced the concept of value chain analysis, a comprehensive framework examining activities involved in product creation or service delivery. It aims to identify areas for improvement, cost optimization, and differentiation, enabling businesses to gain a competitive advantage and achieve sustainable growth. Value chain analysis (VCA) involves a comprehensive examination of various market systems responsible for producing a specific commodity or a group of commodities. The value chain approach serves as an analytical framework to comprehend the market failures that impact competitiveness, the functioning of market systems, evaluate opportunities, and the potential for sustainable and inclusive growth, with the ultimate aim of advancing the sector.

According to Sky Research Forecast (2022), buyer bargaining power has a moderate impact on the market. This implies that buyers hold some influence in commercial decisions and can exert pressure on suppliers for better terms or prices. Factors affecting buyer bargaining power include product differentiation and brand loyalty. If buyers have numerous similar product options and can easily switch between suppliers, their bargaining power is higher. Additionally, strong brand loyalty among buyers can also grant them more influence in purchase conditions.

Regarding to the determinants of competitive rivalry in the European Nuclear Medicine for Diagnostics market, Sky Research Forecast (2022) identified determinant factors such as, product differentiation, brand loyalty, costs of switching, and distribution and sales channels. Product differentiation and brand loyalty can influence the intensity of competitive rivalry, as unique products or strong brand loyalty can reduce rivalry. Moreover, high switching costs or exclusive sales channels may provide a competitive advantage to certain competitors.

In relation to the risk of alternative options or substitutes, it can have a moderate impact on the European Nuclear Medicine for Diagnostics market. Substitutes are products or services that fulfill a similar function in the industry but in a different way. In this context, other diagnostic imaging technologies like Magnetic Resonance Imaging (MRI) or Computed Tomography (CT) could be potential substitutes at same stage of certain diseases. The impact of substitutes depends on their availability, accessibility, acceptance by medical professionals and patients, and cost-effectiveness compared to nuclear medicine.

While nuclear medicine for diagnostics has proven to be an effective and widely used technology in the medical field, the emergence of new technological advancements in medical imaging could pose potential threats in the future. Thus, companies in the nuclear medicine for diagnostics industry should closely monitor technological developments in substitute technologies and continuously seek to improve and differentiate their products to maintain their market position.

In summary, the threat of new entrants is found to be moderate, primarily influenced by high investment costs, legal barriers, and product differentiation. In terms of competitive rivalry, the market demonstrates a moderate level, possibly attributed to a limited number of players, moderate strategies, high innovation, and a rapid growth rate. Moreover, the presence of a supply-demand gap and moderate exit barriers further contribute to the competitive landscape. On the other hand, the bargaining power of buyers appears to be low, driven by factors such as a significant number of buyers, substantial purchase quantities, low switching costs, and a high degree of product dependency. These conclusions highlight the complexities and opportunities within the Europe Nuclear Medicine for Diagnostics market.

2.5.1.2 Market Trends Dynamic Analysis

Sky Research Forecast (2022) presents a comprehensive analysis of the market dynamics pertaining to nuclear medicine for diagnostics in Europe. The report delves into the factors driving and constraining the market, as well as the emerging opportunities for future growth.

One of the key drivers identified in the report is the escalating prevalence of infectious and chronic diseases across Europe. Despite preventive measures, awareness policies, hygiene and education improvement, the incidence of these diseases continues to rise. The report attributes this trend, particularly in developing countries, to the deteriorating nutritional content in diets, which contributes to the prevalence of chronic conditions such as cardiovascular diseases, diabetes, cancer, osteoporosis, neurological diseases, and obesity.

Another significant driver highlighted in the report is the increasing awareness among patients regarding disease diagnosis through nuclear medicine. Advancements in nuclear medicine technology, diagnostic procedures, instruments, and reagents have led to a surge in demand for diagnostic services. Furthermore, changing lifestyles and habits have contributed to the rise of diseases like cardiac diseases, kidney disorders, liver disorders, diabetes, among others, leading to heightened awareness among individuals across developed, developing, and under-developed countries in Europe. The focus on early diagnosis, also known as preventive diagnosis, has become paramount in promoting precise and prompt treatment for various ailments, subsequently bolstering the demand for nuclear medicine in the region.

The referred report also identifies a key restraint in the market, which is the access rate of molecular diagnostic tests. While these tests are known for their precision and rapid results, they tend to be costly in comparison to general diagnostic tests. In developed countries, insurance schemes and reimbursement policies often cover these tests, enabling accessibility for low to middle class populations. In contrast, certain countries lack such coverage, resulting in financial constraints for patients seeking these advanced diagnostic services. This affordability challenge delays the market's overall growth potential.

On a positive note, emerging radioisotopes, and the development of radiotheranostics (combination of both therapeutic and diagnostic elements within a single process) present opportunities for the future, offering innovative diagnostic and therapeutic potentials. The ongoing race in the production processes of radioisotopes is expected to drive the market scenario in the coming years. Moreover, radiotheranostics is gaining momentum as a promising cancer therapeutics approach, potentially guiding various other therapies and providing a robust opportunity for the overall nuclear medicine for diagnostic market in Europe.

2.5.1.3 Future of Nuclear Medicine Market

According to Sky Research Forecast's analysis, the future of the nuclear medicine market shows promising advancements and developments in diagnostic imaging technologies. Functional nuclear medicine, an emerging field, utilizes radioactive isotopes as tracers to analyze metabolic processes in the body. Nuclear medicine is particularly effective in diagnosing and staging cancers and monitoring treatment. The market consists of two segments: positron emission tomography (PET) and single-photon emission computed tomography (SPECT) systems, which are often combined with other imaging modalities to produce hybrid imaging systems.

However, the nuclear imaging industry faces challenges, including reliability, pricing, product positioning, and the erratic supply of radiopharmaceuticals. Nevertheless, promising developments have been observed in some companies, such as NeuSoft's patient-friendly PET/CT system and Molecular Dynamics' innovative whole-body SPECT/CT scanner. These advancements offer faster image acquisition, better image quality, and improved patient comfort, driving progress in the nuclear medicine market.

To further enhance nuclear medicine's potential, researchers are focusing on various aspects, including the development of new radionuclide production technologies, new radiotracers for better understanding of specific organ functions, and multimodality imaging devices like PET/CT and PET/MRI. Additionally, targeted radionuclide therapeutics are being researched for personalized cancer treatments. The increasing incidence of cardiac and cancer diseases, growing awareness, and expanding application segments contribute to the demand for diagnostic applications of radiopharmaceuticals.

Overall, the increasing demand for PET machines and SPECT scanners, along with the growing use of PET and SPECT scans for early and accurate disease diagnosis, is expected to drive the demand for radiopharmaceuticals, especially FDG, in the future. Despite certain challenges, continuous technological developments and research advancements are likely to propel the nuclear medicine market toward more effective and efficient diagnostic imaging and targeted therapies.

2.5.1.4 Key European Market Trends

Upon conducting a thorough examination of the extensive information presented by Sky Research Forecast, the focus has been placed on statistically significant data for this thesis, which is summarized as follows:

According to Sky Research Forecast's market research (2022), the European nuclear medicine market is estimated to be valued at 2,652 million dollars by 2023, with the Diagnostic market segment representing 84% of the total. It is projected that the market will grow at a Compound Annual Growth Rate (CAGR) of 19.2% by the year 2030, maintaining the leading share of the diagnostic sector over molecules intended for Therapy. The diagnostic segment is expected to exhibit an even faster growth rate, surpassing therapy by up to 2.23 percentage points. Figure 10 give a visual representation of the mentioned estimations.

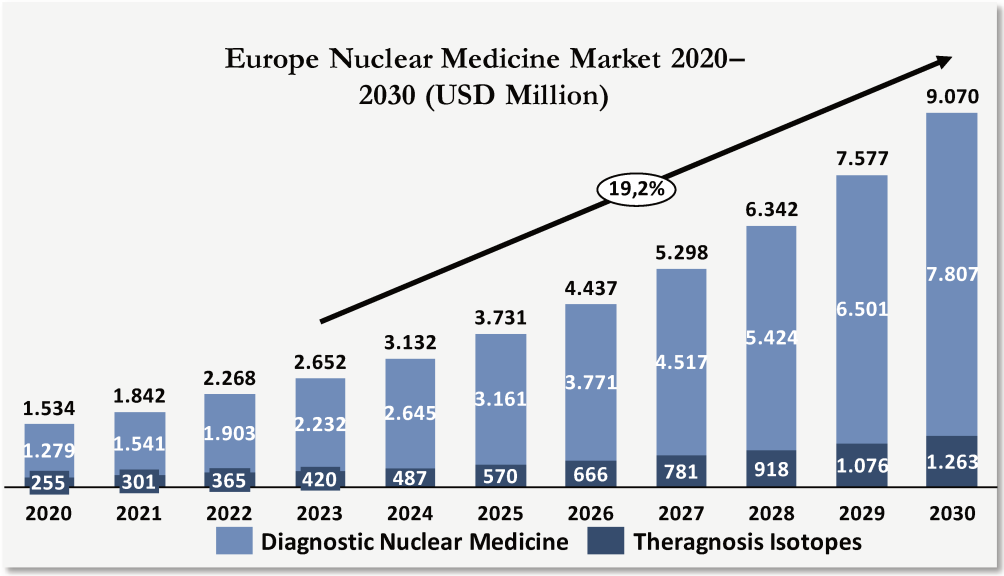

Figure 10: Europe Nuclear Medicine Market 2020–2030 (US Million). Source: SRF Market Research.

In line with the findings from previous chapters, Sky Research Forecast (2022) indicates that while the diagnostic market will experience significant growth in the next seven years, this upward trend is primarily driven by PET diagnostics with a CAGR 21.1%, which is expected to grow at a notably higher rate than SPECT. This observation results logical since the latter technology is trending towards obsolescence and is naturally phasing out. Evidence of this is that by 2030, SPECT will only represent 14% of the total diagnostic market, whereas it accounted for 33% in 2020.

The significant relevance of the Fluor isotope in the PET diagnostic market is noteworthy, as it currently stands as the primary molecule utilized in this segment, representing 80% of the total production and projected to grow to 83% by 2030, as it is reflected in the Figure 11. The consumption of Fluor is expected to experience a dramatic increase in the upcoming years, with a CAGR of 22.6%. This surge in demand can be interpreted as a substantial rise in the utilization of cyclotron capacity, as this isotope is produced through the exploitation of such devices.

Regarding the indications or diseases diagnosed through the application of radiopharmaceuticals in PET units, approximately 72% currently corresponds to oncological conditions. By the year 2030, it is projected that cancer diagnostic procedures will account for 80% of all interventions, indicating an average annual growth rate of 21.5%. The Figure 12 summarizes these facts.

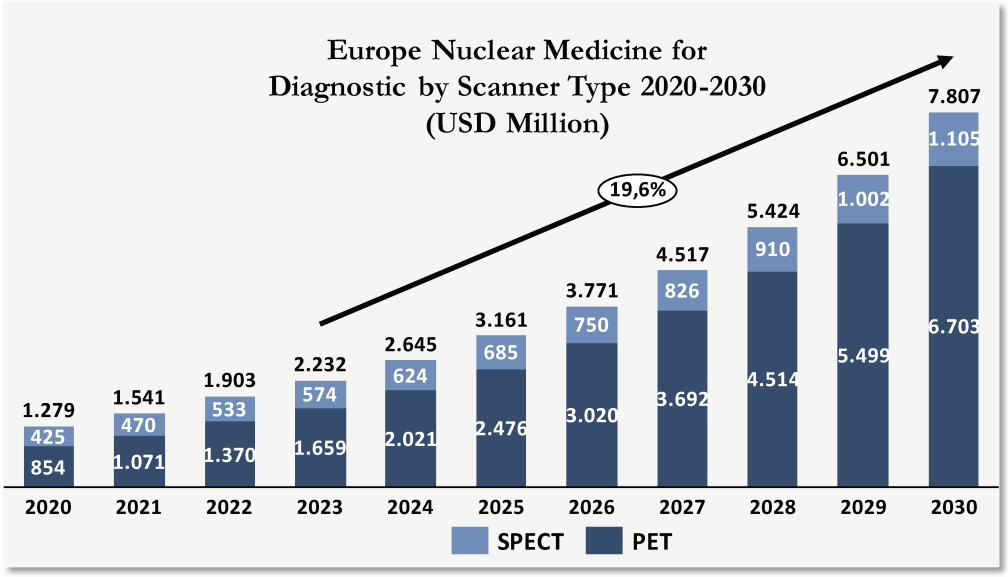

Figure 11: Europe Nuclear Medicine for Diagnostic by Scanner Type 2020-2030 (USD Million). Source: SRF Market Research.

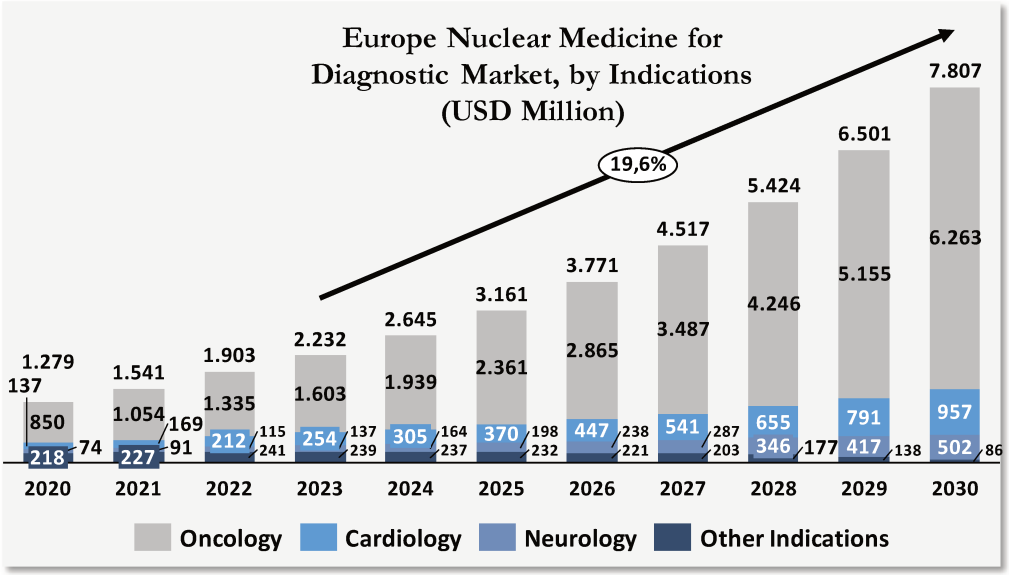

Figure 12: Europe Nuclear Medicine for Diagnostic Market, by Indications (USD Million). Source: SRF Market Research.

2.5.1.5 Main Countries

According to Sky Research Forecast (2022), Europe has advanced and modern healthcare facilities with the latest technology and services. The region has top-notch hospitals, advanced diagnostic centers, and well-trained professionals in the diagnostic field. This has led to significant growth in the overall nuclear medicine market in Europe.

Germany's market has experienced significant growth due to several factors, including a strict legal framework governing the development and manufacturing of radionuclides in nuclear medicine. Additionally, cost-effective diagnostic nuclear medicine tests have ensured accessibility within budgetary limits. The country is also embracing new sensor-based technologies for diagnosing chronic and infectious diseases, which is expected to further drive market growth.

In France, superior healthcare spending makes the market partially cost-sensitive, allowing high-cost nuclear medicine diagnostic tests to be adopted by a broader population. However, overall market growth in France has been stagnant in recent years. The integration of new technologies into the diagnostic system and access to an established healthcare ecosystem are expected to unlock new growth opportunities.

The United Kingdom (U.K.) stands out as a promising market for nuclear medicine diagnostics in Europe, displaying consistent positive growth. Factors contributing to this growth include an increasing geriatric population, rising awareness about disease diagnosis, and the introduction of new diagnostic technologies. Government initiatives supporting diagnostic healthcare funding and the launch of advanced equipment to improve diagnostic precision are further fuelling the expansion of the U.K. nuclear medicine for diagnostic market.

It is worth noting that based on Sky Research Forecast (2022) report, France represents the third most important market in Europe. Currently, this country accounts for 17.5% of the entire European nuclear medicine market, and it is projected to maintain this share in the coming years. Furthermore, estimates indicate that France's growth aligns with the overall European market, with an expected annual growth rate of approximately 18.7%, reaching a significant value of approximately 1,543 million dollars by the year 2030. Figure 13 illustrates the revenue levels generated by the leading countries in the European nuclear medicine industry.

As it is showed in the previous figure, the results presented by Sky Research Forecast (2022) do not reveal any particular trend for the specific case of France; instead, it is characterized by maintaining a close relationship with the projections of the global market.

Additionally, as depicted in Figure 14, the main driver of the nuclear medicine industry is the diagnostic segment, accounting for 85% of the current total, while the therapy segment, being relatively younger, only covers 15%. These proportions of market share are expected to remain relatively stable over the following years with minor variations. The projected average annual growth rates for the diagnostic and therapy segments are believed to be around 19.1% and 16.5%, respectively, by the year 2030.

Furthermore, the report from Sky Research Forecast (2022) indicates that, similar to the rest of Europe, molecules intended for use in PET scanners currently account for 78% of the market in France, and it is projected that by 2030, this proportion will increase to 87%, while the revenues generated from the sale of molecules intended for SPECT will decline.

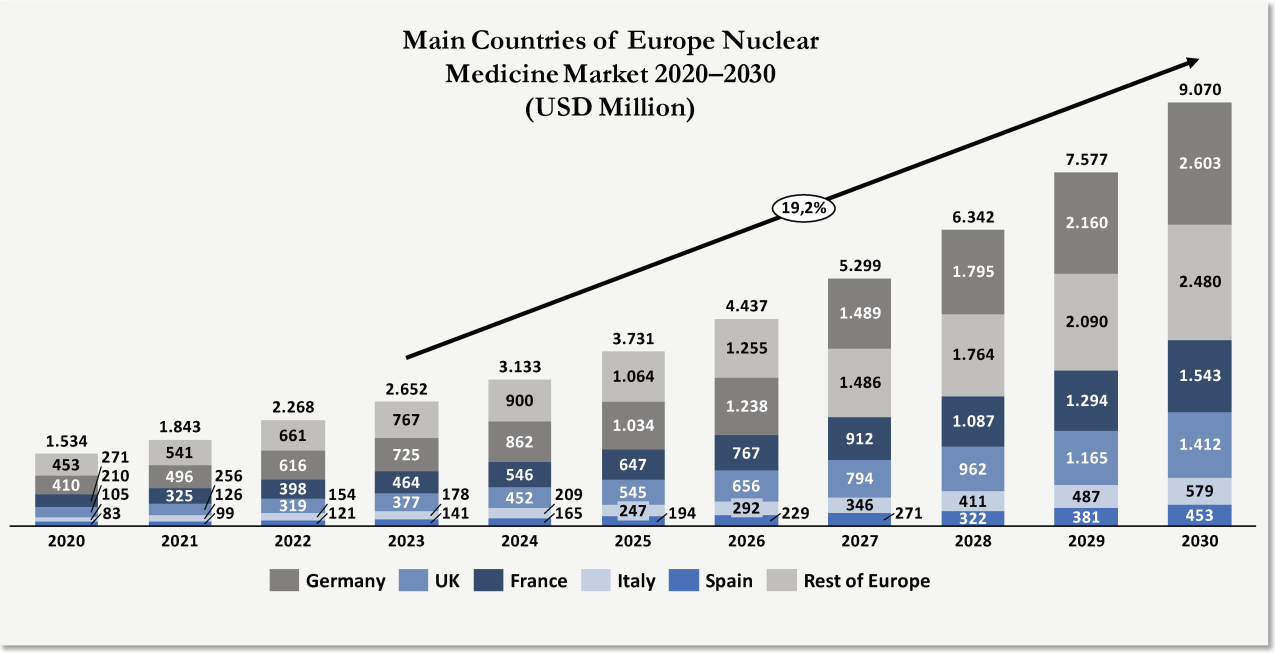

Figure 13: Main Countries Forecast for European Market of Nuclear Medicine. Source: SRF Market Research

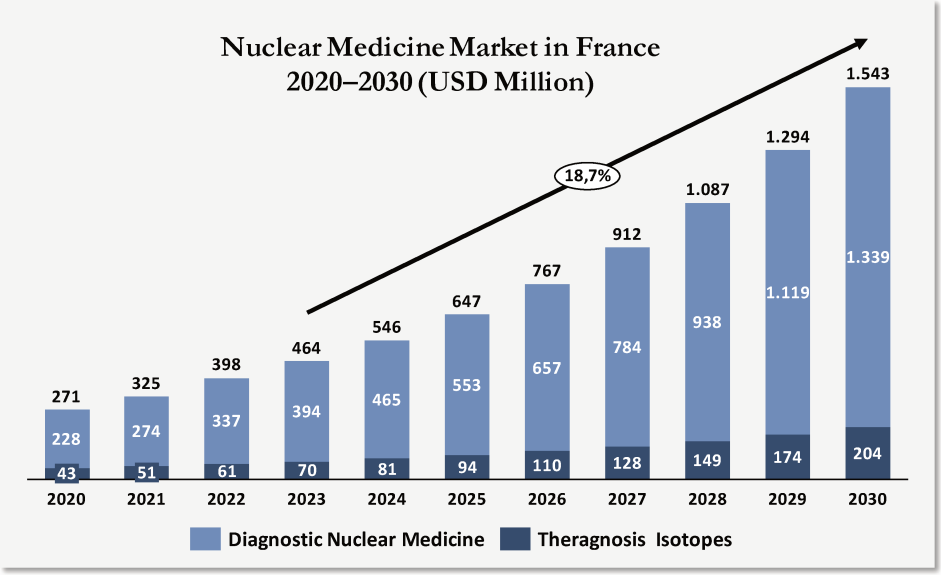

Figure 14: Nuclear Medicine Market in France 2020–2030. Source: SRF Market Research.

2.5.1.6 Competitive Landscape

As per Porter, M. (1998), a comprehensive structural and competitive strategy analysis offers invaluable insights into the competitive forces within an industry, enabling the development of a robust and effective competitive landscape for a certain company. By conducting a detailed examination of the industry's structural dynamics, this analysis empowers businesses to identify their strengths and weaknesses relative to the competitive forces at play. Subsequently, strategic decision-makers can leverage this knowledge to position their firm advantageously, either by reinforcing their defences against existing forces, influencing the balance of competition, or exploiting changes to gain a competitive edge. Ultimately, this strategic approach aids in predicting industry profitability and facilitates informed diversification decisions, ensuring a well-informed and competitive market presence.

There are various techniques available for conducting such analyses, one of which is the "Market Player Positioning Chart." This method involves creating a graphical representation that illustrates the relative positions of different companies or organizations within a specific market, based on specific criteria or attributes. The chart facilitates a visual comparison of market players' strengths and weaknesses, enabling the identification of their competitive positions and strategies in relation to one another. The "Market Player Positioning Chart" serves as a valuable analytical tool widely used in business and marketing to gain insights into the competitive landscape. It is important to note that this concept is a general tool in the realm of competitive analysis and strategic management and does not have a specific individual or organization attributed to its origin. The Figure 15 displays the outcome presented by Sky Research Forecast (2022) concerning the leading players in the nuclear medicine market. It provides a clear indication of the relative positions of each company and the strength of their portfolios.

However, merely applying a single technique does not achieve a comprehensive evaluation of the market and the relative importance of its participants. Therefore, market research studies commonly employ multiple methodologies to reach a more objective and precise conclusion that avoids interpretative biases. Consequently, Sky Research Forecast also introduces the Company Evaluation Matrix. This analytical tool is defined by Gordon, J. (2022) as method of analysis employed to assess a company's strategic position by considering both internal and external strengths and weaknesses. This approach bears resemblance to a SWOT (Strengths, Weaknesses, Opportunities, and Threats) analysis, but it distinguishes itself by assigning numerical weights to the factors under consideration.

The matrix comprises key components, starting with market attractiveness, which gauges the potential for profits and opportunities in the market. Factors considered include market size, growth rate, profitability, competitive intensity, and emerging trends. Next, the market growth potential evaluates a company's growth prospects within the given market, considering historical growth, projected future growth, market penetration, and diversification potential. Moreover, the matrix assesses a company's innovativeness by considering research and development

investment, intellectual property, and product differentiation. Visionary leadership is also appraised, examining the leadership track record, strategic vision, and execution capabilities. Additionally, the evaluation matrix investigates emerging companies to gauge their growth trajectory, innovation potential, and financial stability. Lastly, dynamic differentiators are examined, focusing on the company's unique value proposition, market positioning, and customer loyalty. By combining these factors into a comprehensive matrix, stakeholders gain valuable insights into each company's strengths and weaknesses. Armed with this evaluation, they can make well-informed business decisions, such as investments, collaborations, or strategic partnerships, to maximize potential returns and mitigate risks.

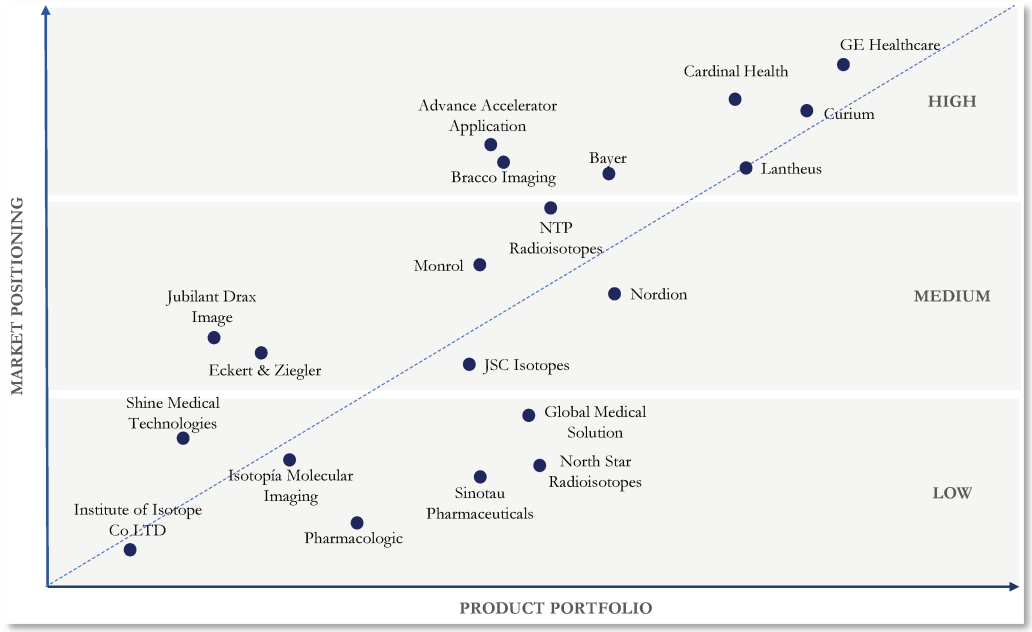

Figure 15: Market Player Positioning Chart 2021. Source: SRF Market Research.

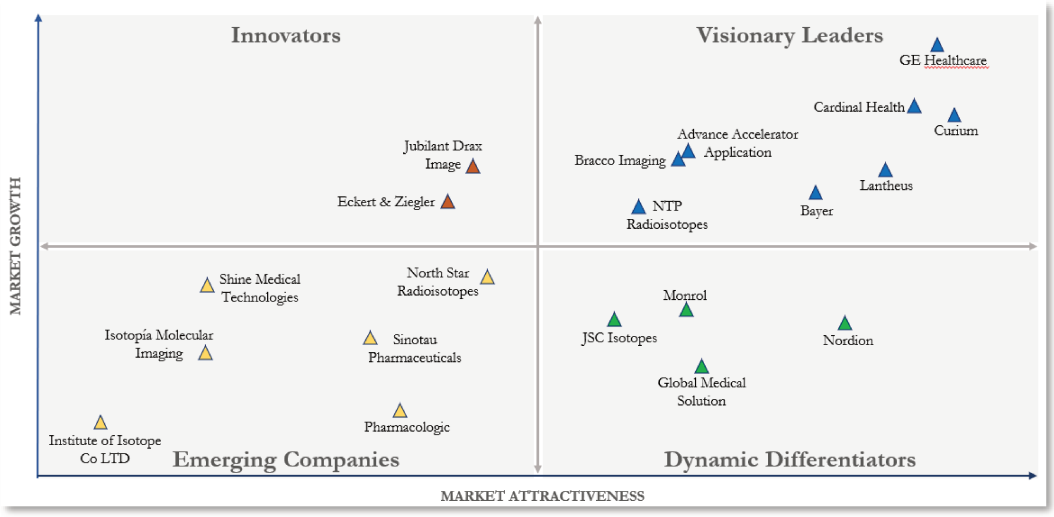

Figure 16: Company Evaluation Matrix 2021. Source: SRF Market Research.

Figure 16 presents the graphical representation of the matrix analysis for the European Market of Nuclear Medicine as of 2021. As a result of the Competitive Landscape analysis, it can be inferred that certain companies, such as GE Healthcare, Curium, Lantheus, and Cardinal Health, exhibit clear leadership. It is expected that this situation will persist in the coming years due to the robustness of their financial and commercial structures.

2.6 Theoretical Fundamentals

Titman and Martin (2016) state that when a company's success is being evaluated, the core focus is to asses how well it adds value for its shareholders and the overall value it creates. Companies that consistently generate value in the long run not only benefit their shareholders and employees but also keep customers satisfied and act responsibly. However, if a company ignores the importance of creating value, it can harm itself and even lead to negative outcomes for the whole society.

As per McKinsey, Koller, T., and Others (2010) the *"Value creation occurs when a company generates cash flows at rates of return that exceed the cost of capital, and accomplishing this goal usually requires that the company has a competitive advantage"*. These authors also explain that, earnings generation and value creation are connected in the long term, but they are not exactly the same thing. Value creation is all about how much money the company brings in (cash flows) and can be divided into two main parts: revenue growth and Return on Invested Capital (ROIC).

If a company's ROIC is higher than what it costs them to borrow money, then increasing growth will make the company more valuable overall. On the other hand, if the ROIC is lower than the borrowing cost, increasing growth will actually make the company less valuable. When the ROIC is the same as the borrowing cost, the company's growth doesn't change its overall value. So, it's important to focus on improving the ROIC because that will positively impact the company's value, regardless of how fast it's growing.

According to Titman and Martin (2016) the discussion revolves around the growth and expansion strategies employed by companies. They can achieve this by either acquiring essential assets or purchasing existing businesses. The primary objective is to generate greater returns than the initial investment. However, it is noted that significant investments may not always yield the expected outcomes. This is attributed to the complex nature of evaluating such decisions and the tendency of managers to rely on intuition and incomplete information. To improve decision-making and enhance the likelihood of successful investments, the authors advocate for the use of analytical tools and computer software. By adopting a more systematic approach, managers can make well-informed choices and potentially attain better results.

Titman and Martin (2016) emphasize the crucial significance of valuation within the realm of financial analysis. Irrespective of whether companies are navigating the assessment of internally generated investment endeavors or considering external acquisitions, valuation stands as an integral precursor. Furthermore, when corporate entities find themselves engrossed in deliberations encompassing share issuances or share repurchases, the entire evaluation procedure takes its initial steps through the valuation of the company's own shares.

This underscores a foundational truth: valuation permeates diverse facets of corporate decision-making. Its presence is instrumental in underpinning the process of gauging the latent value and worth held by investment openings and the company's own shares. In essence, valuation serves as a bedrock, facilitating informed assessments and strategic determinations across various dimensions of corporate operations.

Titman and Martin (2016) highlight five crucial factors to consider when valuing an investment, by addressing these key issues, companies can make informed decisions to maximize returns and minimize risks in their investment ventures:

- **Plausibility and Potential Gains: Does the "story" make sense?**
  This involves determining whether the investment strategy is logical and convincing to decision-makers. It requires assessing if the potential gains justify further investigation and if the firm has the necessary expertise or competitive advantage to benefit from the investment.
- **Assessing Risks: What potential risks are associated with embarking on this investment?**
  Evaluating the associated risks is paramount, even more so than focusing on positive outcomes. Factors like investing in emerging markets and political instability need careful consideration, and their impact on the rate of return must be analysed.
- **Financing Considerations: How can the investment be financed?**
  Securing attractive financing significantly influences an investment's value. Companies should explore various financing options, considering how the firm and project characteristics affect financing decisions and impact project valuation.

- **Impact of Earnings: What is the immediate impact of the investment on earnings in the short term?**
  The investment's effect on the firm's near-term earnings is crucial. Managers must be aware of how it might affect earnings per share, especially when compensation is tied to performance measures, and investors focus on earnings.
- **Inherent Flexibility: Does the investment have inherent flexibilities?**
  Investments with inherent flexibilities allow firms to adapt to changing circumstances. Opportunities like staged investments, follow-on possibilities, or synergies with existing products can enhance the investment's value and decision-making process.

Titman and Martin (2016) propose a standardized process to ensure the successful assessment of any investment, providing a framework for making informed decisions. The investment evaluation process is a structured approach that helps companies make informed decisions when considering investment opportunities. It consists of three phases: Phase I involves generating ideas and analysing potential investments, Phase II includes a managerial review to ensure objectivity and accuracy in the analysis, and Phase III culminates in a top-level executive decision and approval. By following this process, firms can thoroughly assess opportunities, align with strategic goals, and avoid biases, ultimately leading to better investment choices across various industries and firm sizes.

Phase I: Idea Generation and Analysis

During this initial stage, companies explore potential investment opportunities from various sources, such as their own employees, customers, or external organizations. The process involves three essential steps:

1. Strategic Assessment: Here, the underlying strategy or value proposition of the investment is carefully evaluated to ensure its viability. This screening process helps determine whether the investment shows enough promise to move on to further evaluation.
2. Investment Value Estimation: Quantitative analysis is conducted to assess whether the investment has the potential to create value for the firm's shareholders. Various valuation models, such as discounted cash flow and market-based multiples, are used in this analysis to evaluate different sources of value.
3. Investment Evaluation Report: The investment analysis team combines the strategic and quantitative analyses to prepare a comprehensive report summarizing the investment's strategy, estimated value (net present value), and the supporting information and assumptions.

Phase II: Managerial Review and Recommendation

In this phase, a separate group of employees, usually an investment review committee, conducts an independent review of the initial analysis to ensure its accuracy and objectivity. The activities in this stage mirror those of Phase I and include:

1. Assessing Strategic Assumptions: The review committee carefully evaluates the investment's value proposition and its alignment with the overall firm's strategy. Additionally, they consider various financing options and hedging opportunities to identify potential sources of value.
2. Thorough Examination of Estimations: In the second phase, the committee meticulously assesses the quantitative analysis conducted in Phase I. This scrutiny involves a deep dive into the foundational assumptions that underpin the analysis and a comprehensive evaluation of the valuation attributed to potential supplementary options encompassed within the proposal.
3. Crafting an Informed Counsel: Following the comprehensive review, the committee takes proactive steps to rectify any predisposed estimations. Armed with a well-balanced perspective, the committee then proceeds to formulate a robust and substantiated recommendation regarding the contemplated investment.

Phase III: Managerial Decision and Approval

The final phase places the ultimate responsibility for the investment decision on a top-level executive with the appropriate authority. This executive combines the firm's overall business strategy with the recommendation from the investment review committee to make the final decision. The choices may include outright acceptance or

rejection of the proposal or accepting it with certain revisions for immediate or future implementation. For significant investments, board approval is typically required.

In addition, Titman and Martin (2016) highlight that investment decision-making process can be influenced by biases, conflicts of interest, and information disparities. Project champions may be motivated to present proposals optimistically due to financial incentives, while internal review groups, such as the strategic planning committee, play a crucial role in scrutinizing and challenging these proposals to ensure unbiased analysis. A balanced emphasis on all three phases of project evaluation is essential to avoid potential pitfalls and make informed decisions.

2.6.1 Essential Components of a Financial Evaluation

The bibliography on feasibility assessment of investment alternatives suggests a wide range of methodologies available for this purpose. The choice of which methodology to apply depends on various factors such as the nature of the project, the industry it belongs to, the management's preferences, and the specific features of the methods themselves. Among the various techniques, the Discounted Cash Flow (DCF) analysis stands out as one of the most widely accepted and utilized by major companies worldwide. Despite its limitations, the DCF analysis remains popular, mainly due to its simplicity and ease of use. However, it is important to note that the DCF analysis involves making numerous assumptions, which may impact the accuracy of the evaluation. Nonetheless, its widespread adoption indicates its practical value in investment decision-making processes. In this section, the essential components involved in this analysis method are presented.

2.6.1.1 Discounted Cash Flow

As it is presented by Fernando (2023) *"Discounted cash flow (DCF) refers to a valuation method that estimates the value of an investment using its expected future cash flows. DCF analysis attempts to determine the value of an investment today, based on projections of how much money that investment will generate in the future"*. On the other hand, Titman and Martin (2016) state that *"The idea behind discounted cash flow (DCF) valuation analysis is simple: The value of an investment is determined by the magnitude and the timing of the cash flows it is expected to generate. The DCF valuation approach provides a method for assessing the value of these cash flows, and consequently it is a cornerstone of financial analysis"*.

The discounted cash flow (DCF) analysis is a technique that entails the evaluation of the present worth of anticipated forthcoming cash inflows, factoring in a discount rate. This method serves as a pivotal tool for investors to gauge whether the future cash flows projected for a specific investment or project surpass the initial outlay's value. The comparison between the calculated DCF figure and the current investment expenditure yields insights into the viability of the opportunity.

A favorable proposition manifests when the computed DCF value surpasses the current investment cost. This indicates that the investment stands to yield returns exceeding its initial outlay. Conversely, if the DCF value falls short, a more in-depth inquiry and analytical scrutiny may be warranted before any decisions are taken.

Conducting a DCF analysis entails several integral steps. Foremost, investors are tasked with estimating the forthcoming cash flows as well as determining the ultimate worth of the investment or assets under consideration. Moreover, a judicious selection of the appropriate discount rate holds paramount significance. This involves a meticulous assessment of elements like the project's inherent risk profile and the prevailing conditions of the capital market. These considerations collectively shape the accuracy and reliability of the DCF analysis results.

The DCF formula looks as follow:

$$DCF = \frac{CF_1}{(1+r)^1} + \frac{CF_2}{(1+r)^2} + \frac{CF_n}{(1+r)^n}$$

Where:

CF_1 = The cash flow of year one
CF_2 = The cash flow of year one

CF_n = The cash flow of year one
r = The discount rate

As it is stated by Fernando (2016), the DCF analysis is a valuable tool utilized by investors and companies to assess the viability of potential investments. It enables them to estimate the present value of expected future cash flows by applying a discount rate. DCF offers a versatile approach applicable to diverse investment projects with reasonably foreseeable cash flows. Moreover, it allows users to explore multiple scenarios, adjusting projections for various what-if situations. Despite its advantages, DCF does have limitations, primarily stemming from its reliance on estimates rather than precise figures. The accuracy of the discount rate and cash flow predictions becomes critical for meaningful results. Additionally, the uncertainty of future cash flows, influenced by numerous unpredictable factors, calls for careful consideration and supplementation of DCF with other valuation methods. Nonetheless, given its widespread use, DCF remains an essential tool for aiding decision-making in investment evaluations.

2.6.1.2 Cash Flow (CF)

In general, Cash flow refers to the net amount of cash and cash equivalents flowing into and out of a company. A positive cash flow indicates that the company's liquid assets are increasing, enabling it to manage debts, reinvest in its business, distribute dividends to shareholders, and cover expenses. This statement is crucial for evaluating a company's financial health and performance. (Murphy, 2021)

This is in line with the concept presented by Ross, Westerfield, and Jordan (2021) which state that the cash flow is a crucial financial metric that shows the difference between the amount of money received and the amount spent by a business. It is a vital piece of information that can be derived from financial statements and provides valuable insights into a company's financial performance. While there is a standard financial accounting statement called the statement of cash flows, which serves a different purpose, the concept of cash flow discussed here focuses on the actual amount of cash taken out of a business over a specific period. Understanding and calculating cash flow is essential for business owners and investors to gauge the financial health and profitability of a company.

2.6.1.3 Operating Cash Flow

Tuovila (2023) clearly define the Operating Cash Flow as *"a measure of the amount of cash generated by a company's normal business operations. Operating cash flow indicates whether a company can generate sufficient positive cash flow to maintain and grow its operations, otherwise, it may require external financing for capital expansion".*

This author states that the operating cash flow, also referred to as cash flow from operating activities, serves as a tangible reflection of the actual cash impact stemming from a company's net income. This outcome emanates directly from the core business operations of the enterprise. This particular facet of cash flow holds pivotal significance, marked by its position as the foremost component within the cash flow statement. Under the purview of Generally Accepted Accounting Principles (GAAP), two distinct methods are accepted for portraying operating cash flow.

Firstly, the indirect method entails a meticulous adjustment of net income to a cash basis. This recalibration is accomplished by accounting for alterations within non-cash accounts, including but not limited to, accounts receivable, accounts payable, and depreciation. This approach essentially aligns net income with a cash-oriented perspective, enabling a comprehensive understanding of the cash dynamics associated with the company's operational activities.

Conversely, the direct method assumes a more straightforward approach by directly recording all transactions on a cash basis. This comprehensive method provides a detailed overview of the actual cash inflows and outflows that transpired during the specified accounting period. Among the diverse array of transactions considered within the direct method are salaries disbursed to employees, payments made to vendors, revenue

collected from customers, interest and dividend income received, as well as payments made for income tax and interest obligations.

It's worth noting that while the direct method is more straightforward compared to the indirect method, it solely encompasses cash revenues and expenses. Notably, it excludes transactions relating to investments and financing activities. This elucidation is in accordance with insights from Tuovila (2023), highlighting the nuanced intricacies of the direct method's application.

"Operating cash flow is an important number because it tells us, on a very basic level, whether a firm's cash inflows from its business operations are sufficient to cover its everyday cash outflows. For this reason, a negative operating cash flow is often a sign of trouble" (Ross, Westerfield, and Jordan, 2021).

$$Operating\ Cash\ Flow = EBIT + Depreciation - Taxes$$

Where:
EBIT = Earnings Before Interest and Taxes

2.6.1.4 Capital Spending (CAPEX)

As per the definition presented by Ross, Westerfield, and Jordan (2021), *"Net capital spending is money spent on fixed assets less money received from the sale of fixed assets".*

Capital expenditures (CAPEX) refer to the financial resources allocated by a company for the acquisition, improvement, and upkeep of tangible assets, such as property, plants, buildings, technology, or equipment. Typically, CAPEX is directed towards embarking on new projects or ventures. These investments in fixed assets may encompass activities like roof repairs to extend its useful life, procuring new equipment, or constructing a new factory. Such financial outlays are strategically made by companies to expand the scale of their operations or secure potential economic advantages for the future (Fernando, 2023).

2.6.1.5 Net Working Capital

Net Working Capital (NWC) refers to the variance between a firm's current assets and current liabilities displayed on its balance sheet. It serves as a gauge of the company's liquidity and its capacity to fulfil short-term commitments while supporting the business operations. Ideally, the favourable situation entails possessing a surplus of current assets over current liabilities, resulting in a positive net working capital balance (Vipond, 2020).

Typically, a project necessitates the firm to allocate funds not only to acquire long-term assets but also to cover net working capital requirements. The project will often demand a reserve of cash to address any arising expenses. Moreover, an initial investment in inventories and accounts receivable is imperative to manage credit sales. While a portion of the financing for these requirements may come from amounts owed to suppliers (accounts payable), the remaining balance must be furnished by the firm, signifying the investment in net working capital (Ross, Westerfield, and Jordan, 2021).

An essential aspect of net working capital in capital budgeting is sometimes overlooked. As the project reaches its conclusion, inventories are sold, receivables are collected, bills are settled, and cash balances are drawn down. These activities release the net working capital originally invested, akin to a loan provided by the firm. The firm supplies working capital at the project's outset and recuperates it towards the project's culmination (Ross, Westerfield, and Jordan, 2021).

2.6.1.6 Cash Flow from Assets or Free Cash Flow

Ross, Westerfield, and Jordan (2021) define the Cash Flow from Assets as "*The total of cash flow to creditors and cash flow to stockholders, consisting of the following: operating cash flow, capital spending, and change in net working capital".*

The financial metric known as "cash flow from assets" evaluates the net cash generated or utilized by a company's fundamental business activities and its investments in capital assets, such as property, plant, and equipment. This

assessment aims to gauge the company's efficiency in using its resources to generate cash and provides insights into the overall effectiveness of its operations.

$$Cash\ Flow\ from\ Assets = Operating\ Cash\ Flow - CAPEX - Change\ in\ NWC$$

It is not uncommon for an expanding company to experience a cash flow deficit. A negative cash flow indicates that the firm obtained more funds through borrowing and stock sales than it distributed to creditors and stockholders throughout the year (Ross, Westerfield, and Jordan, 2021).

As it is highlighted by Ross, Westerfield, and Jordan (2021) the term Cash flow from assets, is commonly referred as Free Cash Flow, representing the cash that a company has available after meeting its working capital and fixed asset investment requirements. Those authors further explain that the term "free" does not imply that the cash is free to use, but rather that it is not tied up in essential operational needs. Instead, it can be potentially distributed to creditors and stockholders.

2.6.1.7 Cash Flow to Creditors and Stockholders

As outlined by Ross, Westerfield, and Jordan (2021), the cash flows directed towards creditors and stockholders serve as indicators of the total disbursements rendered to both creditors and proprietors during a specific fiscal period. The computation of cash flow to creditors involves the deduction of interest payments from the aggregate of net new borrowing. Conversely, the cash flow to stockholders is calculated by subtracting dividends disbursed from the total of net new equity raised. These assessments of cash flow provide insights into the financial interactions linking the company with its creditors and shareholders. They unveil the company's fiscal well-being and its capacity to fulfil financial commitments and distribute earnings to its owners.

2.6.1.8 Cash Flow Summary

To ensure a comprehensive understanding of the concepts presented, a concise and structured summary is provided below in a waterfall format:

+	*Sales*
-	*Cost of Goods*
=	***Gross Profit***
-	*Operating Expenses*
=	***Earnings before interest and taxes (EBIT)***
+	*Depreciation*
-	*Taxes*
=	***Operating Cash Flow***
-	*CAPEX*
-	*Change in Net Working Capital*
=	***Cash Flow from Assets or Free Cash Flow***

2.6.1.9 Relevant Cash Flow

Based on Titman and Martin (2016) statement, *"Only cash flows that are a direct result of the acceptance of an investment are relevant to the valuation of the project"*. These cash flows are known as incremental cash flows and include the additional cash generated by the investment itself and any indirect effects it may have on the firm's other activities. For instance, when evaluating the introduction of a new product, must be consider not only the projected revenues and costs of the new product but also its potential impact on the sales of existing ones. Additionally, it is crucial to avoid the mistake of considering sunk costs, which are expenses that have already been incurred and are not recoverable. The valuation should focus solely on the incremental revenues and costs resulting from the investment decision.

2.6.1.10 Net Present Value

Net Present Value (NPV) serves as a comprehensive metric for assessing the value of an investment, project, or business by considering all future cash flows, both positive and negative, discounted back to the present. NPV analysis, a widely used method in finance and project management, aids in determining the intrinsic worth of various ventures involving cash flow, such as capital projects, cost reduction programs, and new ventures (Edspira, 2013).

The NPV analysis takes into account the timing of each cash flow, recognizing the impact it can have on the present value of an investment. To address risk, discount rates are adjusted based on the level of risk associated with different investments relative to the risk-free rate, such as United States (US) Treasury bills.

Furthermore, NPV considers the time value of money due to inflation, interest rates, and opportunity costs, emphasizing the higher value of money received sooner. A positive NPV indicates value creation, while a negative NPV implies that the expected rate of return falls short of the required rate of return, resulting in a value-destroying investment. Though widely used, NPV analysis comes with challenges, including the need for making multiple assumptions, sensitivity to small changes in assumptions, and potential manipulation of outcomes. Additionally, it may not capture secondary impacts on other parts of a business and assumes a constant discount rate over time, making accurate risk adjustment challenging.

The Corporate Finance Institute (2023) presents the following formula for the NPV:

$$NPV = CF_0 + \left(\frac{CF_1}{(1+r)^1}\right) + \left(\frac{CF_2}{(1+r)^2}\right) + \left(\frac{CF_3}{(1+r)^3}\right) - X_0$$

Where:

CF_0 = Cash Flow year 0
CF_1 = Cash Flow year 1
CF_2 = Cash Flow year 2
CF_2 = Cash Flow year 3
r = Discount Rate
X_0= Cash outflow year 0 (CAPEX)

Ross, Westerfield, and Jordan (2021) highlight a widely accepted rule for NPV *"An investment should be accepted if the net present value is positive and rejected if it is negative".*

2.6.1.11 Discount Rate

According to Hayes (2023), in the context of DCF analysis, *"the discount rate the discount rate refers to the interest rate used to determine the present value".*

The discount rate, a risk-adjusted factor frequently employed for determining the present value of forthcoming cash flows (Ross, Westerfield, Jordan, 2010), holds significant importance in assessing a company's value. It is imperative that the discount rate adequately accommodates the prevailing risk level. Two prominent approaches for deriving an appropriate discount rate encompass the Required Rate of Return (RRR) and the Weighted Average Cost of Capital (WACC).

2.6.1.12 Required Rate of Return (RRR)

The concept introduced by Palmer (2022) elucidates the minimal anticipated profit that an investor pursues when assuming the inherent risk linked with an investment in stocks or other securities. This concept is recognized as the required rate of return (RRR). RRR is also harnessed to evaluate the potential profitability of a venture in relation to its financing cost. It functions as an indicator, gauging the degree of risk entailed in committing to a

particular investment or project. A heightened return signifies a heightened risk, while a reduced return implies diminished risk.

Within the realm of corporate finance, RRR is extensively employed in investment appraisal, facilitating the computation of potential Return on Investment (ROI). It's important to bear in mind, however, that RRR doesn't factor in inflation. Additionally, it's noteworthy that the requisite rate of return can vary among investors, contingent on their individual levels of risk tolerance.

2.6.1.12 Weighted Average Cost of Capital (WACC)

WACC represents the average cost of capital for a firm, encompassing the costs incurred from both internal and external sources. It can be explained as the weighted average of the cost of debt, which is the interest rate paid to creditors for borrowing, and the cost of equity, which reflects the expected return demanded by shareholders when investing in the company.

$$WACC = I_{(L)}.\left(\frac{L}{E+L}\right).R_{(E)}.\left(\frac{E}{E+L}\right)$$

Where:

L = Total Current Liabilities.

$I_{(L)}$ = Interest paid to creditors.

E = Total Equity.

$R_{(E)}$ = Shareholders Expected Return.

$I_{(L)} . L/(E+L)$ = Cost of Debt

$R_{(E)} . E/(E+L)$ = Cost of Equity

The Cost of Equity is typically estimated using the Capital Assets Pricing Model (CAPM), which provides a precise prediction of the relationship between an asset's risk and its expected return (Bodie-Kane-Marcus, 2010). CAPM factors in the market's overall risk, the risk-free rate of return, and the firm's systematic risk compared to the market risk. This model yields a benchmark rate that can be employed for company valuation.

$$ER_i = R_f + \beta_i.(ER_m - R_f)$$

Where:

ER_i = expected return of investment

R_f = Risk free rate

B_i = Beta of the investment

$(ER_m - R_f)$ = market risk premium

The Capital Asset Pricing Model (CAPM) delineates the relationship between systematic risk, encompassing broader investment hazards, and the projected return for assets, specifically stocks. CAPM represents a financial framework that constructs a linear association connecting the anticipated return on an investment and its associated risk. Rooted in the interplay between an asset's beta, the risk-free rate (typically symbolized by the Treasury bill rate), and the equity risk premium, which signifies the expected market return minus the risk-free rate (Kenton, 2023).

2.6.1.13 Horizon of the Analysis:

The investment horizon refers to the duration during which an investor intends to maintain an investment position before divesting or liquidating it. It holds paramount importance in the process of making investment decisions, as it exerts an impact on the level of risk and potential returns that an investor can anticipate. The investment horizon is subject to variation based on an individual's financial objectives, risk tolerance, and the specific characteristics of the investment under consideration. Generally, short-term investment horizons span from a few months to a year, mid-term horizons encompass a period of one to five years, while long-term horizons extend beyond five years. The selection of the investment horizon significantly influences the appropriateness of various investment approaches and the likelihood of achieving financial goals, (Titman and Martin, 2016).

The timeframe chosen for the Discounted Cash Flow method significantly influences the valuation of a company or a project. Depending on the valuation objectives, different timeframes may be utilized. Generally, short-term is less than a year, mid-term ranges from one to five years, and long-term is beyond five years. These widely accepted timeframes serve as valuable references during the valuation process.

2.6.1.14 Internal Rate of Return (IRR):

Ross, Westerfield, and Jordan (2021) define the IRR as *"The discount rate that makes the NPV of an investment zero"*. This rate serves as a valuable metric for assessing an investment's suitability by providing insights into the project's profitability. The IRR is evaluated using certain key criteria:

- If the IRR exceeds the discount rate: When the IRR surpasses the discount rate applied to future cash flows, it indicates that the project yields a rate of return higher than what's required to attract investors. This typically signals the project's financial attractiveness.
- Comparison with the required rate of return: If the IRR is greater than the investors' required rate of return or the company's cost of capital, the project is likely to be deemed profitable and feasible. Conversely, if the IRR falls below the required rate of return, the project may not be financially attractive or suitable for investment.
- IRR comparison between investments: The IRR allows for a comparison of various projects or investment options. By calculating the IRR for each alternative and considering additional factors and associated risks, the most promising investment can be selected.
- Consideration of risk: It's important to note that the IRR does not account for the investment's risk. Even if two projects have the same IRR, they could have varying levels of risk. Therefore, it's essential to assess other factors such as the time horizon, projected cash flows, financial risks, market stability, and other pertinent aspects.

In summary, a higher IRR relative to the discount rate or the required rate of return indicates greater financial appeal and convenience for the investment. Nonetheless, it's crucial to complement the IRR analysis with other financial and non-financial criteria to make well-informed decisions regarding investment suitability.

2.7 Conclusion

The comprehensive literature review conducted in this Master Thesis has provided valuable insights into the production of radiotracers and the advancements ongoing in the market. The analysis of the market research indicates a promising future for nuclear medicine, with continuous improvements driving its growth. Moreover, considering the existing regulations, which do not impede the utilization of air transportation for nuclear medicine, the context is firmly established for the viability of this mode of transport.

Furthermore, the research has unveiled real-world examples of companies that are currently leveraging air transportation as their primary distribution channel for nuclear medicine. This fact highlights the feasibility and unblocking potential of adopting air transport in the field of nuclear medicine.

As a result of this literature review, a solid foundation has been laid to support the viability and practicality of utilizing air transportation in the distribution of nuclear medicine. The existing market trends, coupled with the absence of regulatory hindrances, offer a promising outlook for the successful implementation of air transportation strategies in this domain. This conclusion covers the way for further investigation and analysis in the subsequent sections of this Master Thesis, contributing to a deeper understanding of the potential benefits and implications of adopting air transport for nuclear medicine distribution.

3. Footprint Expansion: Construction of Additional Production Plants

3.1 Sizing the Potential Market and Investment Scope

As developed in section 1.7, the methodology or strategy for testing the thesis statement consisted of the financial feasibility evaluation of two alternative strategies for a medium-sized company belonging to the nuclear medicine industry. Specifically, the possibility of expanding the company's market to the west of France was studied.

The main objective in the initial stage was to carry out an estimation or sizing of the potential business in the west of France, for which the professional and technical support of an expert in the company's commercial field (SME Commercial Team, personal communication, 2023) was indispensable. The evaluation focused on identifying healthcare centers in the western region of France that currently possess PET diagnostic devices.

Consequently, a total of 77 institutions offering nuclear medicine diagnostic services were identified. Among these, 49% were private companies, 35% were public institutions, and 16% were mixed entities with agreements between public and private institutions. This holds significance as the mode of commercialization varies according to the type of entity involved. Public and certain mixed entities follow a public tender process, while private and specific mixed entities employ a direct sales modality, affording them considerable flexibility in their marketing approach.

To effectively segment potential clients, the company's subject matter experts (SMEs, personal communication, 2023) utilizes specific parameters such as the nature of diagnostic equipment, bed count, staff strength, and laboratory facilities. This enabled them to assess the potential clients' capacity for utilizing annual doses. The established categories spanned a range of 1,500 to 10,000 doses per year. Notably, among the identified potential clients, a significant majority, approximately 62%, demonstrated an annual dose requirement of less than 3,000 doses. In contrast, a mere 9% of the potential clients indicated a need exceeding 6,000 doses annually.

Furthermore, it was observed that the majority of healthcare centers in the western region of France (74%) were equipped with a single PET scanner, while the remaining 22% had 2 and 4% (one center) has 3 PET scanners.

Once potential clients were identified, the focus shifted towards strategically determining ideal locations for the new production plants. Aligned with the technical SMEs (personal communication, 2023) within the company, the recognition arose that, due to the considerable number of potential client centers, it was essential to establish a minimum of two additional plants, hereinafter referred as +2Sites Scenario. This multipronged approach was aimed at ensuring comprehensive service coverage. The rationale behind this decision rested on the understanding that a single supplementary plant would fall short in efficiently accommodating all these centers.

Moreover, placing sole reliance on a single plant could pose a significant risk to operations. Instances of technical shutdowns or exceptional risk scenarios could arise, jeopardizing the company's ability to maintain operations seamlessly. This vulnerability arises from the lack of requisite backup support that is indispensable for skillfully navigating such challenges and safeguarding the continuity of operations.

Having defined potential new plant locations, the evaluation shifted to determining distances to the identified centers. This assessment factored in the practical feasibility of reaching these centers while upholding the requisite quality standards for successful diagnostic procedures. The strategic placement of the new plant sites was meticulously orchestrated to guarantee accessibility to all centers within the western region of France.

The comprehensive analysis revealed that by adopting the suggested locations, a substantial 50.6% of the prospective clients would fall within a 2-hour and 30-minute travel radius. This outcome implied a notably low operational risk. In a similar vein, 27.3% of clients would be reachable within 2 hours and 30 minutes to 3 hours and 30 minutes, signifying a moderate operational risk level. Finally, 22.1% of clients would be situated beyond the 3-hour and 30-minute mark, still adhering to acceptable technical thresholds. This situation would pose a relatively higher but manageable operational risk, mitigated by other factors like the capacity to regulate radioactivity concentrations per vial.

With the operational feasibility of accessing the healthcare centers validated, the assessment led to an estimation of the total market size within the western region of France. This estimation pegged the annual demand at 236,500 doses, based on the predefined categorization of dose requirements. However, a pertinent revelation came to light: 12 healthcare centers were already established clients of the company. To streamline operations and eliminate redundancy, it was deemed more efficient to serve these centers through the new production plants.

To maintain accuracy and prevent distortion of the results, the calculated market size was adjusted to 193,500 doses annually. This correction accounted for a deduction of 43,000 doses attributed to the 12 existing clients. This adjustment was implemented to mitigate the concept of erosion or cannibalization, ensuring a precise representation of the potential market.

The estimated dosage figures provide an assessment of the total market demand within the western region of France. It's important to recognize that the market isn't devoid of competition, as other companies are already catering to these healthcare centers. Considering the company's introduction into this novel territory, an assumption is made that the company possesses the potential to secure a market share of no less than 45%. This optimistic projection is substantiated by the commercial Subject Matter Expertise (SME) derived from the company's accumulated competitive advantages in terms of reliability, efficiency, and quality, honed over time.

Nonetheless, it's crucial to acknowledge that attaining a 45% market share won't be instantaneous. The envisioned achievement requires a gradual process, with the anticipated capture spanning a minimum of 5 years starting from the operational commencement of the new production plants. The journey would begin with a target market share proportion of 40%, with the ultimate goal of reaching the desired 45% share. This considered timeframe accounts for the organic progression and growth trajectory that aligns with market dynamics and the time needed for the company's influence to permeate the region effectively.

According to the previous chapter, the nuclear medicine market is expected to experience substantial growth in the coming years. However, a highly conservative viewpoint was adopted for the dose estimation. In other words, for the purposes of this analysis, it is assumed that the estimated market will remain stable and not experience any growth in the upcoming years. This conservative approach is employed to prevent distortions in the analysis that might arise from overly optimistic projections, given the uncertainty surrounding whether the currently active centers will invest in expanding their capacity. In conclusion, it is assumed that the 193,500 doses represent the maximum production quantities, although in reality, the market holds clear potential for growth, presenting a significant opportunity for the company. Figure 17 summarizes the main characteristics of the market defined in western France.

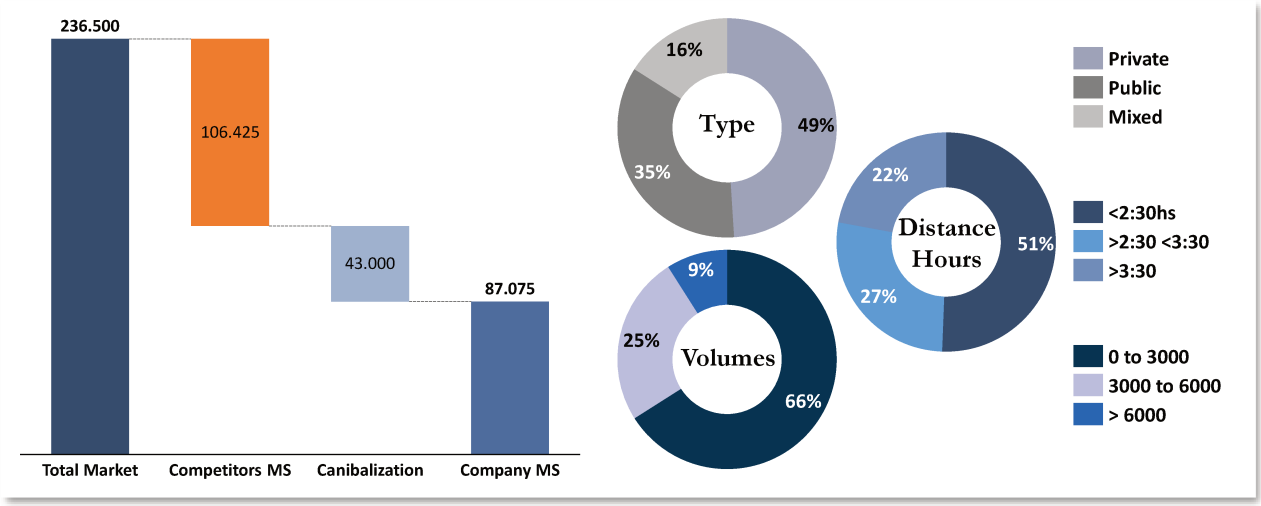

Figure 17: Market sizing of radiopharmaceuticals for PET diagnostics in western France.

3.2 Investment Project Design and Analysis Horizon

In the preceding section, was established the target market size and, based on the geographical dispersion of potential clients, concluded that the simultaneous construction of two production plants is imperative. An

intriguing question naturally emerges: Could it be viable to develop one factory initially and subsequently embark on constructing the second one? This approach might appear to simplify the complexity associated with managing two concurrent investment projects.

However, the insights provided by the company's technical SMEs (personal communication, 2023) paint a different picture. Opting for a single plant construction path would imperil the very success of the expansion strategy. This stems from the fact that the company's footprint in the western region of France is nonexistent (with the exception of the 12 institutions currently served by existing sites, which are maintained at the maximum feasible distance).

The rationale for advocating the establishment of two plants lies in more than just addressing the requirements of new clients. It's underscored by the strategic foresight that having dual plants in the western region of France offers distinct advantages. Notably, these plants would not only fulfill the needs of the expanding customer base but also function as mutually supportive backups in instances of routine technical shutdowns or other operational disruptions. This redundancy provides a robust safeguard, minimizing downtime and upholding operational continuity for the diagnostic procedures crucial to healthcare services.

According to technical and commercial SMEs insights (personal communication, 2023), the completion of an investment of this magnitude ordinarily spans a duration ranging from 2 to 3 years, commencing from the outset of the project's design phase. This timeframe encompasses the orchestration of building construction and the installation of essential equipment. Subsequent to these critical steps, a rigorous process of validation and inspection is embarked upon, overseen by regulatory authorities upon the culmination of the project.

In the context of commercial operations, the process of normalization comes into play. To elaborate, achieving a stable and anticipated level of income from a plant typically materializes around 5 years subsequent to its activation. In simpler terms, it takes approximately 5 years for a plant to attain a consistent level of financial output that aligns with expectations.

This journey towards operational stability extends further. A productive plant attains its anticipated production capacity only after around 8 years from the inception of the initial design project. This timespan underscores the intricate interplay of various factors, including project initiation, development, regulatory compliance, and the gradual maturation of processes.

Thus, it is evident that due to the 8-year timeframe required for the construction and stabilization of a radio-pharmaceutical production plant, feasibility analyses for such investment projects are generally conducted with a significantly longer time horizon compared to other industries. With this in mind, the analysis horizon considered in this thesis is set at 15 years, as a shorter period may lead to distorted results or interpretations.

3.2.1 Core CAPEX Projection

The analysis aims to build up two productive plants in accordance with the new GMP regulations and the standards defined by the International Atomic Energy Agency. The projected capacity assumes that the plants must have a similar capability to the latest plant built by the company in France. The goal is to develop sites with an annual capacity of 1440 lots or batches, with a maximum variable efficiency of 100 doses per lot. The capacity of lots is determined by work shifts and pragmatic time limitations, whereas the efficiency of each lot may vary, with demand being the primary driver for lot utilization. However, conservatively, it is estimated that a maximum of 100 units can be extracted from each lot.

Table 2 presents a breakdown of the required capital for the construction of the two production plants and its temporal allocation by periods. The analysis assumes that the operational launch of the two plants would occur 2.5 years after the project's start.

It is worth noting that investment projects of this nature are made with a very long-term perspective, and the lifespan of a cyclotron or a production line can be extended simply by replacing certain technologies. As mentioned earlier and validated by the Subject Matter Experts, the fundamental operating technology of a cyclotron has

remained unchanged for the past six decades, with only minor automation changes appearing that have not significantly impacted the performance of these devices. Therefore, the capabilities of a cyclotron can last for over 25 years as long as proper maintenance tasks and investments are carried out.

Items	CAPEX Amount	Years		
		0	1	2
Project Management	3,000,000	3,000,000		
Land Acquisition	2,400,000	2,400,000		
Cyclotron	3,600,000	3,600,000		
Production Lines	12,000,000		7,200,000	4,800,000
General Infrastructure	3,400,000		2,040,000	1,360,000
Quality Control	2,200,000		1,320,000	880,000
Radioprotection	1,000,000		600,000	400,000
IT and General Furniture	1,000,000		600,000	400,000
Total	**28,600,000**	**9,000,000**	**11,760,000**	**7,840,000**

Table 2: Capital Expenditure Projection and Time Allocation, for 2 production Sites.

However, for the purposes of this analysis, it is considered that the plant will cease to be operational after the 15th year. When a plant dedicated to the production of radioactive products stops functioning, as per current regulation, all facilities and equipment must be decommissioned, which entails a significant expenditure of money. Based on technical SMEs (Personal communication, 2023) the decommissioning cost of a site is currently estimated to be 3 million Euros, and this would rise to 4.7 million Euros in the 16th year, considering the accumulated inflation over all the analysed periods.

Indeed, it is possible that only the land and certain parts of the building infrastructure could be sold at the end of the project, allowing for the recovery of some value, given a significant portion of the investment would need to be decommissioned. While the decommissioning cost is not technically a capital investment, it is an expenditure that should be considered from the outset, and as such, it has been included in the projections of this thesis analysis.

3.2.2 CAPEX for Maintenance

In the industry under analysis, regular investments are made to preserve and ensure the proper performance of a plant. Technically, these expenditures could be considered as costs impacting operational expenses. However, these outlays are intended to maintain technical capabilities, and an average service life of 5 years is applied.

Based on inputs provided by financial SMEs (Personal communication, 2023), investments in maintenance of production capacity are estimated at approximately 0.4 million euros annually. Since the two plants assumed in the analysis would be built from scratch, maintenance investments only commence from year 5, starting from the operational launch of the plant in the 2.5-year period.

3.3 Revenue Evaluation: Topline Calculation

The previous section initiates by outlining the process used to estimate the potential demand for radiopharmaceutical doses in the western region of the French market. The total market was initially defined, and then specific filters were applied to identify the relevant segment. Within the total market, 12 institutions are already supplied by the company through existing sites, resulting in no incremental revenue potential for the company. Subsequently, the potential market is determined, and it is assumed that the company could capture a 45% market share with 2 additional sites, accounting for the presence of other competitors. Furthermore, it is acknowledged that sales will take approximately 5 years to reach their maximum or normal level.

The calculated doses representing the potential demand for the company in the western region of France are based on the total doses required, without specific identification of brands or products. In essence, the estimation of these doses is derived from the normal capacity of absorption that potential customers can accommodate. Consequently, to estimate revenues, a thorough analysis involving the weighting and allocation of doses by brand or molecule was undertaken.

To determine a reasonable breakdown and avoid additional complexity in alignment with SMEs insights (personal communication, 2023), the average market share of the main brands over the last 3 years was taken into consideration. As a result, the distribution of total doses for the first year is estimated to be 87% for FDG, 2% for FCH, 4% for FDopa, and 8% for FPSMA.

However, the relative market shares of each brand were anticipated to change over time due to the specific indications for which the considered brands are prescribed. As discussed in the literature review chapter, the FPSMA radiotracer, as of the date of this thesis, is a new molecule with specific indications, particularly for Prostate Cancer, which significantly impacts society due to its high prevalence. Hence, it is expected that FPSMA will gradually gain a larger market share in the coming years at the expense of other molecules such as FCH and FDG.

It is crucial to clarify that for the purposes of this analysis, it is assumed that neither potential customers nor the company will expand their capacity beyond the two new plants under consideration. Thus, the analysis presupposes that sales to these potential customers will be limited to the number of doses they can accommodate.

Each diagnostic procedure involving radiopharmaceuticals can vary based on the specific needs of each patient and the requirements indicated by attending physicians. Consequently, each patient receives different dosages according to specific parameters, which impacts the billing and revenue accordingly. Additionally, there are price variations depending on whether the client is treated in a public, private, or mixed institution. To mitigate the complexity arising from these factors and establish a coherent pricing structure for each brand involved in the analysis, equivalent dose-based prices were calculated using billing data and quantities from the last completed commercial exercise.

Regarding prices, it is essential to understand the distinct dynamics of this market, as unlike other industries, radiopharmaceutical prices tend to decline over time. According to Commercial SMEs (personal communication, 2023), this phenomenon is attributed to various factors, including the introduction of new molecules, the entry of new competitors, advancements in technology that enhance efficiency, commercial agreements between firms, and the emergence of new public tenders. In light of this reality, the analysis adopts the assumption that prices will decrease at a rate of 2% every 3 years, reflecting a reasonably accurate representation of market dynamics, even in the absence of a clearly defined pattern.

Figure 18 offers a comprehensive overview of the estimated incremental revenues for the +2Sites Scenario over the next 15 years, taking into account all the aforementioned assumptions. It is imperative to highlight that the declining prices of radiopharmaceuticals impact the projected revenues, resulting in a slight reduction. Additionally, the assumption that the target market will not experience significant growth within the considered time horizon further contributes to the conservative revenue estimates.

Additionally, it is fair to highlight that, due to the confidentiality and limited disclosure agreements signed by the author of this thesis, the prices of the brands considered in the analysis, as well as any other data that could allow their inference, are not presented.

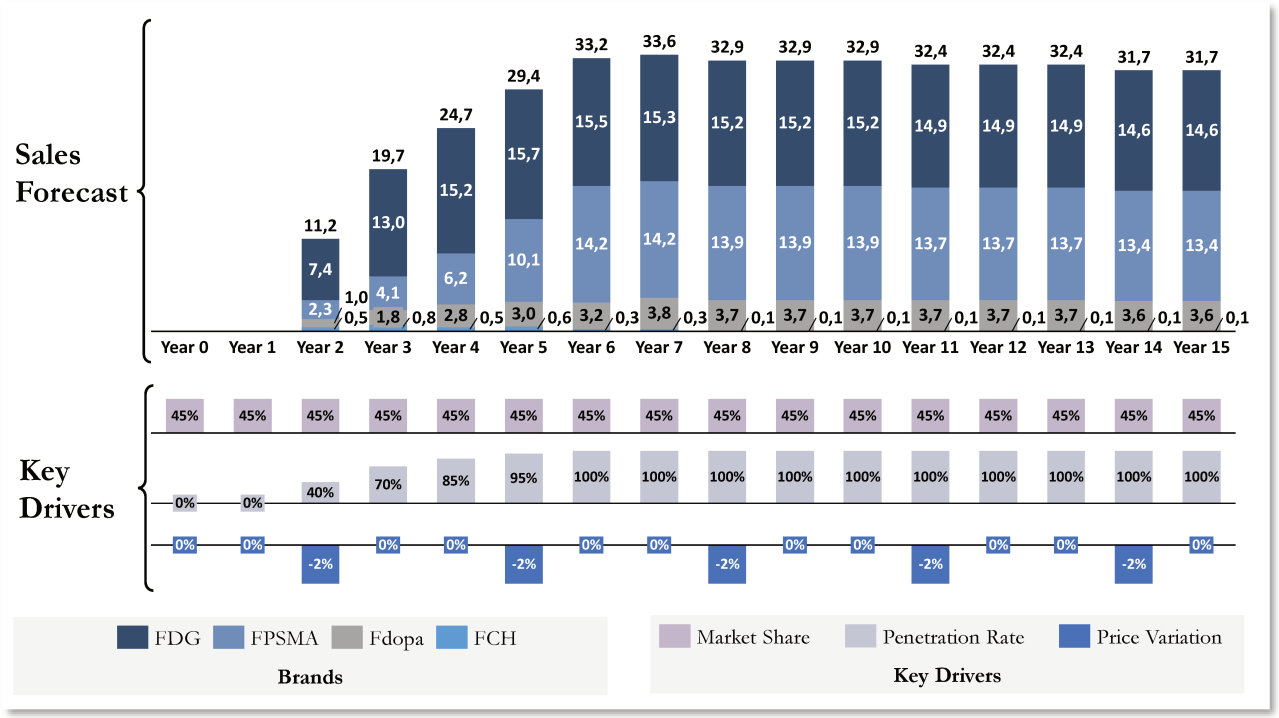

Figure 18: Overview of Projected incremental revenues for +2Sites Scenario.

3.4 Production Costs Analysis

This section provides a comprehensive examination of the costs associated with the production of diagnostic radiopharmaceuticals. It sheds light on the specific dynamics of each cost element and their impact on evaluating the feasibility of investing in the +2Sites Scenario. However, it is fair to mention in advance that most of the assumptions described in this section are also applicable for the scenario considering air transportation.

Following an in-depth analysis of the company's cost structure, the costs were classified into four categories: Materials Cost, Personnel Cost, Transportation or Distribution Cost, and a broader category termed Other Production Costs, which is used for analysis purposes.

3.4.1 Batch Utilization Efficiency: Yield

Before delving into the evaluation of each main cost category, it is crucial to introduce a concept previously mentioned but not given due significance: "batch utilization efficiency" or, as referred to in the industry, "Yield."

In simple terms, "batch utilization efficiency" or "Yield" refers to the number of doses that can be extracted from a production batch, being a this the industrial process through which a dose is obtained. While this explanation may appear straightforward and conceptually assimilated through analogy, its application can become highly intricate when considering the operations of a radiopharmaceutical manufacturing facility. It is important to highlight that production batches are carried out individually for each brand. In other words, two different brands cannot be produced simultaneously in the same batch.

$$Batch\ utilization\ efficiency = Yield = \frac{Number\ of\ Doses}{Number\ of\ Batches}$$

According to technical SMEs (personal communication, 2023) a notable characteristic of a batch or lot is its nearly fixed cost structure, meaning that producing 1 dose or 100 doses incurs virtually the same expenses. The cost variation between producing a small number of doses and a large volume is negligible, as the primary focus in this industry lies in introducing or labeling nuclear energy into another chemical molecule, eventually being placed in a

vial. Consequently, the concentration of activity in each vial does not significantly impact production costs. For instance, a vial intended for patient A with 10 times more radiation than the one intended for patient B does not result in cost differentiation.

In theory, if a radiopharmaceutical production plant had an adequate number of beds and scanners in close proximity, efficient logistics and distribution, and sufficient medical professionals available, the facility could perform hundreds of diagnostic procedures simultaneously with a single production batch.

Hence, the primary driver for production schedules is demand and planning. Batches or lots are produced based on patient requirements, considering the natural limitations of radioactive isotopes. For example, if there are 10 patients to be injected between 8 a.m. and 12 p.m., a batch will be produced in the morning. Conversely, if there are only 2 patients scheduled for 5 p.m. in the afternoon, a separate batch must be produced for them, as the radioactive decay prevents using the remaining production from the earlier batch.

Like any industrial or standardized process, a batch has a specific technical time. Although certain stages of the process can overlap, a radiopharmaceutical manufacturing facility can ultimately produce a limited number of batches per year, depending on the installed capacity and available resources. However, this capacity can be expanded through additional investments or resources allocation.

In summary, the number of batches a facility produces hinges on the efficiency of the planning team and customer service. Efficient scheduling leads to better utilization of each batch, resulting in lower costs.

While it was emphasized the variability and potential for improvement in batch utilization efficiency, it is common for companies in this field to follow standardized patterns. Work teams tend to develop standardized methods to harmonize processes, and the list of frequently served clients remains stable, with low-volatility work systems. Consequently, for the analysis presented, the assumption is that the company maintains static or flat efficiency levels for all periods considered, based on the yields from the previous year.

Table 3 below presents the batch utilization levels disaggregated by product brand. These are the average yields obtained from the last completed annual exercise. It is important to note that throughout the year, the volumes extracted from each batch may vary according to daily planning, making it an ex-post reference variable that provides insights into the efficiency of a specific plant's operations and allows for cost estimation. Additionally, the yield may differ from one plant to another, even if they belong to the same company, as it depends on the demand in the region where the manufacturing facility is located.

	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10	Year 11	Year 12	Year 13	Year 14	Year 15
FDG	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60	60
FCH	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17	17
Fdopa	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14	14
FPSMA	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20

Table 3: Yield Projections for +2Sites Scenario.

In conclusion, the "yield" variable holds a pivotal significance when projecting costs for a radiopharmaceutical manufacturing company. The efficiency of batch utilization directly influences the overall cost structure, making it a critical factor in determining the company's financial health and profitability. As highlighted, the average yields obtained from the last completed annual exercise serve as reference points to estimate costs, considering that daily planning may lead to variations in the volumes extracted from each batch throughout the year.

The careful consideration of yield assumptions is of utmost importance for the accurate projection of costs in a radiopharmaceutical manufacturing setting. Overly optimistic yield assumptions may lead to unrealistic cost estimates, potentially obscuring the true financial picture and creating unrealistic expectations. Conversely, adopting excessively conservative yield assumptions may adversely impact the gross margin and hinder the company's financial performance.

3.4.2 Inflation

During the time of writing this thesis, the European economic landscape was immersed in an inflationary period due to prevailing global circumstances. Considering the impact of inflation was crucial to ensure the projections and analysis maintained a reasonable level of accuracy.

The impact of inflation on production costs is a critical factor that can significantly influence the financial performance of a company engaged in manufacturing or production activities. Inflation refers to the general increase in prices of goods and services in an economy over time, resulting in the erosion of purchasing power. When inflation occurs, the cost of living and operating expenses tend to rise, affecting both households and businesses.

Indeed, it is crucial to highlight that, in terms of prices, it has been previously mentioned that the assumption is for prices to trend downwards due to the factors explained. However, in this section, the introduction of an inflation assumption would further deteriorate the financial health of the company under analysis.

The interplay between declining prices and the impact of inflation introduces an additional layer of complexity to the financial projections. The downward price trend exerts pressure on the company's revenue, reducing the income generated from each unit sold. On the other hand, inflation increases the costs associated with production, labour, and other operational expenses. This combination can potentially lead to a reduction in the company's gross margin and overall profitability.

Therefore, beyond the analysis given this is a real issue, the company should consider potential strategies to mitigate the impact of inflation and counteract the effects of declining prices. This may involve optimizing production efficiency, exploring cost-saving measures, diversifying revenue streams, and implementing pricing strategies that adapt to market dynamics while considering the inflationary environment.

For the analysis, the assumption regarding the inflation variable was based on projections from the Bank of France (2023). According to this financial institution, inflation is expected to hover around 4% annually and subsequently stabilize at 3%.
It is essential to clarify that the same inflation assumption has been uniformly applied to all cost elements, including both production-related expenses and general operational expenses of the company.

3.4.3 Materials Costs:

Like in other industries, this category encompasses all raw materials used during the production process. These materials are consumables with variable characteristics. However, the variability of this cost element is not determined by the final units or doses but rather by the number of batches produced.

Hence, to project the costs of materials per batch, the total costs incurred in the last completed commercial exercise were divided by the quantity of batches produced during the same period, with due consideration of the projected inflation for each period.

$$\boldsymbol{Material\ Cost_{(Year\ A+1)}} = \frac{Total\ Cost\ of\ Materials_{(Year\ A)}}{\#Total\ Batches_{(Year\ A)}} \times \#Total\ Batches_{(Year\ A+1)} \times (1 + Inflation\ Rate)$$

The methodology of dividing the total costs incurred in the last completed commercial exercise by the quantity of batches produced in the same period allows obtaining a reasonable estimate of the unit costs per batch. By considering the effect of inflation on each cost element, a more precise and realistic projection is achieved.

3.4.4 Personnel Costs:

As the name suggests, this cost element includes the direct expenses associated with the workforce dedicated to production. For the purpose of cost projections, the incremental organizational structure resulting from the development of the two analyzed productive plants and the average cost of operational positions were taken into account, along with the effect of inflation.

It is important to emphasize that only the incremental structure is considered for these projections. As mentioned in previous chapters, only marginal variations are deemed relevant, while the existing structure remains unaffected. The sizing of the personnel structure was validated according to the necessary technical requirements for the operational functioning of a productive plant, as per technical SMEs (personal communication, 2023).

The cost of productive labor represents a fixed expense that remains unaffected by production volumes. Nevertheless, due to the fact that production normalization is not achieved until after five years, the structure of operational labor also attains its normalized state at the same five-year mark. Table 4 outlines the personnel requirements to meet the needs of the two plants, broken down by periods and functions.

Functions	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5 and later
Project Management	0	4	4	4	4	4
Site Head	0	2	2	2	2	2
Quality Head	0	2	2	2	2	2
Engineering	0	2	2	2	4	4
Quality Control Manager	0	0	2	2	2	2
Production Manager	0	2	2	2	4	4
Quality Assurance Manager	0	0	2	2	4	4
Technician	0	0	8	8	14	18
Total Head Count	**0**	**12**	**24**	**24**	**36**	**40**

Table 4: Incremental Production Headcounts, +2Sites Scenario.

3.4.5 Transportation Cost:

This cost element is strictly variable since it depends on the doses dispatched to customers.

Estimating this cost element is quite complex, as each treated patient may have unique circumstances that impact the final incurred cost. As previously highlighted, medical centers are located at varying distances and regions, thereby causing transportation and distribution costs to vary for each dose, ultimately influencing the profitability per dose.

To address this complexity, the total transportation cost from the previous year and the doses produced during the same period were used to calculate the average cost of freight, accounting for the effect of inflation.

$$\boldsymbol{Transportation}_{(\boldsymbol{Year\ A+1})} = \frac{Total\ Cost\ of\ Transportation_{(Year\ A)}}{\#Total\ Doses_{(Year\ A)}} \times \#Total\ Doses_{(Year\ A+1)} \times (1 + Inflation)$$

Based on the adopted assumption, all doses would incur the same transportation cost, whereas in reality, each dose carries a different impact depending on the distances and regions where the health center is located. Nevertheless, the assumption resulted in a pragmatic and useful solution for projecting this cost element.

3.4.6 Other Production Costs:

This category encompasses all remaining costs not covered in the previous categories and directly related to production, including expenses for electricity, gas, maintenance, etc.

As with materials costs, these expenses vary based on the batches produced, not according to the doses. For the estimation of these costs, the expenses incurred in the last year and the batches produced during the same period and the consideration of inflation.

$$\boldsymbol{Other\ Pn\ Costs}_{(Year\ A+1)} = \frac{Total\ Other\ Pn\ Costs_{(Year\ A)}}{\#Total\ Batches_{(Year\ A)}} \times \#Total\ Batches_{(Year\ A+1)} \times (1 + Inflation)$$

3.5 Non-Production Costs

Having conducted a detailed analysis of production costs, the following presents an evaluation of the incremental costs not related with the production but involved in the territorial expansion for the company in question.

Non-production costs, such as G&A (General and Administrative Expenses) and M&S (Marketing and Sales), are expenses that are not directly related to the manufacturing of products or to the services provided by the company. Instead of being associated with production itself, these costs are necessary for the overall operation and management of the company.

G&A includes administrative expenses, operating costs of the headquarters, compensation for employees not involved in production, office rent, utilities, insurance, among others. On the other hand, M&S comprises expenses related to promotion, advertising, sales, product development, market research, among others, which are necessary for the marketing and growth of the business.

It is crucial to consider these costs unrelated to production when projecting a cash flow because they represent a significant part of the company's total expenses and can influence its profitability and financial viability. Ignoring or underestimating them in the projections could lead to incorrect decisions or an incomplete view of the financial health of the company.

By including G&A and M&S in the cash flow projections, a more complete and accurate picture of the company's operating costs and how they affect its profitability can be obtained. This allows for better financial planning and informed decision-making to ensure the long-term success and sustainability of the business.

It should be noted that the company already has an established infrastructure beyond its production structure, encompassing all support functions necessary for the proper functioning of the firm and the achievement of its mission and objectives. Therefore, when expanding its commercial reach, the company will only expand those relevant and necessary functions that will cover the new regions.

In this regard, it is assumed that to achieve its expansion objectives, based on the previously estimated dosages and the territories to be covered, the company will need to expand its sales force, customer service team, planning team, and scientific support for patients and healthcare service providers. Table 5 provides a detailed view of the incremental variations in the organizational structure unrelated to production according to insights provided by commercial SMEs (personal communication, 2023).

To project the incremental costs due to the increase in the workforce, an average cost based on the last completed fiscal year has been used. This means considering the total labor cost unrelated to production and the number of employees in these functions at the commercial closing date.

It is important to highlight that the new hires do not all occur simultaneously, but rather the company's penetration rate was considered. This rate assumes that the company will reach normalized volumes after 5 years of operational and commercial launch.

Functions	Year 0	Year 1	Year 2	Year 3	Year 4	Year 5 and later
Sales Manager	0	2	2	2	2	2
Sales Assistant	0	0	1	2	2	2
Scientific Affairs	0	0	1	2	2	2
Logistic and Planning	0	0	2	2	2	4
Customer Services	0	0	2	2	2	2
Total Head Count	**0**	**2**	**8**	**10**	**10**	**12**

Table 5: Incremental Commercial and General Head Counts, +2Site Scenario.

Similarly, it is assumed that there will be other incremental costs necessary and unrelated to production or personnel. Thus, it was identified that once the operational and commercial launch of the new plants occurs, additional expenses for promotion and advertising, human resources services, technology and IT', and Finance would be incurred. The total budget for these activities is estimated at 1.1 million Euros for the first year of operations, representing 9% of the revenues. Afterward, when the activity normalizes, they represent approximately 4% of the topline. Like the other costs previously analyzed, the effect of inflation also applies to these costs, Finance SMEs (personal communication, 2023).

3.6 Other relevant variables for analysis

In addition to production costs, other fundamental variables that influence financial projections and strategic decision-making for the company have been evaluated. These variables include variations in working capital, the corporate income tax rate, and the discount rate.

3.6.1 Changes in working capital:

In the financial analysis, changes in Net Working Capital (NWC) have been considered as a critical variable for projecting the company's future cash flows. To calculate changes in NWC, specific assumptions have been applied for variations in inventories, accounts receivable, and accounts payable.

Regarding inventories, it has been assumed that they represent approximately 10% of the company's generated revenues. This estimation is based on the historical relationship between the value of inventories and the company's total revenues. By using this assumption, inventories are projected to vary directly based on sales, reflecting an increase or decrease in line with revenue growth or decline.

On the other hand, for accounts receivable, it has been assumed that collections are generated 35 days after sales are made. This means that the company expects to receive payments from its customers approximately 35 days after selling them products or services. A year of 360 days has been used for the calculation to provide a more accurate projection of cash flows.

Regarding accounts payable, it has been estimated that the company makes payments with an average term of 65 days. This means that the company has a period of about 65 days to settle its debts with suppliers and other creditors after having received goods or services. As with accounts receivable, a year of 360 days has been used for the calculation to facilitate comparison and analysis of the results.

The formula used to calculate the change in NWC is as follows:

$$Changes\ in\ NWC = (10\%\ Revenues) + \left(\frac{Revenues}{360}.35\ days\right) - \left(\frac{Expendable\ costs}{360}.35\ days\right)$$

By applying this formula, a clear and consistent estimate of how inventories, accounts receivable, and accounts payable affect the company's cash flow based on the adopted assumptions is obtained. This data is fundamental for accurate financial projection and allows identifying how changes in NWC can influence liquidity and the overall financial health of the company.

3.6.2 Corporate income tax rate:

In the financial analysis, the applicable tax rate in France has been considered as a fundamental part of projecting the company's cash flow. To determine this rate, information provided by the country's tax authority, which is the official entity responsible for establishing and administering tax regulations, has been used (www.impots.gouv.fr).

The tax rate is directly applied to the EBIT (Earnings Before Interest and Taxes), which represents the income generated by the company before deducting interests and taxes. By using this direct rate, it is assumed that no possible mitigating or aggravating factors applicable under the current tax regulations in France are considered.

For example, in some circumstances, companies may be entitled to tax deductions or tax advances that would reduce the final amount of taxes to be paid. However, in this analysis, it was chosen not to consider these possible variables and apply the tax rate directly to the EBIT.

This approach can simplify the projection of taxes to be paid and provide a more conservative and realistic view of the company's tax burden. By not taking into account potential tax benefits, underestimating future taxes is avoided, ensuring a more prudent estimate of the cash flows available to the company.

It is important to note that this is a standard approach in many financial analyses, and although it may not reflect all the specific circumstances of a particular company, it provides a solid basis for evaluating the overall tax situation.

3.6.3 Discount rate:

The discount rate used in calculating the Net Present Value (NPV) of the alternative under study is based on the rate that the company applies for this type of investment in France. In this case, the applied rate was 8% (Finance SMEs, personal communication, 2023).

To determine the 8% discount rate, the company uses the Weighted Average Cost of Capital (WACC) methodology. This methodology considers several relevant factors for the company, including the costs of accessing current capital, the risk-free rate, and the weighting of each component.

As previously explained, WACC is a metric that combines the cost of debt financing and the cost of equity capital for the company, considering the proportions in which the operations are financed. The resulting discount rate is used to discount the future cash flows associated with the investment and calculate its net present value.

The risk-free rate represents the return obtained from a risk-free investment, such as government bonds. This rate serves as a benchmark for the minimum expected profitability of a risk-free investment and is used as a key component in calculating WACC.

The costs of accessing current capital for the company include both the cost of debt financing and the cost of equity (or cost of equity shares). The weighting of each component is based on the proportion in which the company uses each source of financing.

In summary, the 8% discount rate used for the calculation of NPV is based on the rate that the company applies for this type of investment in France and was determined using the WACC methodology, considering the costs of accessing current capital, the risk-free rate, and their appropriate weighting.

3.7 Conclusion: Feasibility and Value Creation Potential

After completing the data collection process and defining the pragmatic assumptions to represent a simplified reality, a cash flow analysis was developed to evaluate the viability of the investment alternative under consideration. The results provided a clear positive outlook and validated that territorial expansion through the construction of new plants is a viable strategy with considerable potential to generate additional value for the company.

It is important to note that the feasibility of the analyzed investment alternatives is attributed to the focus on the entire western region of the country. Had a smaller region with lower population density been evaluated, the results would have differed significantly. Therefore, for the industry in question, a commercial expansion strategy must necessarily target regions with a large population base and logically have health service providers equipped with PET cameras to facilitate diagnostic procedures.

Years	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Sales																	
FDG	-	-	7.4	13.0	15.2	15.7	15.5	15.3	15.2	15.2	15.2	14.9	14.9	14.9	14.6	14.6	-
FCH	-	-	0.5	0.8	0.5	0.6	0.3	0.3	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	-
Fdopa	-	-	1.0	1.8	2.8	3.0	3.2	3.8	3.7	3.7	3.7	3.7	3.7	3.7	3.6	3.6	-
FPSMA	-	-	2.3	4.1	6.2	10.1	14.2	14.2	13.9	13.9	13.9	13.7	13.7	13.7	13.4	13.4	-
Total Revenue	**-**	**-**	**11.3**	**19.7**	**24.7**	**29.4**	**33.2**	**33.6**	**32.9**	**32.9**	**32.9**	**32.3**	**32.3**	**32.3**	**31.6**	**31.6**	**-**
Growth Rate		0%	0%	75%	25%	19%	13%	1%	-2%	0%	0%	-2%	0%	0%	-2%	0%	-100%
COGS																	
Materials	-	-	(1.3)	(2.3)	(2.9)	(3.6)	(4.1)	(4.3)	(4.5)	(4.6)	(4.7)	(4.9)	(5.0)	(5.2)	(5.3)	(5.5)	-
Direct Labor	-	(1.1)	(2.2)	(2.3)	(3.5)	(4.0)	(4.1)	(4.2)	(4.3)	(4.5)	(4.6)	(4.8)	(4.9)	(5.0)	(5.2)	(5.3)	-
Transportation	-	-	(1.8)	(3.2)	(4.0)	(4.6)	(4.9)	(5.1)	(5.2)	(5.4)	(5.6)	(5.7)	(5.9)	(6.1)	(6.3)	(6.5)	-
Other Production	-	-	(0.6)	(1.1)	(1.4)	(1.7)	(1.9)	(2.0)	(2.1)	(2.1)	(2.2)	(2.3)	(2.3)	(2.4)	(2.5)	(2.6)	-
Total COGS	**-**	**(1.1)**	**(5.8)**	**(8.8)**	**(11.7)**	**(13.8)**	**(15.1)**	**(15.6)**	**(16.1)**	**(16.6)**	**(17.1)**	**(17.6)**	**(18.2)**	**(18.7)**	**(19.3)**	**(19.9)**	**-**
COGS/Sales	0%	0%	-52%	-45%	-48%	-47%	-45%	-47%	-49%	-50%	-52%	-55%	-56%	-58%	-61%	-63%	0%
Gross Margin	**-**	**(1.1)**	**5.5**	**10.9**	**12.9**	**15.6**	**18.1**	**17.9**	**16.8**	**16.3**	**15.8**	**14.6**	**14.1**	**13.6**	**12.4**	**11.8**	**-**
Gross Margin/Sales	0%	0%	48%	55%	52%	53%	55%	53%	51%	50%	48%	45%	44%	42%	39%	37%	0%
SG&A																	
Marketing and Sales	-	(0.2)	(0.9)	(1.1)	(1.1)	(1.4)	(1.4)	(1.5)	(1.5)	(1.6)	(1.6)	(1.7)	(1.7)	(1.8)	(1.8)	(1.9)	-
General Administration	-	-	(1.0)	(1.1)	(1.1)	(1.1)	(1.2)	(1.2)	(1.2)	(1.3)	(1.3)	(1.4)	(1.4)	(1.4)	(1.5)	(1.5)	-
Total SG&A	**-**	**(0.2)**	**(1.9)**	**(2.2)**	**(2.2)**	**(2.5)**	**(2.6)**	**(2.7)**	**(2.8)**	**(2.9)**	**(2.9)**	**(3.0)**	**(3.1)**	**(3.2)**	**(3.3)**	**(3.4)**	**-**
SG&A/Sales	0%	0%	-17%	-11%	-9%	-9%	-8%	-8%	-8%	-9%	-9%	-9%	-10%	-10%	-10%	-11%	0%
EBITDA	**-**	**(1.3)**	**3.6**	**8.8**	**10.7**	**13.0**	**15.5**	**15.2**	**14.0**	**13.5**	**12.9**	**11.6**	**11.0**	**10.4**	**9.0**	**8.4**	**-**
Gross Margin/Sales	0%	0%	32%	44%	43%	44%	47%	45%	43%	41%	39%	36%	34%	32%	29%	26%	0%
D&A	-	-	(2.5)	(2.5)	(2.5)	(2.5)	(2.7)	(2.6)	(2.8)	(3.1)	(3.3)	(3.3)	(1.5)	(1.5)	(1.4)	(1.3)	(1.2)
Tax	-	0.3	(0.3)	(1.6)	(2.1)	(2.6)	(3.2)	(3.2)	(2.8)	(2.6)	(2.4)	(2.1)	(2.4)	(2.2)	(1.9)	(1.8)	0.3
EBIT	**-**	**(1.0)**	**0.8**	**4.7**	**6.2**	**7.9**	**9.6**	**9.5**	**8.4**	**7.8**	**7.2**	**6.2**	**7.1**	**6.6**	**5.7**	**5.3**	**(0.9)**
Gross Margin/Sales	0%	0%	7%	24%	25%	27%	29%	28%	25%	24%	22%	19%	22%	21%	18%	17%	0%
D&A add Back	-	-	2.5	2.5	2.5	2.5	2.7	2.6	2.8	3.1	3.3	3.3	1.5	1.5	1.4	1.3	1.2
Operating Cashflow	**-**	**(1.0)**	**3.3**	**7.2**	**8.6**	**10.4**	**12.3**	**12.1**	**11.2**	**10.9**	**10.5**	**9.5**	**8.6**	**8.1**	**7.1**	**6.6**	**0.3**
CAPEX	(9.0)	(11.8)	(7.8)	-	-	(0.9)	(1.0)	(1.0)	(1.0)	(1.1)	(1.1)	(1.0)	(0.9)	(0.6)	(0.2)	(0.1)	(0.9)
Change in NWC	-	0.0	(1.3)	(1.1)	(0.7)	(0.6)	(0.5)	0.0	0.2	0.1	0.1	0.2	0.1	0.1	0.2	0.1	3.0
Free Cash Flow	**(9.0)**	**(12.7)**	**(5.8)**	**6.1**	**8.0**	**8.9**	**10.8**	**11.1**	**10.4**	**9.9**	**9.5**	**8.7**	**7.8**	**7.6**	**7.1**	**6.6**	**2.4**
DFCF	(9.0)	(11.7)	(5.0)	4.8	5.9	6.0	6.8	6.5	5.6	4.9	4.4	3.7	3.1	2.8	2.4	2.1	0.7
NPV	(9.0)	(20.7)	(25.7)	(20.9)	(15.0)	(9.0)	(2.2)	4.3	9.9	14.9	**19.3**	23.0	26.1	28.9	31.3	33.4	**34.1**
Regular Payback	5.8 Years																
Discounted Payback	7.0 Years																
IRR	23%																

Table 6: Financial Analysis, P&L, Free Cash Flow, and NPV Calculation for Building up 2 Sites in western France Footprint Expansion +2Site Scenario.

Table 6 presents the complete cash flow development corresponding to the alternative of expanding the company through the construction of two plants in western France. Some particularities are highlighted, such as the initial rapid growth of revenues driven by the effort to capture the entire market share, followed by a slight decline due to price reductions, while doses remain stable. It is worth mentioning that the effect of inflation and decreasing prices leads to a deterioration in the cost-revenue relationship in the second half of the analysis horizon, which cannot be avoided under the assumption of price decreases, as this would not be realistic.

Furthermore, it is crucial to emphasize that the final liquidation period of the analysis does not significantly distort the final result, unlike other cases where the potential value generated is highly influenced by the methodology itself, beyond the nature of the business under analysis. This highlights the solidity and coherence of the approach used in the financial evaluation of the proposed expansion.

The detailed cash flow analysis has allowed for a precise examination of revenue and cost behavior over the analysis horizon, providing a realistic and well-founded view of the viability of the expansion. Despite the challenges identified in terms of the cost-revenue relationship, the cash flow analysis has demonstrated that the alternative of building two additional plants is feasible and offers clear potential for value generation for the company.

In summary, the cash flow analysis provides a comprehensive understanding of the financial aspects and profitability of the +2Sites Scenario. The calculation of the Net Present Value (NPV) yielded favorable results of

19.3 million Euros for a 10-year period and 34.1 million Euros for a 15-year period. In terms of potential value creation, the analyzed alternative of building two additional plants presents itself as a viable strategy.

Regarding the regular payback period, it was calculated to be approximately 6 years, while the discounted payback period is 7 years. As anticipated in previous chapters, investment payback periods in this industry tend to be significantly prolonged by nature. Hence, the analysis was conducted with an unusually extended horizon.

Additionally, with the development of the cash flow analysis, the Internal Rate of Return (IRR) was calculated, resulting in a rate of 23%. This result provides further support for the viability of the analyzed alternatives. The IRR is a crucial metric for evaluating the attractiveness of an investment, as it reveals the potential profitability of the project. In the context of this analysis, the calculated IRR surpasses the discount rate employed to assess future cash flows. This result indicates that the project's return exceeds the minimum rate required to attract investors. In summary, the fact that the IRR exceeds the discount rate is a strong indicator of the project's financial appeal. It demonstrates that the investment holds promising prospects for generating significant returns and is, therefore, an appealing opportunity from a financial perspective.

In conclusion, the analyses carried out through the cash flow analysis, NPV, and IRR strongly support the viability and potential value generation associated with the investment alternative of territorial expansion through the construction of new plants (+2Sites Scenario). Furthermore, this analysis provides a solid reference base for evaluating the expansion strategy involving the implementation of air transportation as the main distribution channel.

4. Footprint Expansion via Air Transportation

In the preceding chapter, a detailed analysis of the +2Scenario was undertaken, confirming the viability of the traditional strategy adopted in the European market. This approach has demonstrated its positivity and potential to create substantial value for the company. The outcomes derived from this analysis serve as a crucial benchmark for the central theme of the current section.

This chapter presents a detailed analysis of carrying out an expansion strategy by leveraging on the existing idle capacity, with the introduction of air transportation as the main driver.

It is crucial to bear in mind that the inherent characteristics of radioactive isotopes employed in nuclear medicine have led the European market to adopt a particular approach in term of broadening market reach. This approach revolves around the expansion of production plant networks to ensure broader patient outreach, primarily relying on ground transportation for distribution. Nevertheless, this approach presents a limitation by restricting companies from accessing untapped patient segments. Therefore, this thesis proposes an innovative solution: the integration of a more agile transportation mode, such as air transport. This shift could have the capacity to open up access to currently unreachable regions without necessitating significant extra investments.

The analysis of this expansion strategy, considering the feasibility of transporting radiopharmaceuticals by air, largely aligns with the estimates made in the previously developed strategy in the previous chapter, which involved a capital investment in two new plants. However, this new proposal presents specific characteristics and assumptions that justify its independent and detailed description.

4.1 Potential Market

Initially, all the assumptions made for sizing the target market in the +2Site scenario would be applicable to the air transportation scenario being examined in this chapter. However, since these are two highly distinct strategies, certain specificities have been identified that could impact the sizing of the market and potentially lead to non-identical estimations for each of the scenarios.

Likewise, it is important to highlight that when referring to the incorporation of air transportation, it does not mean that a dose will leave the factory and reach a healthcare centre solely through an airplane. Ground transportation will continue to be prevalent and significant throughout the logistical system. The main difference lies in avoiding the need to build a new factory and leveraging the existing idle capacity.

Given the air transportation scenario does not consider additional production plants, determining the starting points for ground journeys becomes crucial. In this sense, destination airports become the starting point of the ground transportation stage.

Consequently, two critical issues raised. Firstly, identifying which of the company's plants were close to an airport with a significant daily flow of departures to ensure the supply of the final product without interruptions. Secondly, identifying airports close to the main cities where potential customers were located.

Airport	Time from Production Facility	Flight/Day
Bordeaux	75	2
Nantes	85	2
Paris	65	6
Toulouse	70	0.5
Brives	125	2

Table 7: Candidate Destination Airports for Distribution Hubs.

By employing a synergistic approach that leveraged Google tools such as Maps and Flights, the identification of airports was successfully executed to address the previously raised inquiries. This process led to the identification of five potential destination airports that meet the mentioned requirements. The results are presented in Table 7. The departure airport is not disclosed in order to prevent the exposure of sensitive data that could potentially lead

to an inference of the identity of the company under study. This decision aligns with the confidentiality and limited disclosure agreements signed by the author.

The airport selection process, to guarantee operational viability, not only considered the travel time from the factory to the nearest airport but also evaluated the distance from the destination airport to the location of the new potential customers. In other words, the total transportation time, from leaving the factory to reaching the patient, was analysed to ensure that this time range preserves the quality of the product to be injected.

This analysis revealed that out of the 77 potential customers, 11 of them would experience an increase in total transportation time, going from being in the average range of below 2:30 hours to being in the range of 2:30 to 3:00 hours. At the same time, 7 potential customers would have transportation times exceeding 3:30 hours. This increase in transportation time implies an increased risk, meaning a higher likelihood that the doses may not arrive in optimal conditions for their use. Table 8 summarizes the comparison of the calculated risk for both alternatives under analysis.

Range	Risk Level	Ground Transportation		Air + Ground Transportation	
<2:30hs	Low	39	50.6%	21	27.3%
>2:30 <3:30	Medium	21	27.3%	32	41.6%
>3:30	High	17	22.1%	24	31.2%

Table 8: Analysing Temporal Distances for Potential New Customers using Various Distribution Methods

As a measure to counteract the heightened risk, it is suggested to adopt an assumption whereby the company's potential market share is adjusted downward to 33%, compared to the original 45%. This practical approach recognizes the possibility that certain customers might not be effectively reached by the new strategy. Figure 19 visually presents the maximum attainable quantities for the company, taking into account the re-evaluated market share assumption and the resulting projected revenue, while factoring in the increased risks associated with longer transportation times.

It's important to emphasize the substantial influence of revising this assumption on the company's revenue. This reassessment results in a notable 27% decrease in the projected topline by the final analysed period. Figure 20 displays a comparison between the projected revenues for the Air Transportation Scenario and those calculated for the +2Sites Scenario.

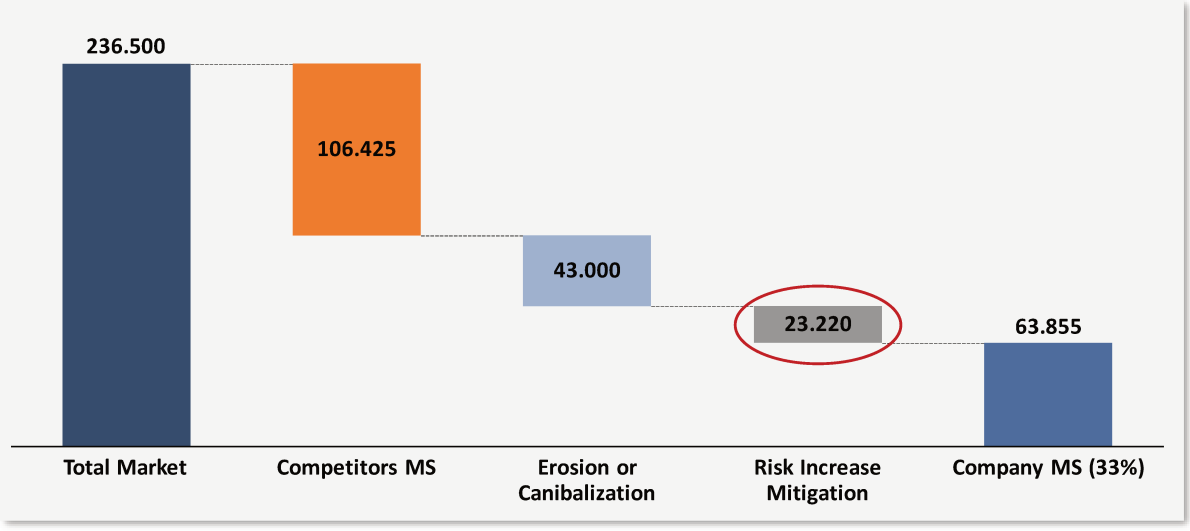

Figure 19: Market Sizing after Market Share Reconsideration.

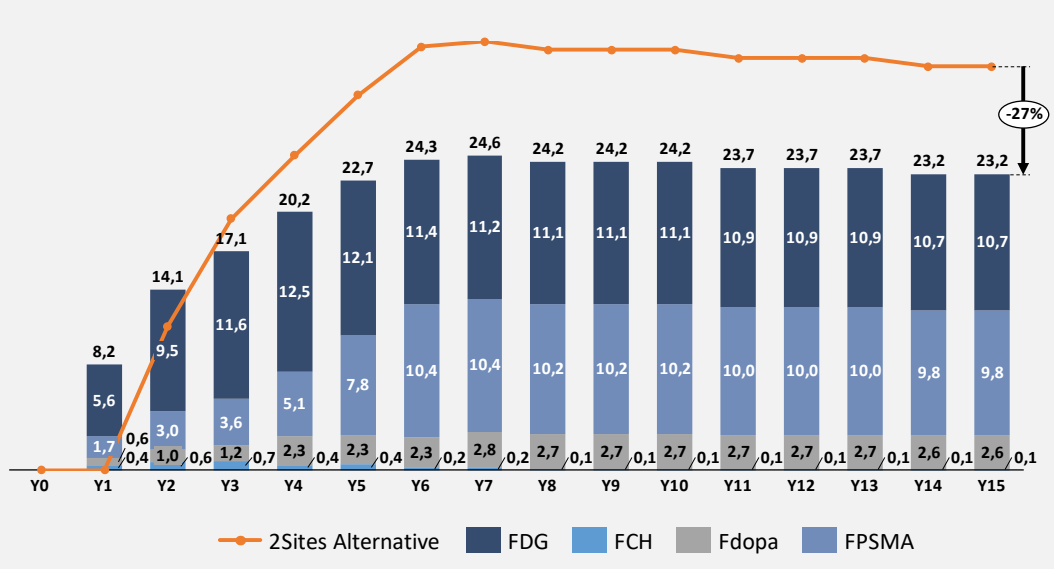

Figure 20: Sales projections Air Transportation vs +2Sites Scenario

4.2 Installed Capacity Utilization

The present thesis is based on the hypothesis that the company has sufficient installed capacity to serve a considerably larger market than the current one, while maintaining relatively stable costs. This feasibility would be achieved through an improvement in the efficiency of production batches (yield), thus avoiding the need for extensive capital investment.

It has been previously mentioned that certain plants have a limited daily production capacity of batches due to two main reasons: first, the processes are standardized with fixed and unchangeable times, and second, the working hours of the healthcare centers to which the radiopharmaceuticals are supplied influence the planning. Unlike other industries that can operate 24 hours a day, in this business, production schedules must adapt and coordinate with the availability of patients. Therefore, considering the work shifts and the characteristics of the currently operating plants, the maximum capacity in terms of batches is 1,440 per year.

It is important to clarify that a radiotracer production plant can annually produce an equal or lesser quantity of batches, depending on the efficiency of batch utilization and planning. Additionally, reaching the maximum batch capacity does not imply subjecting the production structure to stress or overload, as seen by the relatively low batch utilization rates.

In the preceding section, a specific plant of the company was chosen due to its proximity to an airport with a substantial volume of flights heading towards destinations in the central-western region of France. The objective was to assess the viability of utilizing the dormant capacity within this chosen facility. To achieve this, an examination was conducted involving the plant's present production rates, as well as forecasts for the quantities of doses and batches to be manufactured over a comprehensive 15-year analysis period. The visual representation of these projections and actual production levels for doses and batches pertaining to the chosen plant can be found in Figure 21.

It can be observed that, in terms of batches, the company currently operates at 52% of its idle capacity in the selected plant. This is because producing larger batches than the current demand levels is not justified, and there is a considerable margin to improve yields and, consequently, reduce the number of batches.

The assumption adopted for the yield in the projections presented in Figure 21 is that it will remain constant throughout the years in line with current efficiency levels (FDG 60, FCH 17, FDopa 14, and FPSMA 20). Consequently, the idle capacity is estimated to be reduced to 38% for the last year considered in the analysis. This reduction in unused capacity is due to the doses increasing at a compounded annual growth rate of 2%, and

theoretically, the plant covers the incremental doses with additional number of batches instead of improving its efficiency.

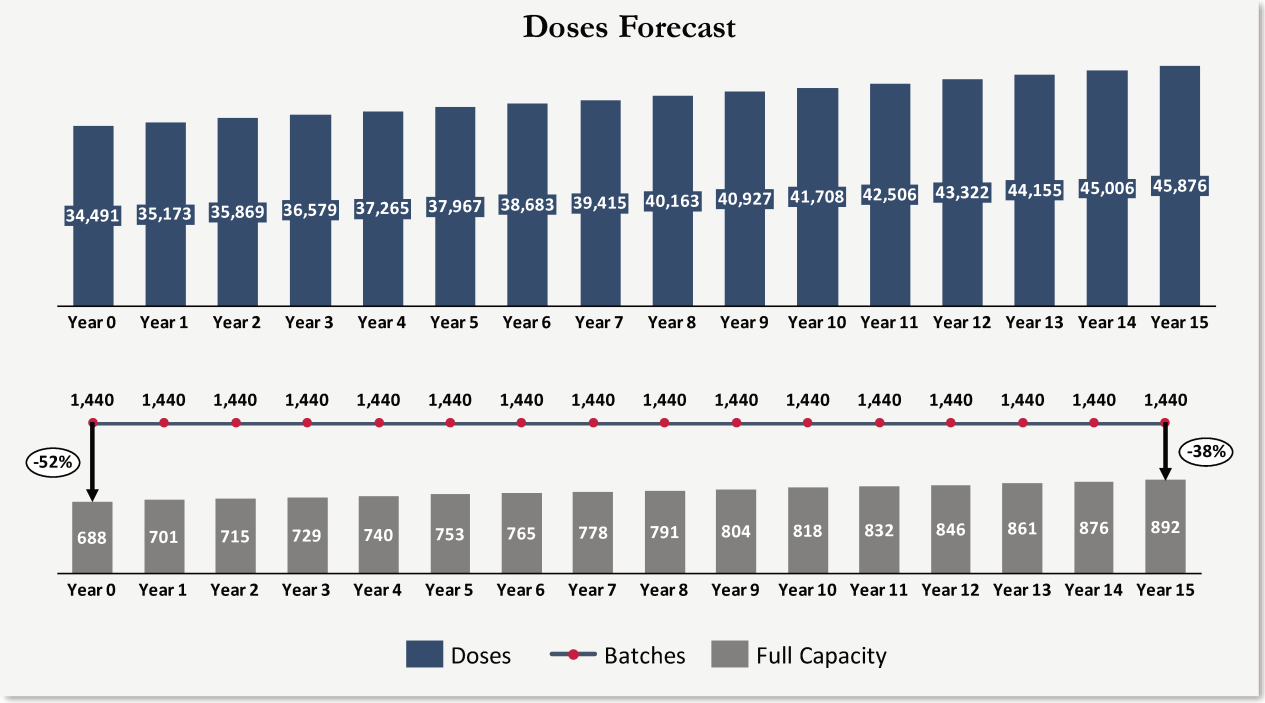

Figure 21: Idle Capacity Assessment of selected Company's Site.

The operational projections of the selected plant represent a very promising initial reference point, and it is interpreted that the plant has sufficient idle capacity to absorb incremental demand while still serving existing clients. From this preliminary conclusion, two questions arise: firstly, what proportion of the new market could be served by improving efficiency without the need for additional batches? And secondly, can the additional batches required to cover the remaining portion of the new demand, be produced with the current installed capacity?

As explained in previous chapters, the maximum utilization of a batch depends strictly on demand, and if all intervening factors were harmonized, several hundred patients could be served at once. However, in reality, this is unlikely to happen, and, according to technical SMEs of the company, a maximum of 100 doses per batch is considered acceptable.

To address the questions posed, it was simultaneously evaluated how much of the new demand could be met by utilizing the number of batches projected for the current demand (enhancing the yield) and how many additional batches should be produced to supply the remaining new doses, provided that the improvement in yield does not exceed 100 doses or the batches do not exceed the maximum 1,440 lots.

Consequently, it was calculated that the yield should gradually improve between 5% and 55% for this alternative to be viable. This increased batch utilization could progressively develop over 6 years without the need for a more accelerated trend.

Table 9 presents a detailed analysis of how the viable production levels were calculated to meet current and future demand from an existing plant, considering a gradual increase in batch utilization. For simplicity, only the first 8 periods are shown.

Installed Capacity Utilization Assessment									
Years	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Current Site - Efficiency per Batch by Brand									
FDG	60	60	60	60	60	60	60	60	60
FCH	17	17	17	17	17	17	17	17	17
Fdopa	14	14	14	14	14	14	14	14	14
FPSMA	20	20	20	20	20	20	20	20	20
Current Site - Production Forecast for existing market - Doses									
Total	34,491	35,173	35,869	36,579	37,265	37,967	38,683	39,415	40,163
Current Site - Production Forecast for existing market - Batches									
Total	688	701	715	729	740	753	765	778	791
Current Full Operational Capacity									
Batches	1,440	1,440	1,440	1,440	1,440	1,440	1,440	1,440	1,440
Efficiency Optimization									
% Improvement	0%	5%	15%	25%	35%	45%	55%	55%	55%
Resulting Yield per Brand after Optimization									
FDG	60	63	69	75	81	87	93	93	93
FCH	17	18	20	21	23	25	26	26	26
Fdopa	14	15	16	18	19	20	22	22	22
FPSMA	20	21	23	25	27	29	31	31	31
Resulting Batches to cover current site demand									
Total	688	668	622	583	548	519	494	502	510
New Market Forecast Doses									
Total	-	25,542	44,699	54,277	60,662	63,855	63,536	63,536	63,983
Incremental Doses Absorved by Efficiency Optimization									
Total	-	1,759	5,380	9,145	13,043	17,085	21,276	21,678	22,090
Incremental Batches to cover New Market									
Total	-	497	755	802	851	868	835	852	854
Resulting Total Batches for all doses (Current + New Market)									
Batches	688	1,165	1,376	1,385	1,400	1,387	1,328	1,354	1,364

Table 9: New Market and Installed Capacity Assessment.

4.3 Incremental CAPEX and OPEX to ensure efficiency improvement

In the previous section, the existence of idle capacity that could be exploited was highlighted. However, according to technical SMEs of the company, the immediate utilization of this flexibility margin could be limited and barely sustained over time without complementary investments that ensured superior performance compared to the current operational level.

In other words, the company's current operational structure meets the current demand with the selected plant. Although in the face of abrupt demand growth, it could be managed to some extent without the need for additional resources, it was determined that the desired efficiency improvement, reaching 55% of maximum efficiency, and the volume of doses required for the new market significantly exceeded the current operational capacity. Therefore, achieving these objectives with the current resources are unlikely.

Next, a detailed overview of the additional CAPEX and OPEX requirements needed to achieve the aforementioned goals is presented.

4.3.1 CAPEX

To achieve the efficiency levels proposed in the previous section, it was necessary to incorporate two new production lines that allowed for the labelling and dispensing of a considerably larger volume of doses than the

currently operated plant. As mentioned earlier, the Cyclotron has the capacity to generate a large amount of activity without major inconveniences but introducing that radioactivity into the vials through the existing production lines could cause bottlenecks and put the entire batch at stake. Table 10 provides a breakdown of the investment required to carry out this expansion and the percentage comparison with the previous alternative (2Sites Scenario).

Item	Service Life	Year 0	Year 1	Year 2
Project Management (20%)	10	600,000	-	-
Production Line (50%)	10	-	3,600,000	2,400,000
Quality Control (20%)	10	-	264,000	176,000
General Infrastructure (20%)	10	-	408,000	272,000
Total		**600,000**	**4,272,000**	**2,848,000**

Table 10: Incremental CAPEX to ensure efficiency improvement and serve new market.

Additionally, it is important to consider that increased utilization of installed capacity would result in increased maintenance expenses. To reflect the impact of these additional expenses, it was assumed that the variation would align with the calculated efficiency increases.

4.3.2 OPEX

4.3.2.1 Production Costs

Having developed an in-depth analysis, it is crucial to highlight that not all production costs would be affected in the same way. Those elements whose main drivers are the number of batches (Materials and Other Production Costs) would increase in relation to the additional batches, while elements dependent on the total number of doses would vary according to the total projected doses for the entire new market (transportation), regardless of whether they are produced through efficiency improvements or new batches.

Regarding labor costs, it was projected that an increase in personnel would be necessary to ensure efficiency improvement. With the significant expansion of production volumes, hiring more staff becomes essential. Table 11 outlines the new positions and the estimated number of employees required. It is worth noting that existing leadership positions in the selected plant would not require new hires for these functions.

Functions	Year 0	Year 1	Year 2	Year 3	Year 4 and later
Engineering	0	1	1	1	1
Quality Control Manager	0	1	1	1	1
Production Manager	0	1	1	1	1
Quality Asurance Manager	0	2	2	2	2
Technician	0	10	10	10	10
Total Head Counts	**0**	**15**	**15**	**15**	**15**

Table 11: New Hiring estimate Air Transportation Scenario.

For the consideration of unit costs of Materials, Labor, and Other Production Costs, the same assumptions developed for the alternative of constructing two plants were applied. However, the transportation cost deserves a more detailed explanation.

4.3.2.2 Transportation Cost

It is relevant to recall that the incorporation of air transport does not replace ground transportation but rather suggests avoiding the expansion of the cyclotron network and utilizing idle capacity to cover longer distances within technically acceptable time ranges.
Therefore, the cost of ground transportation should still be considered in this scenario. After identifying the destination airports that could be used as connection points between the selected plant and the identified health centers, it was determined that the distances to customers improved significantly. In other words, after the air transportation stage, the distances to be covered by land were considerably reduced, as shown in Table 12.

KM	Distance from Site to Customer		Distance from Airports to Customer	
	Number of Customers	%	Number of Customers	%
≤100	9	12%	19	25%
>100 <200	15	19%	34	44%
≥200	53	69%	24	31%

Table 12: Distance Comparison for ground transportation stage in Air Transportation Scenario.

Despite the shortened distances representing an improvement in transportation efficiency, the incorporation of air transport also brings an increase in risk in terms of organization, planning, and coordination. As a mitigating factor for the risk raised, it was assumed for the analysis that the unit transportation cost per dose remains unchanged in relation to the alternative of constructing new plants. In this manner, an attempt was made to offset the more challenging to quantify higher risk in a pragmatic way that influences costs.

4.3.2.3 Estimation of Air Transport Cost

As reiterated multiple times throughout this thesis, the European nuclear medicine market currently does not employ air transportation as its primary distribution channel, let alone a key driver for expansion. Nevertheless, air transport is utilized sporadically and under exceptional circumstances. In this context, it is noteworthy to highlight that the company under study exclusively serves one of its clients in Spain via airplanes.

The fact that the company is not entirely unfamiliar with this distribution method has provided the foundation for the assumption made in estimating the cost of air transportation. In this sense, according to Logistic and Planning SMEs of the company, the current price in Spain is on average 400 euros per container, and each container has a capacity to transport a range of 1 to 10 equivalent doses.
In the context of the air transportation scenario, technical experts who are Subject Matter Experts (SMEs) propose that it would be more efficient to contemplate the transport of radiopharmaceuticals in bulk or in equivalent doses. Put simply, this approach would involve sending to each healthcare center the quantity of activity required to serve the scheduled patients within a specific range of time.

Based on the relatively higher service costs in France compared to Spain, it was assumed that the cost of transporting a container by air would be approximately 25% more expensive. Thus, this pragmatic assumption allows us to estimate a reasonable cost of 500 euros per container. Likewise, it was assumed that, on average, containers with 5 equivalent doses would be transported daily. Table 13 presents the rationale behind the estimation made, using only 5 periods for simplification.

Functions	Year 0	Year 1	Year 2	Year 3	Year 4
AVG Working Days/Year	240	240	240	240	240
Doses per day to be transported	-	106	186	226	253
Doses per Container	5	5	5	5	5
Number of Container	-	21	37	45	51
Cost per Container	(500)	(520)	(536)	(552)	(568)
Total Container Cost per Day	-	(11,068)	(19,950)	(24,952)	(28,724)
Total Air transportation	**-**	**(2,656,368)**	**(4,788,103)**	**(5,988,549)**	**(6,893,877)**

Table 13: Air Transportation Cost Estimate Calculation.

4.3.2.4 Other Costs and Assumptions

Regarding other costs not related to production, an evaluation was made of the impact that the development of this expansion strategy would have. The result showed that, although this scenario does not consider the construction of the two plants, it does not imply that the sales force, planning, and customer service should not be expanded. Although not exactly the same functions would be required, additional hires are necessary to support the strategy and ensure its success. Table 14 presents the hiring plan for new employees.

Unlike the first scenario developed, it is not considered necessary to increase human resources and finance administration expenses in this one since the existing structures would be used. However, it would be necessary to

rent offices in different locations of the new region to be covered, and it was assumed that this expense could represent approximately 240,000 euros in the first year. Also, there is a need to increase IT expenses by approximately 50,000 euros annually, representing significant savings compared to the other strategy, as the requirements become much simpler to implement.

Functions	Year 0	Year 1	Year 2	Year 3	Year 4 and later
Sales Manager	0	2	2	2	2
Sales Assistant	0	1	1	1	1
Scientific Affairs	0	1	1	1	1
Logistic and Planning	0	5	5	5	5
Customer Services	0	1	1	2	2
Total Head Counts	**0**	**10**	**10**	**11**	**11**

Table 14: Non-production Headcounts new hiring for Air Transportation Scenario.

Regarding the other assumptions considered in the analysis of the expansion strategy through the construction of two plants, such as changes in NWC, inflation, discount rate, among others, which have not been explained in this section, they were used in the same way in this scenario.

4.4 Feasibility and Value Creation Potential

This chapter has presented a detailed analysis of the main assumptions and estimations used to model the financial impact of incorporating air transportation as a central element in an expansion strategy. In terms of revenue, it was observed that this alternative project has a significantly lower reach compared to the +2Sites Scenario. This is primarily due to two factors: firstly, the total transportation times are to increase, affecting the quantity of doses delivered; and secondly, to operate a larger quantity of doses, much higher efficiency would be required, which trigger the needs of incremental CAPEX.

An important observation to highlight is that the gross margin gradually erodes in the air transportation scenario, even though 18% of the doses required by the new market are covered using existing idle capacity (at an existing cost). This is primarily attributed to the substantial increase in transportation costs.

In general, in the +2Sites Scenario, the COGS represents an average of 52%, with a maximum of 63%. However, in the scenario that includes air transportation, this ratio significantly increases, with an average of 72% and a maximum of 86%. This implies that producing a dose becomes much more expensive in this scenario, with the primary driver of this variation being the transportation cost, which went from representing 33% of the total cost to 46%.

Despite the gross margin being affected in this scenario, it remains positive and sufficient to cover non-production-related costs. Comparatively, the gross margin in the +2Sites Scenario averaged 48%, while in this scenario, it has an average margin of 28%.

Regarding general non-production-related costs, it is estimated that this alternative would save approximately 9 million euros over the analyzed time horizon. However, in terms of the relation to total revenues, there would be no significant variations, as both scenarios maintain these costs at an average of 10%.

It was demonstrated that the alternative of using airplanes to avoid the construction of new plants does not exempt the company from making capital investments. On the contrary, carrying out these investment projects is essential to guarantee improved efficiency. However, considering the entire capex (capital investment + maintenance) over 15 years, the company would save approximately 27 million euros by avoiding the construction of new plants.

Finally, the viability of this proposal was evaluated using the Net Present Value (NPV) methodology, which yielded a positive result. It is estimated that this expansion strategy using air transportation could generate value for the company in the range of approximately 14 million euros over 10 years and 18 million euros over 15 years. Although the results indicate that this alternative would be viable considered isolated, it is observed that it has the capacity to generate only the half value compared to the +2Sites Scenario (52%).

However, the alternative with air transportation proves more attractive in terms of regular payback period (4 years and 9 months) and discounted payback period (4 years and 10 months), improving by 1 and 2 years, respectively, compared to the +2Sites Scenario. Additionally, it was verified that the internal rate of return (IRR) of this strategy is 16 percentage points higher than that of the +2Sites Scenario, yielding a rate of 39%.

In conclusion, the alternative that includes air transportation is fully viable from a financial perspective, although the results are less favorable compared to the +2Sites Scenario. The complete calculation of discounted cash flows for this alternative is presented in Table 15.

Years	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Sales																	
FDG	-	5.6	9.5	11.6	12.5	12.1	11.3	11.2	11.1	11.1	11.1	10.9	10.9	10.9	10.7	10.7	-
FCH	-	0.4	0.6	0.7	0.4	0.4	0.2	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	-
Fdopa	-	0.6	1.0	1.2	2.3	2.3	2.3	2.8	2.7	2.7	2.7	2.7	2.7	2.7	2.6	2.6	-
FPSMA	-	1.7	3.0	3.6	5.1	7.8	10.4	10.4	10.2	10.2	10.2	10.0	10.0	10.0	9.8	9.8	-
Total Revenue	**-**	**8.2**	**14.1**	**17.1**	**20.2**	**22.7**	**24.3**	**24.6**	**24.2**	**24.2**	**24.2**	**23.7**	**23.7**	**23.7**	**23.2**	**23.2**	**-**
Growth Rate		0%	72%	21%	18%	12%	7%	1%	-2%	0%	0%	-2%	0%	0%	-2%	0%	-100%
COGS																	
Materials	-	(0.8)	(1.2)	(1.3)	(1.5)	(1.5)	(1.5)	(1.6)	(1.6)	(1.7)	(1.7)	(1.8)	(1.8)	(1.8)	(1.9)	(2.1)	-
Direct Labor	-	(1.3)	(1.4)	(1.4)	(1.4)	(1.5)	(1.5)	(1.6)	(1.6)	(1.7)	(1.7)	(1.8)	(1.8)	(1.9)	(1.9)	(2.0)	-
Transportation	-	(3.9)	(7.0)	(8.8)	(10.1)	(11.0)	(11.3)	(11.6)	(12.0)	(12.4)	(12.8)	(13.1)	(13.5)	(13.9)	(14.4)	(14.8)	-
Other Production	-	(0.4)	(0.6)	(0.6)	(0.7)	(0.7)	(0.7)	(0.7)	(0.8)	(0.8)	(0.8)	(0.8)	(0.8)	(0.9)	(0.9)	(1.0)	-
Total COGS	**-**	**(6.4)**	**(10.2)**	**(12.2)**	**(13.7)**	**(14.7)**	**(15.0)**	**(15.5)**	**(16.1)**	**(16.5)**	**(17.0)**	**(17.5)**	**(18.0)**	**(18.5)**	**(19.1)**	**(19.9)**	**-**
COGS/Sales	0%	-77%	-72%	-71%	-68%	-65%	-62%	-63%	-66%	-68%	-70%	-74%	-76%	-78%	-82%	-86%	0%
Gross Margin	**-**	**1.9**	**3.9**	**5.0**	**6.5**	**8.0**	**9.3**	**9.1**	**8.1**	**7.6**	**7.1**	**6.2**	**5.7**	**5.1**	**4.1**	**3.3**	**-**
Gross Margin/Sales	0%	23%	28%	29%	32%	35%	38%	37%	34%	32%	30%	26%	24%	22%	18%	14%	0%
SG&A																	
Marketing and Sales	-	(1.0)	(1.1)	(1.2)	(1.3)	(1.3)	(1.3)	(1.4)	(1.4)	(1.4)	(1.5)	(1.5)	(1.6)	(1.6)	(1.7)	(1.7)	-
General Administration	-	(0.5)	(0.5)	(0.5)	(0.5)	(0.6)	(0.6)	(0.6)	(0.6)	(0.6)	(0.6)	(0.7)	(0.7)	(0.7)	(0.7)	(0.7)	-
Total SG&A	**-**	**(1.5)**	**(1.6)**	**(1.7)**	**(1.8)**	**(1.8)**	**(1.9)**	**(2.0)**	**(2.0)**	**(2.1)**	**(2.1)**	**(2.2)**	**(2.3)**	**(2.3)**	**(2.4)**	**(2.5)**	**-**
SG&A/Sales	0%	-19%	-11%	-10%	-9%	-8%	-8%	-8%	-8%	-9%	-9%	-9%	-10%	-10%	-10%	-11%	0%
EBITDA	**-**	**0.3**	**2.4**	**3.3**	**4.7**	**6.1**	**7.4**	**7.2**	**6.1**	**5.6**	**5.0**	**4.0**	**3.4**	**2.8**	**1.7**	**0.9**	**-**
Gross Margin/Sales	0%	4%	17%	19%	23%	27%	30%	29%	25%	23%	21%	17%	14%	12%	7%	4%	0%
D&A	-	-	(0.0)	(0.8)	(0.8)	(0.8)	(0.9)	(0.9)	(1.0)	(1.0)	(1.0)	(1.1)	(1.1)	(0.3)	(0.3)	(0.3)	(1.1)
Tax	-	(0.1)	(0.6)	(0.6)	(1.0)	(1.3)	(1.6)	(1.6)	(1.3)	(1.1)	(1.0)	(0.7)	(0.6)	(0.6)	(0.4)	(0.1)	0.3
EBIT	**-**	**0.3**	**1.8**	**1.8**	**2.9**	**4.0**	**4.9**	**4.7**	**3.8**	**3.4**	**3.0**	**2.2**	**1.8**	**1.9**	**1.1**	**0.4**	**(0.8)**
Gross Margin/Sales	0%	3%	13%	11%	14%	17%	20%	19%	16%	14%	12%	9%	7%	8%	5%	2%	0%
D&A add Back	-	-	0.0	0.8	0.8	0.8	0.9	0.9	1.0	1.0	1.0	1.1	1.1	0.3	0.3	0.3	1.1
Operating Cashflow	**-**	**0.3**	**1.8**	**2.6**	**3.7**	**4.8**	**5.8**	**5.6**	**4.8**	**4.4**	**4.0**	**3.2**	**2.8**	**2.2**	**1.4**	**0.7**	**0.3**
CAPEX	(0.6)	(4.3)	(2.9)	(0.1)	(0.2)	(0.2)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.4)	-
Change in NWC	-	(0.4)	(0.5)	(0.2)	(0.3)	(0.3)	(0.3)	0.0	0.2	0.1	0.1	0.2	0.1	0.1	0.2	0.1	0.9
Free Cash Flow	**(0.6)**	**(4.5)**	**(1.6)**	**2.3**	**3.3**	**4.3**	**5.2**	**5.4**	**4.7**	**4.2**	**3.8**	**3.1**	**2.6**	**2.0**	**1.2**	**0.5**	**1.2**
DFCF	(0.6)	(4.1)	(1.4)	1.8	2.4	2.9	3.3	3.1	2.6	2.1	1.8	1.3	1.0	0.7	0.4	0.1	0.3
NPV	(0.6)	(4.7)	(6.1)	(4.3)	(1.9)	1.0	4.3	7.5	10.0	12.1	**13.9**	15.2	16.3	17.0	17.4	17.5	**17.9**
Regular Payback	4.8	Years															
Discounted Payback	4.8	Years															
IRR	39%																

Table 15: Air Transportation Strategy financial assessment, NPV Calculation.

4.5 Sensitivity, Risk and Opportunities Analysis

This section focuses on a crucial aspect for any financial assessment, sensitivity analysis. In the financial environment, uncertainty and variability are inherent elements that must be understood to ensure the robustness and reliability of every evaluation.

Sensitivity analysis is a powerful tool that allows us to explore various scenarios and evaluate how financial outcomes react in response to changes in the assumptions and estimates used in the model. Through this

methodology, it is possible to identify potential risks, uncover hidden opportunities, and assess the feasibility and profitability of a project or strategy under different conditions.

Throughout the development of this thesis, a thorough analysis of the main assumptions and estimates used in the financial model has been carried out. However, it is important to recognize that reality is dynamic and subject to changes and unforeseen events. It is precisely in this context where sensitivity analysis becomes fundamentally relevant, as it allows us to anticipate alternative scenarios and understand how key factors can influence the results.

The key aiming of this section is to present the results of this analysis, illustrating how financial projections are modified when the main parameters of the model vary. It will focus on analyzing the most sensitive factors, those that have the greatest impact on the Net Present Value and discuss their implications for decision-making and financial management.

Sensitivity analysis represents an essential complement to traditional financial analysis, as it goes beyond static results and allows us to understand the underlying dynamics of a financial project or strategy. Its correct application and interpretation provide a realistic and complete overview of the environment in which it operates, which will contribute to making solid and strategic decisions. Figures 22 and 23, provide a summary of the results obtained from the sensitivity analysis of the most relevant factors that can be studied mathematically.

It is relevant to emphasize that both alternatives exhibit a very similar sensitivity to the examined factors, with the most significant ones being market growth, market share, inflation, discount rate, and price.

It's important to clarify that the sensitivity analysis of the yield variable is not relevant to the air transportation scenario, or its outcomes would lack realism. This is because the existing idle capacity is already being utilized under the assumptions of this scenario, through the enhancement of the yield. As a consequence, there is a limit to how much the yield can be improved – it cannot exceed 100 units. Therefore, this operational margin of improvement exists only for a limited number of years.

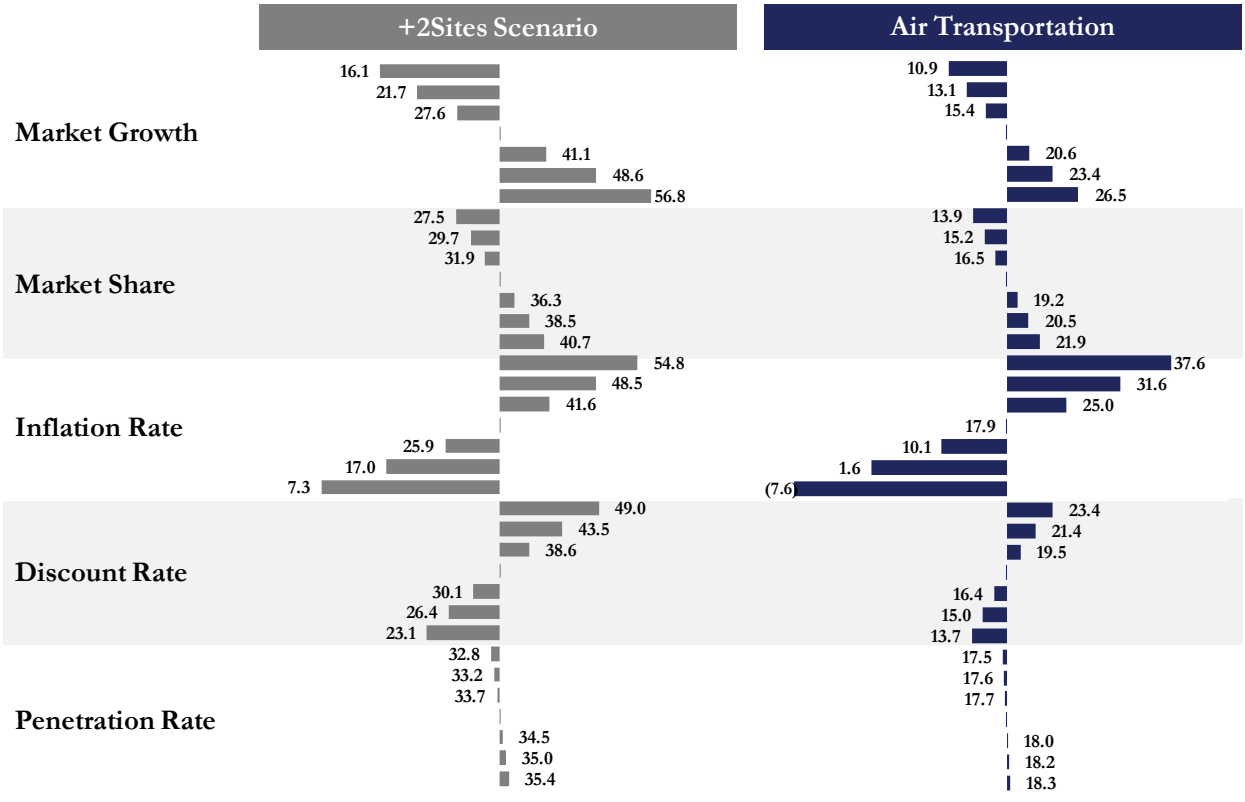

Figure 22: Sensitivity Analysis, +2Sites vs Air Transportation Scenario (1/2)

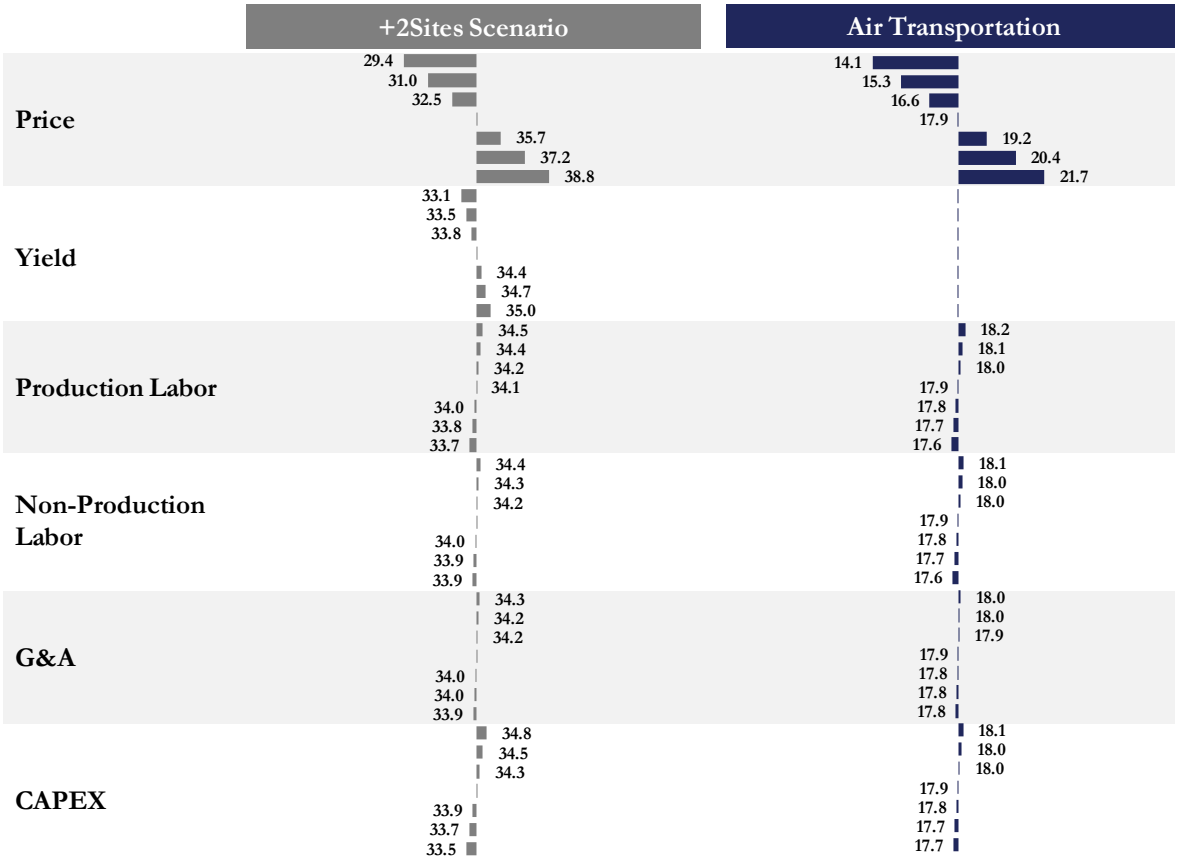

Figure 23: Sensitivity Analysis, +2Sites vs Air Transportation Scenario (2/2)

4.5.1 Market Growth Rate and Market Share

The impact of these factors can indeed be logical and expected, and the mitigation of positive or negative changes in market size will depend on the company's adaptability. However, in both alternatives, the potential versatility in the face of change is interpreted very differently in opposing directions.

If the market were to grow, naturally, the net present value of both alternatives would increase. In the case of the +2Sites Scenario, there would be ample idle capacity to meet higher demand, and if this growth were sustained over time, it would likely require only additional employees. Consequently, the added value presented in the graph becomes significant, and under these conditions, the achieved results would be attainable.

However, in the air transportation alternative, as the existing idle capacity would already be in use, this room for maneuver would be diminished. This implies that if the market were to grow for short periods, the company could potentially capture those sporadic increases. But if there were a consistent growth, the company would encounter a limit rapidly. To continue growing, significant investments, such as incorporating a new cyclotron, would be necessary.

Now, if the market were to decline, the interpretation is opposed to what was mentioned in the previous paragraphs. If the chosen market turns out to be significantly smaller than estimated, divesting in the +2Sites Scenario would be much more expensive than the air transportation alternative. The ease of transitioning out of operations in the case of air transportation becomes straightforward and immediately applicable without major costs.

4.5.2 Inflation Rate and Price

These factors significantly impact on the net present value to be generated by both alternatives, as they influence almost all lines of the profit and loss statement (P&L), while prices simultaneously tend to decline. At the time of

writing this thesis, Europe is experiencing an inflationary process, and consequently, it is estimated that the inflation rate will continue to gradually increase in the short term.

Given the high sensitivity to this factor, the most favorable scenario would be if the inflation rate stabilizes at relatively low levels, around 3%, which would positively contribute to the company's finances and enable it to achieve the estimated value. However, if inflation were to grow or remain at high levels, it would undermine the estimated value, as prices in this industry tend to decline. In the event of an unfavorable inflation scenario, it would be imperative to seek attenuation strategies or engage in negotiations aimed at updating prices to offset the negative impact of inflation.

4.5.3 Discount Rate

The high degree of sensitivity of this factor is explained by its technical nature; it is normal that variations in this rate have a significant impact on the results of an analysis, as it constitutes a primary reference factor for evaluating an investment alternative. Its relevance is evident during the evaluation and analysis stage, but once a decision is made for one alternative or another, attention is no longer given to variations in this variable. Instead, the focus will be on the influence of changes in other projects evaluated in the future.

4.5.4 Other Factors

Mathematically, it has been demonstrated that factors such as market penetration speed, yield, incremental costs, or capex itself have a low impact on potential changes, providing a high reliability of estimates concerning these variables. Once the projects are executed, it could be estimated that, if budget deviations occurred within reasonable ranges, they would not generate a significant impact on the final value created by the investment.

4.5.5 Adaptability Margin

In line with what was mentioned when discussing market growth and market share, it is important to further extend this analysis, which is not straightforward to calculate, and present it in a simplified graph.

The +2Sites Scenario proposes the construction of two new plants following the business model adopted by the company as of today. These new plants would operate at similar levels to the ones already in operation. As previously mentioned, in the event of market growth, these new plants, in collaboration with the expanding cyclotron network, would have full capacity to meet incremental demand. It is estimated that with these two new plants, the entire French market would be satisfied, and in the future, only a greater number of investments in OPEX would be needed.

On the contrary, the cost of disinvestment would be extremely high, and the entire investment would be lost if the estimates were incorrect, and it would not be justified to maintain the new regions if they were not profitable.

Regarding the air transport alternative, the situation is very different, as the main driver of this strategy is the utilization of idle capacity. Therefore, initially, the ability to address incremental demand would be limited. However, if this alternative were to be developed, the company could serve customers from any of its plants and not be limited to the plant selected for the analysis. Moreover, there is even the possibility of supplying new customers from other countries.

The versatility of the air transport scenario is significantly higher when negative forecasts are considered, as the cost of disinvestment is extremely low and rapidly applicable.

While the utilization of air transport is presented as a key pillar for an expansion strategy, there is nothing preventing the most viable approach from being a combination of both alternatives. This opens up a highly valuable opportunity for the company, where expansion can begin with the use of air transport for initial stages, and once the new market achieves a certain consolidation, construction of a plant can proceeds in regions that justify it.

5. Conclusion:

In conclusion, this thesis has conducted a comprehensive holistic analysis of the radiotracer production business for diagnosis, encompassing from the foundational pillars of nuclear medicine to the assessment of an expansion strategy based on air transport. It has delved into the technical and conceptual fundamentals underpinning the nuclear medicine industry, delineating the product, its functionality, production, and distribution. Subsequently, the commercial dynamics and strategies that have led the industry to its current state have been explored.

In this research, it has been demonstrated that air transport is a viable alternative for the distribution of radiopharmaceuticals from a regulatory and legal perspective. It has been confirmed that there are no regulatory obstacles prohibiting the use of airplanes for transporting radioactive substances intended for medical purposes, provided that the established safety standards are strictly adhered to.

The discovery of real success cases in utilizing air transport as a primary distribution channel, with examples from companies in Canada and Australia, validates the practical viability of this strategy. Furthermore, a market analysis supports the perspective of ongoing growth in the nuclear medicine industry, underscoring the relevance of versatile expansion strategies in alignment with market expectations.

The proposal to implement an expansion strategy based on air transport has been substantiated by detailed financial modeling, indicating that it could generate substantial value for the company. However, it's acknowledged that traditional territorial expansion through the construction of new plants remains appealing from a value creation perspective.

Despite the historical lack of connection between the nuclear medicine and aerospace industries, untapped potential in collaboration between the two has been identified. The advanced flight network in Europe could enhance access to accurate diagnostics for underserved regions. To achieve this collaboration, the role of a logistics company bridging both industries is crucial.

As was mentioned, airplanes have primarily been utilized for exceptional or sporadic transportation rather than forming a consistent connection between these sectors. However, the extensive flight network in Europe offers a promising opportunity to enhance patient access. Despite this potential, a smooth and continuous collaboration between these two industries has not been fully developed. This lack of established ties makes it challenging to envision a seamless partnership between them, even though Europe's airport network, destinations, and flight frequencies are highly developed.

For progress to be made, it's essential for a nuclear medicine company to take the initiative and kickstart the process of connecting these industries. This would require the establishment of a bridge between the nuclear medicine and aerospace sectors, potentially facilitated by a logistics company.

While financial analysis indicates that integrating air transport is a highly feasible option, it's important to acknowledge that this step would introduce a notable increase in both risk and complexity to the business operations. Presently, European companies are not well-acquainted with utilizing air transport on a large scale. Implementing such a system would necessitate the creation and enforcement of new operational protocols and work systems to ensure the effective and safe distribution of radiotracers.

Currently, the majority of companies specializing in diagnostic tracer production operate a network of manufacturing facilities spread across various regions. Successfully implementing an aerial distribution system would present the opportunity for significant flexibility, reducing the significance of geographic limitations. In practical terms, companies could supply their clients from multiple factories, even across different countries, according to varying demands and work schedules. In the present scenario, clients are primarily served by the nearest production plant, with exceptional circumstances occasionally leading to supply from more distant facilities.

The societal importance of companies expanding their reach through the use of air transport for radiopharmaceutical distribution cannot be overstated. The improved accessibility to accurate diagnostic tools that this strategy offers would have far-reaching positive implications for society as a whole.

Currently, there are regions with limited healthcare infrastructure, commonly referred to as underserved or poorly attended regions. In these areas, individuals often lack access to advanced diagnostic procedures due to practical constraints. These individuals might resort to less precise methods like ultrasound due to the unavailability of more accurate options. By employing air transport to distribute radiopharmaceuticals, companies can overcome the geographic barriers that have hindered the delivery of advanced medical technology to these underserved regions. This would ensure that people in these areas can benefit from more accurate and effective diagnostic tools, ultimately leading to better healthcare outcomes.

Moreover, despite significant advancements in various fields, health disparities persist globally. Certain regions continue to face challenges in accessing modern healthcare solutions. Diseases like cancer, heart conditions, and neurological disorders have a substantial impact on public health. Implementing an efficient air transport system for radiopharmaceuticals could make a significant difference in the fight against these diseases by ensuring that timely and accurate diagnostic tools reach even the remotest areas. By enhancing their reach, companies would contribute to saving lives and improving the overall health and well-being of society.

In summary, the societal benefits of companies expanding their reach through air transport are evident in the improved access to accurate diagnostics for underserved populations. By overcoming geographical limitations, this strategy has the potential to address health disparities, provide timely diagnoses, and ultimately contribute to saving lives and enhancing healthcare outcomes on a broader scale.

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List of Abbreviations

18F Fluor Isotope 18
ASN Autorité de Sûreté Nucléaire
BNI Basic Nuclear Installations
Bq Becquerel
Bq/g Becquerel per gram
CAGR Compound Annual Growth Rate
CAPEX Capital Expenditures
CAPM Capital Assets Pricing Model
CCS Containment Control Strategy
CEO Chief Executive Officer
CF Cash Flow
COGS Cost of Goods Sold
CT Computed Tomography
DCF Discounted Cash Flow
DOPA Dihydroxyphenylalanine
DOTA 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid
EBIT Earnings Before Interest and Taxes
EU European Union
F Fluor
FAPI Fibroblast Activation Protein Inhibitors
FCF Free Cash Flow
FCH Fluorocholine
FDG 18F-fluorodeoxyglucose FDG
Ga-68 Gallium 68 Isotope
GAAP Generally Accepted Accounting Principles
GE General Electric
Ge-68 Germanium-68
GMP Good Manufacturing Practice
IAEA International Atomic Energy Agency
IBC Intermediate Bulk Containers
INES International Nuclear and Radiological Event Scale
IRR Internal Rate of Return
IRSN Institute for Radiation Protection and Nuclear Safety
USD United States Dollar

VCA Value Chain Analysis

WACC Weighted Average Cost of Capital

IT Information Technology
kPa Kilopascals
LOR Lines of Response
LSA Low Specific Activity
MeV Mega Electron Volts
MOX Mixed Oxide Fuel
MRI Magnetic Resonance Imaging
MS Market Share
NIBIB National Institute of Biomedical Imaging and Bioengineering
NPV Net Present Value
NWC Net Working Capital
OPEX Operating Expenses
P&L Profit and Loss
PET Positron Emission Tomography
PET CT Positron Emission Tomography Computed Tomography
PSMA Prostate-Specific Membrane Antigen
QC Quality Control
RABS Restricted Access Barrier Systems
ROIC Return on Invested Capital
RRR Required Rate of Return
SCO Surface Contaminated Objects
SME Subject Matter Expert
SPECT Single Photon Emission Computed Tomography
SRF Sky Research Forecast
SSR Specific Safety Requirements
SWOT Strengths, Weaknesses, Opportunities, and Threats
TBq Thera Becquerel
TSN Transport Safety Nuclear
UK United Kingdom
US Ultrasound
US United States

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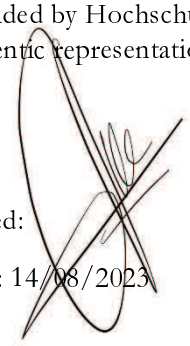

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