FINANCIAL FEASIBILITY STUDY OF INCREMENTAL MODIFIED DRUGS DEVELOPMENT BY DOMESTIC PHARMACEUTICAL INDUSTRY

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A Thesis Submitted in Partial Fulfillment of the Requirements
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การศึกษาความเป็นไปได้ด้านการเงินของการพัฒนารูปแบบยาสำหรับยาใหม่ชนิดที่เป็นตัวยาเดิม โดยอุตสาหกรรมการผลิตยาภายในประเทศ

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Thesis Title	FINANCIAL FEASIBILITY STUDY OF INCREMENTAL MODIFIED DRUGS DEVELOPMENT BY DOMESTIC PHARMACEUTICAL INDUSTRY
By	Miss Manthana Laichapis
Field of Study	Social and Administrative Pharmacy
Thesis Advisor	Assistant Professor RUNGPETCH SAKULBUMRUNGSIL, Ph.D.

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มัณฑนา ไล่ชะพิษ : การศึกษาความเป็นไปได้ด้านการเงินของการพัฒนารูปแบบยาสำหรับยาใหม่ชนิดที่เป็นตัวยาเดิมโดยอุตสาหกรรมการผลิตยาภายในประเทศ. (FINANCIAL FEASIBILITY STUDY OF INCREMENTAL MODIFIED DRUGS DEVELOPMENT BY DOMESTIC PHARMACEUTICAL INDUSTRY) อ.ที่ปรึกษาหลัก : ผศ. ภญ. ดร.รุ่งเพ็ชร สกุลบำรุงศิลป์

อุตสาหกรรมยาในประเทศไทยได้เน้นการพัฒนาตามแผนยุทธศาสตร์ชาติ เพื่อให้เกิดการพึ่งพาตนเองในระยะยาว ผ่านการวิจัยและพัฒนา วัคซีน ยาและผลิตภัณฑ์ทางชีวภาพ อย่างไรก็ตามด้วยสถานการณ์ปัจจุบันมูลค่ายานำเข้ามีค่าสูงกว่ายาที่ผลิตโดยอุตสาหกรรมภายในประเทศ แสดงให้เห็นว่าศักยภาพในการวิจัยและพัฒนาของอุตสาหกรรมยาภายในประเทศจำเป็นต้องมีการพัฒนา ซึ่งการวิจัยยาใหม่จากยาเคมีเดิม (IMDs) เป็นการสนับสนุนให้อุตสาหกรรมสามารถพึ่งพาตนเองได้และมีเสถียรภาพ งานวิจัยนี้จึงมีวัตถุประสงค์เพื่อประเมินความเป็นไปได้ด้านการเงินในการพัฒนายา IMDs เพื่อสนับสนุนการตัดสินใจเชิงนโยบายและการลงทุน วิธีการการศึกษาเป็นงานวิจัยแบบผสมผสาน ประกอบด้วยกระบวนการ ได้แก่ การเลือกประเภทของ IMDs การพัฒนาแบบจำลองให้เหมาะสมสำหรับอุตสาหกรรมยาภายในประเทศ การระบุโครงสร้างต้นทุนและการประมาณค่าที่เกี่ยวข้องกับการลงทุนในอุตสาหกรรมผลิตยา IMDs และการวิเคราะห์ความเป็นไปได้ทางการเงินของ IMDs รวมถึงการวิเคราะห์ความอ่อนไหวและการวิเคราะห์สถานการณ์ทางอุตสาหกรรม ผลการศึกษาพบว่า ยาออกฤทธิ์เนิ่นยาเม็ดแตกตัวในปากและยาพ่นจมูกเป็นตัวเลือกที่ได้รับความนิยมในอุตสาหกรรมยาในประเทศ เมื่อใช้แบบจำลองเพื่อวิเคราะห์ตามช่วงเวลาของการคืนทุนที่นักลงทุนรับได้พบว่า การวิจัยและพัฒนารูปแบบยาเหล่านี้ใช้เวลา 7-13 ปี ซึ่งนานกว่ายาสามัญใหม่เนื่องจากการพัฒนาสูตรตำรับและอัตราการล้มเหลวที่สูงกว่า ต้นทุนในการพัฒนายาเหล่านี้อยู่ระหว่าง 50.95 - 708 ล้านบาท โดยรายได้ที่นักลงทุนจะต้องทำได้เพื่อให้คืนทุน ขึ้นอยู่กับช่วงเวลาของการคืนทุนที่คาดหวังและระยะเวลาในการลงทุนเพื่อการวิจัยและพัฒนา โดยช่วงเวลาการคืนทุนที่ยาวนำไปสู่ความต้องการรายได้ต่ำลง นอกจากนี้ปัจจัยเช่น วงจรชีวิตของยา อัตราการเติบโตของยอดขาย การแข่งขัน และนโยบายของรัฐล้วนมีผลต่อความเป็นไปได้ สรุปได้ว่าเพื่อให้เกิดการพัฒนายาใหม่ภายในประเทศควรได้รับการสนับสนุนโดยรัฐบาลเพื่อสนับสนุนการวิจัยและพัฒนายาใหม่อย่างยั่งยืน

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Manthana Laichapis : FINANCIAL FEASIBILITY STUDY OF INCREMENTAL MODIFIED DRUGS DEVELOPMENT BY DOMESTIC PHARMACEUTICAL INDUSTRY. Advisor: Asst. Prof. RUNGPETCH SAKULBUMRUNGSIL, Ph.D.

The Thai pharmaceutical industry aims to achieve self-reliance in vaccines, drugs, and biologics as per the National Strategic Master Plan. Challenges include low research capacity and higher drug imports compared to domestic production. To promote self-reliance, more research on incrementally modified drugs (IMDs) is essential. This study analyzes the financial feasibility of developing IMD dosage forms for policy and investment decisions. A mixed-method approach, including type selection, investment models, cost structures, and financial analysis, was employed. Results favor sustained release, oro-dispersible tablet, and nasal spray formulations. IMD research and development took 7 to 13 years due to formulation complexity and higher failure rates. Development costs ranged from 50.95 to 708 million THB. Longer payback periods correlated with lower annual income requirements, influenced by factors like drug life cycle, sales growth rate, competition, and government policies. The findings underscore the importance of clinical studies, research duration, drug selection, and market feasibility in investment decisions. Policymakers can utilize this insight to foster the growth and sustainability of Thailand's pharmaceutical sector.

Field of Study:	Social and Administrative Pharmacy	Student's Signature .....
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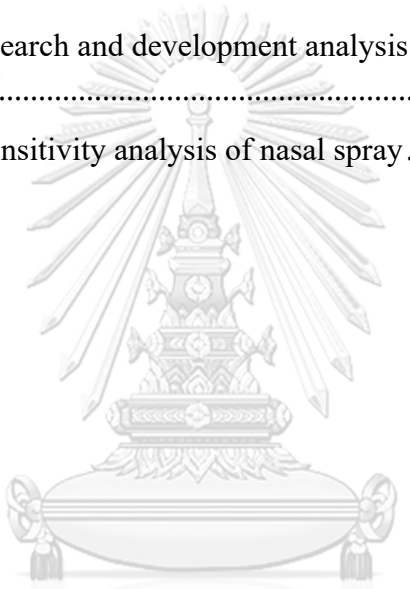

CHAPTER I
INTRODUCTION

BACKGROUND AND RATIONALE

The Thai pharmaceutical industry has aligned itself with the National Strategic Master Plan (2018-2037) to concentrate on the strategy for national drug system development and the enhancement of pharmaceutical manufacturing within the country(Secretariat of the National Strategy Committee, 2016). This commitment involves implementing the 3rd national drug policy in 2011 and the national drug system development strategy from 2011 to 2016, with the objective of fostering stable and sustainable growth in the pharmaceutical industry, biologics, and herbal medicines to achieve self-reliance (National drug system development committee, 2011). The primary focus lies in enhancing capabilities and elevating the pharmaceutical industry through research, development, and production of vaccines, drugs, and biologics, as well as promoting local pharmaceutical industries and services to reduce imports and increase exports.

Within Thailand's pharmaceutical industry, the current state of the Thai pharmaceutical manufacturing sector predominantly operates downstream. Most manufacturers import active pharmaceutical ingredients (API) from foreign countries and combine them with pharmaceutical excipients to produce finished products in various forms such as tablets, coated tablets, capsules, solutions, and injected drugs. These products primarily consist of generic drugs or new generic drugs (Committee on Thai drug system, 2020).

Regarding research and development in the pharmaceutical manufacturing sector, the majority of Thai pharmaceutical manufacturers concentrate on producing generic drugs (with an average of 540 drugs approved per year) and new generic drugs (with an average of 35 drugs approved per year) after patent expiration. Many of these manufacturers develop formulations for finished products to enhance properties such as drug stability and dissolution. Over the past decade, pharmaceutical manufacturing companies have invested in research and development, adopting new technologies to develop various forms of finished products.

Based on the relatively low research and development capacity and the trends observed in Thai pharmaceutical manufacturing and importation over the past two decades (Kessomboon & Manomayitthikan, 2019), the value of domestically produced
drugs exceeded that of imported drugs from 1995 to 2002. However, since then, the value of imported drugs has surpassed that of domestically produced drugs, indicating a decline in domestic drug stability over the past two decades.

However, the development and approval of new drug formulations in Thailand have faced constraints due to the unpreparedness of the pharmaceutical manufacturing industry and relevant regulatory agencies, as well as the absence of explicit guidelines for the registration of new drugs produced in the country. Currently, research and development in this area are becoming more defined. The Thailand Food and Drug Administration (FDA) has categorized "new drugs" into seven types, including new chemical entities (NCEs), new indications, new combinations, new delivery systems,

new routes of administration, new dosage forms, and new strengths. Types 2-7, often referred to as incrementally modified drugs or IMDs in many countries, encounter challenges in NCE research and development in Thailand due to inadequate investment, technology, and personnel capacity (Committee on Thai drug system, 2020)

To support the policy on the pharmaceutical manufacturing industry, it is crucial to conduct research and development on incrementally modified drugs (IMDs) that share similar compounds and efficacy with original drugs but possess altered properties and characteristics. This can be achieved by leveraging advanced technology platforms to foster the self-reliance of the Thai pharmaceutical industry in a sustainable manner.

Previous studies have conducted financial analyses of generic drugs, encompassing infrastructure establishment and production unit setup (Department of industries ministry of economic affairs royal government of Bhutan, 2009). However, the research and development phase has not been taken into account. Consequently, this study aims to investigate the financial feasibility of developing dosage forms of incrementally modified drugs by the local pharmaceutical manufacturing industry. This aspect holds significant importance in providing an investment proposal for the development of such dosage forms, thereby contributing to policymaking and investment decision-making from industrial perspectives.

OBJECTIVES

To analyze financial feasibility for developing a dosage form of IMDs.

RESEARCH QUESTIONS

Is it financially feasible to develop IMDs by domestic pharmaceutical industry?

CONCEPTUAL FRAMEWORK

The present study adopts a mixed methods research design, encompassing a comprehensive literature review, a survey, and in-depth interviews. The data collection process entails engaging specialists in the field of IMDs and conducting a meticulous examination of pertinent literature related to IMDs to ensure the meticulousness and precision of the data. To ensure the selection of knowledgeable and relevant participants, the researchers employed a purposive sampling technique. Subsequently, the collected data underwent rigorous analysis performed by field experts to identify the key factors associated with the financial feasibility assessment of developing dosage forms of IMDs by the local pharmaceutical manufacturing industry, as visually depicted in Figure 1.

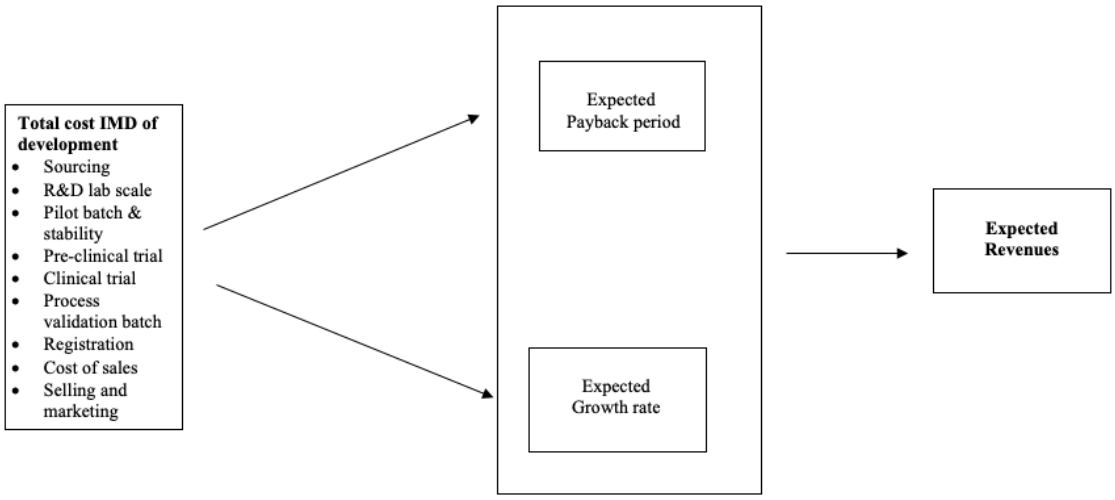

Figure 1 research conceptual framework

This study aims to evaluate the financial scenario and forecast the future conditions of IMDs development by the domestic pharmaceutical industry, with a specific focus on total cost requirements, expected profitability, and investment considerations. To conduct a comprehensive financial feasibility analysis, this study incorporates four key constructs:

1. Total cost estimation for IMDs development involves classifying costs according to the functions of the drug development process.

2. The expected payback period estimation focuses on determining the duration within which businesses can anticipate recovering their capital investments.

3. The estimation of the expected growth rate is based on the growth rate profile of the drug, taking into account the interests of the business.

4. The estimation of expected revenue involves determining the sales needed to break even or generate a profit.

By examining these four constructs, this study aims to provide a thorough assessment of the financial aspects associated with IMD development in the domestic pharmaceutical industry.

EXPECTED BENEFITS

1. A proposed measure should be implemented to inform policymaking in the IMDs manufacturing industry. This measure would support investment decisions and facilitate supplementing the decision-making process concerning investments in incrementally modified drug manufacturing.

2. The local industry possesses the capability to develop IMDs manufacturing, leading to a reduction in imported drugs from foreign countries and an increased accessibility of drugs for patients.

3. It serves as a valuable exemplar for conducting financial feasibility assessments for the development of IMDs within the local pharmaceutical manufacturing industry.

CHAPTER II
LITERATURE REVIEW

The concept of incremental drug modification involves purposeful alterations to an existing drug, including changes to its chemical structure, dosage form, delivery method, or combination with other therapeutic agents. These modifications aim to optimize drug efficacy, improve patient compliance, reduce toxicity, and overcome limitations associated with conventional drug treatments. By building upon existing drug compounds and formulations, researchers can enhance the overall quality and effectiveness of drug products.

This literature review has two primary objectives. Firstly, it aims to provide a comprehensive overview of the existing literature on the research and development of drug products by the Thai pharmaceutical industry. It also aims to present guidelines for the nonclinical and clinical evaluations of new drug products derived from previously approved drug substances.

Secondly, the review aims to identify the cost and financial feasibility process related to drug formulation. This includes examining costing methods, principles of feasibility studies, financial statements, financial indicators, and the existing literature on financial feasibility studies of drug formulation. By exploring these aspects, the review seeks to provide insights into the financial considerations associated with drug development.

Research and development of drugs product by Thai pharmaceutical industry

Research and development in the Thai pharmaceutical industry encompasses various types of finished drug products. These types can be classified as follows, based on the Committee on Thai Drug System (2020):

1. Research and development of generic drugs in conventional dosage forms: Generic drugs and new generic drugs are the most commonly found drugs in Thailand. Although both groups undergo similar research and development procedures, they differ in terms of the bioequivalence study requirements. Bioequivalence studies are costly, complex, time-consuming, and demand researchers and developers with extensive knowledge and expertise. As a result, only a limited number of pharmaceutical manufacturing companies have the potential to develop such products. This limitation is reflected in the average number of new generic drugs approved by the Thai FDA, which is 35 drugs per year (from 2002 to 2018), compared to an average of 590 generic drugs approved per year.

2. Research and development of generic drugs using a high technology platform: Certain drugs require advanced technology for formulation or production, such as modified-release drugs, sterile lyophilized products, inhalers, and nasal sprays. If research and development, along with substantial investment, focus on this group of drugs, it can reduce the need for drug imports and enhance accessibility for patients. Manufacturers utilizing high technology platforms in production have the advantage of facing fewer competitors in the market.

3. Research and development of new drugs: The number of newly developed and approved drug formulations in Thailand is relatively small. One notable example is the approval and registration of GPOVIR. This limited progress can be attributed to the unpreparedness of the pharmaceutical manufacturing industry and relevant agencies, as well as the absence of explicit guidelines for the registration of new drugs

produced in Thailand. Currently, research and development in this area are becoming more defined. The Thailand Food and Drug Administration (FDA) defines seven types of "new drugs": new chemical entities (NCEs), new indications, new combinations, new delivery systems, new routes of administration, new dosage forms, and new strengths. These types, collectively referred to as incrementally modified drugs or IMDs in many countries, are now receiving increased attention in research and development efforts (Committee on Thai drug system, 2020).

In addition, the review includes guidelines for the nonclinical and clinical evaluations of new drug products derived from previously approved drug substances, as outlined by the Thai Food and Drug Administration (FDA) in 2019. These guidelines provide a framework for ensuring the safety and efficacy of new drug products based on existing drug substances.

Guideline for nonclinical and clinical evaluations of new drug products from previously approved drug substances (Thai food and drug administration, 2019)

	Non-clinical study			Clinical study	
Topics	Pharmacology	Pharmacokinetics	Toxicology	Phase I	Phase II & III
General studies	Non-clinical trials could be waived if previously approved products have demonstrated the following: 1. Former studies have provided sufficient information to support and meet the current standards. 2. Systemic exposure of IMDs is not greater than that of the previously approved products.			Information for this aspect can be obtained from existing approved products, serving as a bridge for the necessary information.	
				- Pharmacokinetic studies of IMDs should be conducted in cases where previously approved drugs differ in dosage form, delivery, strength, route, or target population. -Data on intrinsic and extrinsic factors from literature or previous approved drugs can be used as a reference, provided there is a valid scientific justification	- Exposure-response relationship information from former approved products could be used to bridge efficacy and safety when applicable - Safety analysis should be done by gathering clinical trial phase I data of IMDs and studying previously approved drugs

	Non-clinical study			Clinical study	
Topics	Pharmacology	Pharmacokinetics	Toxicology	Phase I	Phase II & III
New dosage form	Not required			should be conducted to assess the effect of food on drug absorption	It is not required to conduct bioequivalence studies if equivalence to a reference product can be demonstrated
New delivery system	Required when a new delivery system is expected to affect the pharmacological performance of the drug Ex. liposome	Required when a new delivery system is expected to affect the pharmacokinetics performance of the drug Ex. Liposome, depot injection	Required when a new delivery system is expected to affect the toxicology performance of the drug Ex. Liposome, depot injection	1. Modified release oral products: effect of food and the effect of alcohol on dose dumping. 2. Depot injection: effect of injection site and in vitro and in vivo investigations to evaluate drug diffusion characteristics. 3. Liposomal products: pharmacodynamic studies, as applicable 4. Device-associated products: usability human factors	Required clinical efficacy and safety studies when new delivery system has potential to change pharmacological and/or toxicological performance

New route	Required when indication is changed	Conducted comparing with previously approved dosing route	For the intended route, repeated toxicology studies are required. Additionally, route-specific studies are necessary. Ex. dermal products, parenteral products and nasal	Route-specific studies are required.	Clinical efficacy and safety are required unless scientifically justified.
New combination	Studies (literature based or experimental) to focus on pharmacodynamic interactions ex. additive, synergistic, antagonistic	Studies (literature based or experimental) to focus on pharmacokinetics interactions	Studies (literature based or experimental) to find toxicities with the combination not seen when given either compound alone	Drug interaction studies	Required clinically efficacy and safety trial, unless scientifically justified
New strength	Study not required in case no alternated indication	Generally, not required	Probably required for higher strength products	Generally, not required	Clinical efficacy and safety are required unless scientifically justified.

New indication	Required study for new target disease or mechanisms	Generally, not required	Generally, not required	Indication specific studies	A clinical efficacy and safety trial is required to support a new indication.

Costing

Costing methods serve specific purposes and there are various methods available. Product costing methods, for example, are used to determine the manufacturing cost of a product. Other important methods include process costing, job costing, direct costing, and throughput costing, each chosen based on the type of production and decision-making environment (Tamplin, 2021)

Costing Methods Mandated by Accounting Standards

- Job costing involves tracking the costs associated with specific production jobs, including labor, materials, and allocated overhead costs. It is typically used for unique batches or individual products that are directly billed to clients.
- Process costing, on the other hand, sums up the labor, materials, and overhead costs for an entire process and then allocates them to each unit. This method is commonly used in long production runs. (Accounting Tools, 2023)

Incremental Costing

When considering the incremental cost of producing additional units, staff often focus on profitability. Two main methods in this category are direct costing and throughput costing.

- Direct costing gathers all costs associated with production and selling, and the resulting cost is used to determine the minimum selling price that will still generate a profit.
- Throughput costing, on the other hand, analyzes the impact of additional units passing through bottleneck operations on the overall business throughput, which is the difference between sales and total variable costs. (Accounting Tools, 2023)

Costs also have their own characteristics, and they can be classified based on common characteristics. This classification of costs helps in grouping and analyzing them effectively. (E-finance management, 2021)

Cost classification

Type of cost	Definition
Classification of Cost by Element	
Material cost	The cost of goods supplied which are involved in the production process
Labor cost	The cost of employee compensation, including salaries, wages, and commissions
Expenses	Including cost of services that provided to process of business and the cost of asset such as building, electricity expenses and depreciation of machine etc.
Classification of Cost by Nature	
Direct costs	The cost is directly to seek. Such as raw materials and labor employed in production process.
Indirect costs	Indirectly seek able cost. Such as factory rent, factory insurance, and salary of the factory manage

Cost Classification by Behavior or variability	
Variable costs	The costs change in directly way if the output of production changes. These costs tend to be getting higher or lower depend on production or sales such as direct raw material cost, direct wages, direct expenses, and commission.
Fixed costs	The costs that remain unchanged even sales or output volumes change such as rent, rates, taxes, insurance charges
Semi-variable or semi-fixed costs	the costs that have characteristics like fixed and variable costs which are likely to vary depend on the change of output or sales volume but not in a directly way such as repairs and maintenance costs for plants, machinery, and buildings
Cost Classification by Controllability	
Controllable costs	The costs which could be directly influenced by others cost center or supervision of specified persons
Uncontrollable costs	The costs which could not be influenced by specified person
Cost Classification by Normality	
Normal or unavoidable costs	Normally cost that happen from the output in normal condition so as to this cost could not be avoided
Abnormal or avoidable costs	Costs that are not normally incurred at a given level of output under the conditions for which that level of output is attained
Cost Classification by Function	
Production costs	The cost of processing and using raw materials to produce the output such as cost of materials, cost of labor, other factory expenses, and packing cost
Administration costs	The cost that happened from generating business policies, managing organization, and controlling the operations of the process. So as to these costs are not relevant to research, development, production, distribution, or selling activities.
Selling costs	Cost happened to generate and enhance demand such as cost of marketing
Distribution costs	Costs are related with the sequence of the process which commences from

	product packing until facilitating the availability of reconditioned, returned, and empty packages for re-use
Classification by Time	
Historical costs	Determined costs after these have been happened so as to these costs will be identified after products have been produced.
Predetermined costs	The costs that are calculated in advance based on specifics circumstances that may affect the cost
Cost Classification by Relevance to Decision-Making and Control	
Marginal costs	The total costs that have been changed in case that the volume of product is rosed or reduced by one unit
Sunk costs	The costs that have already happened and could not change by any decisions in the future and become non-related costs for later decisions.
Out-of-pocket costs	The present or future cost depend on decisions and could vary by making decisions so as to the cash expenditure could be influenced by decisions management
Opportunity costs	Term of earning revenue from using the resources to alternative project
Imputed costs	Hypothetical characteristics cost and not contained in costs, but could be used for decisions management
Differential costs	The difference in total costs between two projects. In case choosing more costly project is known as incremental costs
Shut-down costs	Costs that will be happened even though the plant is temporally shutting down
Postponable costs	Postponable cost that will not affect to current situation. However, this is not avoidable cost and business have to pay later
Replacement costs	The costs that substitute an asset at the current price or market
Abandonment costs	The costs that have already removed fixed assets from the cost while fixed assets are no longer use

Financial feasibility

The World Health Organization Centre for Health Development defines financial feasibility as the projected ability of a provider to cover the capital and operating costs associated with delivering a proposed service (Onwujekwe et al., 2018). It involves studying the capability of investors to invest the total capital and performance costs required for a particular service. Financial feasibility is closely linked to financial analysis, which is an analytical tool used to assess the financial viability of an investment. The purpose of this tool is to evaluate the current financial situation and forecast future conditions of the business (WHO Centre for Health Development, 2004).

Conducting a financial feasibility study before starting a project is crucial to prevent financial losses and make informed decisions about project commencement. There are several reasons why conducting a financial feasibility study is essential:

1. It helps specify the objectives of the project and outline alternative approaches.
2. It narrows down project alternatives and identifies new opportunities throughout the process.
3. It determines whether to proceed with the project or not by identifying reasons for and against it.
4. It increases the likelihood of success by identifying and mitigating factors that could impact the business.
5. It provides high-quality data for decision-making.
6. It documents that the project has been thoroughly investigated, providing confidence to investors.
7. It assists in securing funding from various sources.
8. It helps attract equity investment.

When conducting a financial feasibility analysis, Hofstrand and Holz-Claus recommend estimating three key factors:

1. Total capital requirements: This includes start-up costs, facility, and equipment costs, working capital, seed capital, contingency costs, etc.
2. Sources of money and credit needs: Addressing capital availability, identifying credit sources, assessing expected financing requirements, and establishing debt-to-equity levels.
3. Budgeting expected costs and returns on investment: Estimating expected costs, revenue, profit margin, net profit, sales, or usage needed to break even, returns based on manufacturing, pricing, and sales levels. It is important to assess the reliability and validity of assumptions, benchmark against industry averages or competitors, and investigate limitations or constraints of the analysis.

However, the reliability of the outcomes depends on the accuracy of the input data. Therefore, it is crucial to collect estimated and forecasted data from the project owner and experts in the specific field.

Remer and Nieto (1995) categorize evaluation methods into five basic types: net present value methods, rate of return methods, ratio methods, payback methods, and accounting methods. For evaluating financial feasibility, two methods are particularly suitable. Firstly, accounting profits derived from financial statements can provide insights into the financial activities of a business. However, this method is not suitable for assessing planned projects as it does not consider the time value of

money. Secondly, the projected cash flows method, which accounts for the time value of money, is more appropriate for evaluating the performance of planned projects. Therefore, the cash flow method is preferred over accounting profits in measuring financial feasibility (Björnsdóttir, 2010) .

Profitability

Profit is a measure of the income generated by a business that exceeds its expenses. It is recorded on the income statement of the company. The primary goal of any business, regardless of its size, is to generate profit from its investments. However, profitability, while similar to profit, focuses on the company's ability to achieve profit relative to its size. It is a measure of the company's effectiveness and its competence in achieving success. Additionally, profitability refers to the company's ability to generate a return on investment when compared to other investments. Therefore, profitability is also an essential goal as it is closely tied to the company's sustainability and existence.

Profitability is calculated using revenue and expenses. Revenue represents the amount of money generated by the business, while expenses refer to the costs incurred in conducting business activities. There are various methods to calculate profitability, with the two most widely understood criteria being net present value (NPV) and internal rate of return (IRR). Additionally, there are other criteria used to assess whether a project is profitable, such as the payback period, discounted payback period, average accounting rate of return (AAR), and the profitability index (PI) (Horton, 2021).

Net present value (NPV)

Net present value (NPV) is a criterion used to determine whether a business should invest in a project based on the projected returns to investors. NPV is calculated by taking the difference between the present value of cash inflows and cash outflows associated with the project. The calculation of NPV takes into account the interest rate,
which is used to discount the cash flows. The minimum attractive rate of return (MARR) is often used as the interest rate for this calculation. (Björnsdóttir, 2010)

$$NPV(i) = \frac{A_0}{(1+i)^0} + \frac{A_1}{(1+i)^1} + \ \dots \ + \frac{A_N}{(1+i)^N}$$

$$= \sum_{n=0}^{N} \frac{A_n}{(1+i)^n}$$

In financial analysis, several terms and formulas are used to assess the viability and profitability of investment projects. One such measure is the net present value (NPV), which takes into account the timing and magnitude of cash flows. In NPV calculations, variables such as net cash flow at the end of a period (An), interest rate (i), and the project period (N) are considered. If the NPV at a given interest rate (NPV(i)) is positive, it indicates that the project has generated a value of cash inflows greater than the outflows, resulting in profitability.

The interpretation of NPV is as follows:

- If NPV > 0, the investment is considered acceptable.

- If NPV = 0, the investment is regarded as indifferent, meaning it neither adds nor reduces value.
- If NPV < 0, the investment is deemed unfavorable and is rejected.

However, it is important to acknowledge the limitations of NPV. Firstly, NPV assumes reinvestment of periodic cash flows at the discount rate, which may not always reflect the reality of actual reinvestment opportunities. Secondly, when comparing two projects of unequal sizes, using NPV alone may yield different results compared to using the internal rate of return (IRR), another commonly used financial metric. It is crucial to consider these limitations and employ additional evaluation methods to make well-informed investment decisions.

Internal rate of return (IRR)

The Internal Rate of Return (IRR) is the interest rate or discount rate that results in a net present value (NPV) of zero for a project. It represents the expected annual rate of growth for the project and is calculated using the same principles as NPV. The Minimum Attractive Rate of Return (MARR) is the rate at which investors would be willing to invest their money and can be used as a benchmark for investment decisions. (Björnsdóttir, 2010)

$$NPV(i^*) = \sum_{n=0}^{N} \frac{A_n}{(1+i^*)^n} = 0$$

The interpretation of IRR is as follows:
- If IRR > MARR, the project is considered acceptable.
- If IRR = MARR, the project is regarded as indifferent, meaning it neither adds nor reduces value.
- If IRR < MARR, the project is rejected.

However, it is important to recognize the limitations of IRR. Firstly, like NPV, IRR assumes reinvestment of cash flows at the IRR rate, which may not always reflect the actual reinvestment opportunities available. It is important to consider additional factors and evaluation methods to ensure comprehensive decision-making.

Financial ratios

Financial activities of a business are documented in financial statements, which provide a record of past transactions and financial performance. While financial statements may not offer a forward-looking perspective of the business, they play a crucial role in helping investors assess the project's performance. By analyzing financial statements, investors can gain insights into factors such as revenue, expenses, profitability, and financial stability. These statements provide valuable information that aids in evaluating the historical financial performance and current financial position of the business. However, it's important to note that financial statements alone may not provide a complete understanding of the future prospects and potential risks associated with the project. Additional analysis and evaluation methods are necessary to make informed decisions about the project's viability and potential for success.

Liquidity Ratios

Liquidity ratios are essential tools for assessing a business's ability to meet its short-term financial obligations. These ratios establish a connection between a

company's assets and its available cash in relation to its current liabilities. By examining liquidity ratios, investors and analysts can gain insights into the company's financial health and its capacity to pay off debts as they become due. These ratios provide a clear picture of the company's liquidity position by considering the relationship between its assets, including cash and other easily convertible assets, and its current liabilities.

Current ratio = Current assess / Current liabilities

If the current ratio decreases, it indicates that a company's current liabilities are growing at a faster pace than its current assets. This situation suggests that the business may be experiencing financial difficulties. A declining current ratio means that the company's ability to cover its short-term obligations is weakening, potentially leading to cash flow challenges and difficulty in meeting financial commitments. It serves as a warning sign that the business may be facing financial hardship and should prompt further investigation into its financial health and stability.

Profitability ratios

Profitability ratios provide valuable insights into a business's ability to generate profits by examining its income, expenses, and debt. Among these ratios, the return on investment (ROI) stands out as a key indicator for evaluating the performance of the capital employed and aiding decision-making processes.

The ROI ratio quantifies the profitability of an investment by comparing the return to the amount of capital invested. It measures the efficiency and effectiveness of utilizing capital resources to generate profits. By analyzing the ROI ratio, stakeholders can assess the profitability of an investment opportunity and make informed decisions regarding its feasibility and potential returns.

ROI = earnings before interests and taxes/total liabilities and shareholder's equity

The return on equity (ROE) ratio is a profitability ratio that calculates the rate of return for investors. It measures the efficiency and profitability of a company in generating returns on the equity invested by shareholders. A higher ROE indicates a greater return for investors, reflecting a more favorable performance of the company in utilizing shareholder equity to generate profits. The ROE ratio is a valuable metric for assessing the profitability and attractiveness of an investment opportunity from the perspective of shareholders.

ROE = net profit after taxes/ shareholder's equity

The payback periods.

The payback period is a measure that represents the amount of time required for a company to recover its initial investment through cash flows. A shorter payback period is generally preferred as it indicates a quicker recovery of the investment. However, it is important to note the limitations of using payback periods as a criterion for decision-making.

Firstly, the payback period does not take into account the time value of money. It fails to consider that cash received in the future is worth less than the same amount received in the present due to factors such as inflation and the opportunity cost of tying up funds.

Secondly, the payback period does not explicitly consider the salvage value of an investment. It focuses solely on recovering the initial investment without

accounting for any additional value that may be derived from the investment beyond the payback period. As a result, the payback period may not provide a comprehensive measure of the profitability or long-term viability of an investment.

These limitations should be considered when using the payback period as a criterion for investment analysis, and other financial metrics that incorporate the time value of money and profitability should be used in conjunction to make well-informed decisions. (CFI team, 2020)

$$\text{payback period} = \frac{\text{initial investment} - \text{openning cumulative cash flow}}{\textit{closing cumulative cash flow} - \textit{openning cumulative cash flow}}$$

Discounted payback period

The discounted payback period is a revised variant of the payback period that incorporates the concept of the time value of money. Both measures serve the purpose of determining the duration required for a project to reach its "break-even" point, where the generated net cash flows cover the initial project cost. Both the payback period and the discounted payback period are valuable tools for assessing the profitability and feasibility of a particular project.

In this measurement, anticipated cash flows are projected and modified to account for the time value of money. It represents the duration for a project to produce cash flows that result in the cumulative present value of those cash flows equaling the initial investment cost.

One drawback of using discounted payback period analysis is its disregard for cash flows that occur after the payback period. As a result, it fails to provide corporate managers or investors with insights into the investment's performance beyond that point and the overall value it may contribute. This limitation can potentially lead to decisions that conflict with the findings of the net present value (NPV) analysis.

Adjusted present value (APV)

The adjusted present value (APV) represents the net present value (NPV) of a project or company when funded exclusively by equity, along with the present value (PV) of any financial advantages, which encompass the added effects resulting from debt. By considering these financing benefits, the APV incorporates elements like tax shields, such as those arising from deductible interest.

The APV formula can be expressed as follows:

APV = Unlevered Firm Value + Net Effect of Debt (NE)

Unlevered firm value, also known as the enterprise value, is a financial metric that represents the total value of a company's operations without taking into account the impact of its capital structure (debt and equity financing)

The Net Effect of Debt (NE) refers to the additional value resulting from the use of debt financing in a project or investment. It takes into account the tax shields and other financial benefits associated with having debt in the capital structure.

In practical applications, the adjusted present value method is not as widely utilized as the discounted cash flow approach. While it is more commonly regarded as an academic calculation, it is often perceived to yield more precise and accurate valuations.

After reviewing the reasons, methodologies, and indicators that indicate the profitability of financial analysis, it is important to consider a more comprehensive example of feasibility analysis for drug formulation.

Feasibility analysis of drug formulation in Bhutan

This study aims to conduct a feasibility study for the establishment of a drug factory that specializes in manufacturing tablets, capsules, and powder for domestic hospital supplies. The primary products of focus include paracetamol, antacid, and iron-folic acid in tablet form, vitamin B complex in capsule form, and oral rehydration solution (ORS) in powder form. In undertaking this study, several project assumptions are considered.

Particular	Rate/amount
Total project cost	126.03
Debt	70%
Equity	30%
Rate of interest	12%
Depreciation (Building)	SLM* 10 years
Depreciation (Machinery)	SLM* 20 years
Tax	30%
Construction cost (Building)/ sq.m.	6000
Construction cost (Shed)/ sq.m.	3500
Repayment period of debt	8 years
Moratorium period	1 year
Installed capacity (units in lacs)	1625
Capacity utilization	90%
Working capital cycle	1 month

* Straight line method

Total project cost

The results of the financial analysis conducted in this study reveal positive indicators for the proposed investment with the total project cost is Rs. 126.03 lacs. The internal rate of return (IRR) on the investment is 23%, which is notably higher than the interest rate of 12%. Additionally, the net present value (NPV) at a discounted rate of 12% is Rs. 76.36 lacs, further indicating a positive outcome. Furthermore, the payback period for the investment is estimated to be 3 years and 6 months.(Department of industries ministry of economic affairs royal government of Bhutan, 2009)

Throughout this literature review, author will critically analyze and synthesize a diverse range of scientific literature. By identifying the gaps, challenges, and future directions in the field of incremental modified drugs.

The knowledge gaps and challenges identified in existing studies include the limited resources for IMDs development and the absence of financial analysis for new drugs, specifically encompassing the research and development phase. The current analysis primarily focuses on generic drugs and establishing a production unit, overlooking the research and development process. Additionally, the financial feasibility process, analytical model, and costing methods should be adapted from the existing study to address the aforementioned reasons.

Consequently, there is a pressing need to conduct a comprehensive financial analysis for new drugs, taking into account the research and development phase. This approach is vital to fill the research gap and ensure the long-term stability and sustainability of the domestic pharmaceutical industry.

CHAPTER III
RESEARCH METHODOLOGY

The financial and investment feasibility assessment, or financial and investment decision analysis, focuses on evaluating investment models specific to the dosage form of incrementally modified drugs (IMDs). The assessment involves the following steps:

1. Select the type of IMDs based on the results obtained from the feasibility study conducted by the domestic pharmaceutical industry(Sakulbumrungsil et al., 2022). The study identified the three most preferable types of IMDs using Thai FDA data, analyzing drug research and development trends, and employing the prediction market method.

Result from prediction market of feasibility study of incremental modified drugs development by domestic pharmaceutical industry

The results from the prediction market feasibility study of incremental modified drugs development by the domestic pharmaceutical industry showed the utilization of prediction market and the Delphi method. The Delphi method offers advantages such as non-disclosure, allowing participants to freely express their thoughts, and being suitable for addressing complex questions. On the other hand, the prediction market method provides precise answers and is particularly useful for predicting sales, allowing for future predictions of new dosage forms. The combination of these two methods enables participants to provide reasoning through the Delphi method, resulting in a more accurate study. However, it is important to note that this study primarily focuses on the industrial perspective and does not encompass the consumer aspect. In conclusion, based on the market scoring rule (MSR) method, the expected outcomes from the prediction market indicate that the three most preferable types of incremental modified drugs are sustained release, oro-dispersible tablets, and nasal sprays.

2. Developing investment models suitable for the IMDs manufacturing industry in Thailand, considering the specific situation and capabilities of the country. The industrial perspective is taken into account during this process.

3. The assessment includes identifying the cost structure and estimating the costs associated with the investment in the IMDs manufacturing industry. The defined cost structures used are derived from the Impact of Thai-EU Free Trade Agreement (FTA) concerning Intellectual Property Rights on the Pharmaceutical Supply Chain in Thailand study (Liangrokapart et al., 2013). These cost structures encompass various stages of drug development, including estimated sales, sourcing, R&D lab scale, pilot batch & stability, pre-clinical trial, clinical trial, commercial batch, registration, cost of goods sold (COGS), and selling and marketing.

4. The financial and investment feasibility assessment is conducted by setting assumptions and collecting data from various variables, which are utilized in the modular architecture as illustrated in Figure 2. After gathering the relevant variables, sensitivity analysis and scenario analysis are performed to further evaluate the investment models. Overall, the assessment aims to provide a comprehensive analysis of the financial and investment feasibility of the investment models in IMDs. It

involves considering multiple factors, making assumptions, and analyzing various scenarios to support informed decision-making in the pharmaceutical industry.

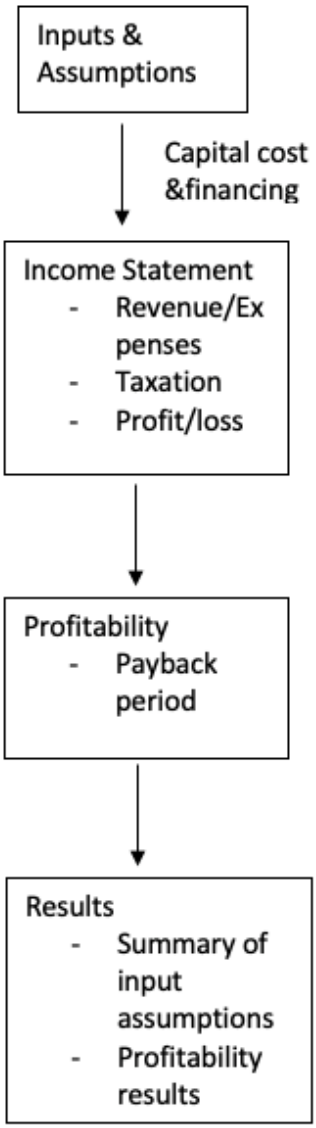

Figure 2 Modular architecture model and the flow of data used for financial and investment feasibility assessment.
(Applied from Björnsdóttir A. R. (2010). University of Iceland 2010. Building and Using Assessment Models for Financial Feasibility Analysis of Investment Projects.)

5. A stakeholders' meeting was held to discuss policy recommendations based on the outcomes of the financial feasibility study, and this meeting will help validate the policies.

The study employs a mixed methods approach, incorporating literature review, survey, and interviews to conduct processes 2 to 4.

Literature review

The literature review conducted to examine the different dosage forms used in the production of existing IMDs, as well as the manufacturing processes involved in IMDs, from the upstream process to the downstream process. Data for the model was collected through the literature review and related documents to assess the situation and ability to manufacture IMDs in Thailand. An interview instrument was developed to interview relevant experts.

Survey

The survey method was used to identify and estimate costs based on the defined cost structures, which were derived from the 'Impact of Thai-EU Free Trade Agreement (FTA) concerning Intellectual Property Rights on the Pharmaceutical Supply Chain in Thailand' study (Liangrokapart et al., 2013)

Survey process:

1. The collection forms with pre-defined cost structures were sent to 5 IMDs (Industrial Manufacturing and Development) experts.
2. The experts provided estimated costs and comments to make the cost structure more valid.

Interview

The interview process involved selecting experts and individuals with expertise in assessing the situation and ability to manufacture IMDs in Thailand

A.) Demographic of informants

The sampling method employed for this study was the snowball sampling technique until data saturation was reached. Participants were recruited from 15 local pharmaceutical industry companies, of which 5 were company owners, and the remaining participants were individuals associated with IMDs development.

B.) Interview process:

1. The researcher sent interview questions to research participants and schedule individual online interviews. Each interview is expected to take approximately 1 hour. The researcher sought permission from participants to record the interview for data analysis purposes (audio recordings will be destroyed at the end of the project).
2. Participants' agreement to participate in the research and their decision to participate in the online interview were considered as consent. Participants were not required to sign a letter of consent.
3. Participants who complete an online interview received remuneration of 1,000 baht per person.

C.) Question guidelines:

1. What are the costs associated with the research and development of a dosage form for IMDs?
2. What are the procedures involved in the research and development of a dosage form for IMDs, and what are the associated costs?
3. What are the costs related to manufacturing technology?
4. What are the costs of conducting clinical and non-clinical studies?

Assumption of financial and investment feasibility analysis

1. It is assumed that the company already has an existing business in place.
2. The cost determination in this analysis is based on incremental costs compared to existing technology. The focus is on identifying the additional costs associated with the development and implementation of the IMDs.
3. The cost estimation is done by classifying costs based on their functions and aligning them with the drug development process. This allows for a more accurate estimation of costs at each stage of the process.
4. A fixed interest rate of 3% is assumed for the analysis. This rate is used to calculate the interest expenses and the impact of borrowing on the financial feasibility of the investment models.
5. A discount rate of 3% is also applied in the analysis. The discount rate is used to determine the present value of future cash flows and assess the overall financial viability of the investment models.

Data analysis

In this study utilizes a modular architecture model created in Microsoft Excel. Excel has been chosen as it is an efficient tool for assessing financial feasibility. The model is designed to accommodate the flow of data, allowing analysts to use different data sheets to generate various modules or conduct different analyses as needed. The flexibility of Excel enables the effective organization and manipulation of data, facilitating accurate and comprehensive financial assessments.

Sensitivity analysis

Sensitivity analysis examines the impact of various factors on financial feasibility.

1. Revenue growth rate: The annual increase in revenue is influenced by the drug's profile and competitiveness in the market.
2. Duration of the drug research and development process: The complexity of the research and development process affects both the timeline and budget allocated to it.
3. Acceptable payback period for investors: The duration of the payback period that investors are willing to accept varies depending on factors such as the type of drug being developed.

By conducting sensitivity analysis on these factors, the study aims to assess the robustness of the financial feasibility model and evaluate the potential impact of changes in these variables on the overall investment viability.

Scenario analysis

The purpose of scenario analysis is to assess the investment viability in specific scenarios based on regulatory requirements and the clinical trial process for each dosage form.

Sustained release tablets

Scenario 1: Conduct only clinical trial phase I In this case, if the particular drug has sufficient non-clinical data from a previous product and the clinical trial phase I demonstrates bioequivalence between the new drug and the reference drug, there is no need to conduct phase II-III studies.

Scenario 2: Conduct clinical trial phase I-III In this scenario, although the non-clinical data for the new drug from a previous product study provides enough information to demonstrate efficacy, safety, and toxicity, additional clinical data is still required.

Oro-dispersible tablets

Scenario 1: Conduct only clinical trial phase I In this scenario, the new drug has sufficient non-clinical data from a previous product and meets the required standards. However, a clinical trial phase I needs to be conducted specifically to evaluate the intentional swallowing of the tablets and compare the drug-food effect between the new drug and the reference drug. Additionally, as the new drug's indication is not altered for a new group of patients, clinical trial phases II-III are not necessary.

Scenario 2: Conduct clinical trial phase I-III In this scenario, although the non-clinical data from the previous product study is appropriate to support the oro-

dispersible tablets, the new drug will be used in new populations. Therefore, a full clinical trial is required, starting from phase I through phase III.

Nasal spray

Scenario 1: Conduct non-clinical trial only pharmacokinetics and pharmacotoxicity part and clinical trial phase I-III

In this scenario, as the route of administration is changed for the nasal spray, additional studies are needed to evaluate the pharmacokinetics and pharmacotoxicity of the IMDs. Furthermore, a full clinical trial from phase I to phase III is still necessary to gather sufficient evidence for the efficacy, safety, and toxicity of the nasal spray.

Scenario 2: Conduct non-clinical trial and clinical trial phase I-III

In this scenario, both non-clinical trials and a full clinical trial from phase I to phase III are conducted for the nasal spray. This is because the route of administration has been altered, and there is not enough existing evidence from former drugs to support the development of the IMDs

Ethical approval

AF 02-12

The Research Ethics Review Committee for Research Involving Human Research Participants, Group I, Chulalongkorn University
Jamjuree 1 Building, 2nd Floor, Phyathai Rd., Patumwan district, Bangkok 10330, Thailand,
Tel: 0-2218-3202, 0-2218-3049 E-mail: eccu@chula.ac.th

COA No. 176/2021

Certificate of Approval

Study Title No. 129.1/64 : FEASIBILITY STUDY OF DOSAGE FORM DRUG DEVELOPMENT FOR INCREMENTALLY MODIFIED BY DOMESTIC PHARMACEUTICAL INDUSTRY

Principal Investigator : Assistant Prof. RUNGPETCH SAKULBUMRUNGSIL, Ph.D.

Place of Proposed Study/Institution : Faculty of Pharmaceutical Sciences, Chulalongkorn University

The Research Ethics Review Committee for Research Involving Human Research Participants, Group I, Chulalongkorn University, Thailand, has approved constituted in accordance with Belmont Report 1979, Declaration of Helsinki 2013, Council for International Organizations of Medical Sciences (CIOM) 2016, Standards of Research Ethics Committee (SREC) 2017, and National Policy and guidelines for Human Research 2015.

Signature: Prida Tasanapradit (Associate Prof. Prida Tasanapradit, M.D.)
Chairman

Signature: Raveenan Mingpakanee (Assistant Prof. Raveenan Mingpakanee, Ph.D.)
Secretary

Date of Approval : 5 August 2021 Approval Expire date : 4 August 2022

The approval documents including:

1) Research proposal
2) Participant Information Sheet and Consent Form
3) Researcher
4) Guideline questions

Protocol No. 129.1/64
Date of Approval - 5 AUG 2021
Approval Expire Date - 4 AUG 2022

The approved investigator must comply with the following conditions:

1. *It's unethical to collect data of research participants before the project has been approved by the committee.*
2. *The research/project activities must end on the approval expired date. To renew the approval, it can be applied one month prior to the expired date with submission of progress report.*
3. *Strictly conduct the research/project activities as written in the proposal.*
4. *Using only the documents that bearing the RECCU's seal of approval: research tools, information sheet, consent form, invitation letter for research participation (if applicable).*
5. *Report to the RECCU for any serious adverse events within 5 working days.*
6. *Report to the RECCU for any amendment of the research project prior to conduct the research activities.*
7. *Report to the RECCU for termination of the research project within 2 weeks with reasons.*
8. *Final report (AF 01-15) and abstract is required for a one year (or less) research/project and report within 30 days after the completion of the research/project.*
9. *Research project with several phases; approval will be approved phase by phase, progress report and relevant documents for the next phase must be submitted for review.*
10. *The committee reserves the right to site visit to follow up how the research project being conducted.*
11. *For external research proposal the dean or head of department oversees how the research being conducted.*

CHAPTER IV
RESULTS

According to the prediction market conducted as part of the feasibility study on the development of incrementally modified drugs by the domestic pharmaceutical industry, it was found that the three most preferred dosage forms are sustained release, oro-dispersible tablets, and nasal sprays. Therefore, these dosage forms will be the focus of the financial analysis.

Table 1 Input data and assumptions for the financial model and financial feasibility study

	Details	Source of data
Cost of sales	According to "how did the public U.S. drugmakers' sales, expenses and profit change over time?" it was found that the cost of sales accounts for approximately 25% of revenues.	Literature review (Jiang & Kong, 2021)
Operational expense	From "how did the public U.S. drugmakers' sales, expenses and profit change over time?" and statement report of Teva pharma, it was reported that operational expenses represent approximately 40% of revenues.	Literature review (Jiang & Kong, 2021) Expert interview
Discounted rate	From the study "On discount rates for economic evaluations in global health" it was stated that the discount rate commonly used for health economics studies is 3%.	Literature review (Haacker et al., 2020)
Interested rate	Interest rate for business is 3%	Interview with experts
Tax rate	Based on feasibility analysis of drug formulation in Bhutan stated that tax rate is 20%	Literature review (Department of industries ministry of economic affairs royal government of Bhutan, 2009)
Expected payback period	The payback period that investors are willing to accept ranges from 5 to 10 years. The specific timing depends on the drug's life cycle, considering factors such as the acceptable period for antibiotics, which is typically shorter than that for non-communicable disease	Interview with investors

	Details	Source of data
	(NCD) drugs due to the development of drug resistance.	

These input data and assumptions will provide the foundation for the financial model and feasibility study, enabling a comprehensive analysis of the financial viability of the incrementally modified drug investment.

Mock design for financial feasibility analysis

The financial feasibility analysis model used in this research differs from other financial models as it focuses on estimating revenues, expenses, and profits from product marketing in order to analyze the payback period and net present value (NPV). The study specifically focuses on the financial feasibility of research and development investments in IMDs at the dosage form level. Since the dosage form can be developed with various active ingredients, it is not possible to estimate sales revenue and market growth accurately, as it depends on the specific active ingredient being studied.

Given the unique design of the financial model in this research, a methodology that differs from traditional financial feasibility analysis is employed. Investors are given the ability to determine the payback period and market growth rate based on their business capabilities, which are then inputted into the model. The financial model aims to estimate the income an investor can earn in order to recoup their capital within the specified period, considering the market growth rate expected by the company based on its business capabilities. This information is crucial for investors to assess the financial feasibility of investing in the research and development of specific pharmaceutical forms with their desired active ingredients.

The financial model in this study is divided into two main parts:

1. Cost of research and development model: This model incorporates the cost information required at various stages of research and development. The collected cost data includes investments made and the respective years of investment. The annual investments are adjusted to the value at year 0 of investment, considering a discount rate of 3%. The model allows investors to adjust the duration of research and development, as different developers may have varying abilities and experiences. The costing model calculates the total cost value at the end of the research and development year, taking into account the investor-specified interest rate. This year marks the launch of the product (year 0). Income generated from product sales begins in year 1 within the revenue and payback model.
2. Sales revenue model: This model calculates the profit margin required to recoup the investment made. Investors determine the desired payback period and the market growth rate based on their business capabilities each year. Once the required profit margin to recoup the investment in year 1 is determined, the model calculates the annual profit margin required for the specified payback period based on the investor-specified market growth rate. It then calculates the corresponding income from product sales each year, which must be achieved within the specified payback period. This model allows investors to assess the financial feasibility of different study drugs and serves as a decision-making tool for the development of IMDs. Investors have the flexibility to adjust various variables, including the payback period and market growth

rate, to determine the required sales revenue for capital recoupment within a specific timeframe.

Financial feasibility study of sustained release dosage form

Sustained release drugs are a subset of modified release formulations that adhere to the definition set by the US Pharmacopoeia. They are designed to provide a specific mode of action and/or targeted drug delivery. Compared to conventional drugs, sustained release formulations are engineered to have a longer duration of action. Initially, the drug is released at a level that achieves a therapeutic effect, followed by a continuous release over time until the drug concentration gradually decreases.

Modified release pharmaceuticals can be categorized based on their structure and mechanism of drug release, such as matrix systems or membrane control systems (Paeratakul, 2018). Among these categories, the matrix system requires relatively lower investment for the development of a phased dosage form. Interviews conducted with the domestic pharmaceutical industry have indicated that the production of sustained release formulations using the matrix system is the most feasible option (Phad et al., 2014) This choice is supported by the fact that existing manufacturing machines can be utilized for production purposes(Houngsaitong, 2016).

There are six phases involved in the research and development of sustained release tablets. These phases include data and raw materials sourcing, R&D lab scale, pilot scale, clinical study, registration, and process validation batch.

Table 2 Sustained release drug research and development processes and data source.

Process	Information Source
Sourcing - drug selection - academic research - raw material sourcing - package material sourcing	Interview with experts
R&D lab scale - formulation development (FD) - lab scale production - analytical method development /validation - finished product specifications - preliminary stability study	Interview with experts
Pilot scale - pilot batch production - stability study	Interview with experts
Clinical study	
-Phase I	IMDS regulation guideline Interview with experts Literature review: What Are Clinical Trials and Studies? (National Institute on Aging, 2023)
-Phase II	IMDS regulation guideline (Thai food and drug administration, 2019) Interview with experts
-Phase III	

Process	Information Source
Registration	Interview with experts
Process validation batch	Interview with experts

The process of researching and developing sustained release dosage forms by the domestic pharmaceutical industry

1. New drugs launched:

Once new drugs from the originator have been released to the market, they serve as important reference products for the research and development of new pharmaceutical products. These drugs must be approved by the Food and Drug Administration as important chemical drugs for registration as new drugs.

2. Sourcing:

Local manufacturers who aim to produce a new drug in the form of an IMDs select a reference drug based on various considerations. These considerations include marketing information, the needs of drug users, issues encountered with drug use, sales data, patent information, as well as the drug itself, the main raw materials, and suitable dosage forms for the drug. The cost of this process, as estimated from expert interviews, is about 0.6-0.7 million baht. The duration ranges from 9 to 15 months, depending on factors such as the difficulty of obtaining information, related wages, and the availability of raw materials in the market.

3. R&D lab scale:

The research and development department conducts studies to develop suitable formulations for sustained release drugs at the lab scale. This includes the development of analytical methods for the drug form and the determination of finished product specifications (FPS). The estimated cost of this process, based on expert interviews, is approximately 2.25 - 5.2 million baht. The duration ranges from 12 to 36 months and depends on factors such as the complexity of the formula (e.g., special effects, BCS class, drug-excipient interaction), the price of raw materials used, and the cost of analytical tools and labor.

4. Pilot batch production:

After successful drug research and development, pilot batch production begins, and stability studies are conducted, including the determination of shelf-life specifications. In the case of sustained release drugs, drug instability often arises from polymer degradation, making this a high-risk step. If the study is successful, the results are reported to the Food and Drug Administration (FDA). The cost of this process, estimated from expert interviews, is about 9.5-23 million baht. The duration ranges from 18 to 48 months, depending on the availability and modification requirements of the tools. This also includes an increasing number of topics to analyze.

5. Non-clinical trial:

Sustained-release drugs are classified as novel drug delivery systems, which are variants of immediate release oral drugs. Additional studies may not be required, and non-clinical study data from the reference product can be referenced. The original data must be sufficient and consistent with currently accepted standards, ensuring that the total amount of drug absorbed by the body does not exceed that of the reference product.

6. Clinical trial:

Phase I: Samples from the pilot batch production are used to study the effect of food on bio-efficacy through a bioequivalence study, as well as to evaluate the effect of alcohol on dose dumping. The estimated cost of this process, obtained from expert interviews and literature reviews (National Institute on Aging, 2023), is approximately 10 million baht, with a duration of 12 months. The duration depends on factors such as the number of participants and the time required to recruit them, including the drugs being studied.

Phase II and III: If the pharmacokinetics of a new drug are not significantly different from those of the reference drug, Phase II and III studies of the new drug may not be necessary, and reference product data can be used (Thai food and drug administration, 2019). The estimated cost of this process, obtained from expert interviews and literature reviews(National Institute on Aging, 2023), is approximately 150-450 million baht. The duration is 24 months, depending on factors such as the number of participants, the time required to recruit them, the drug used in the study, and the study design.

7. Process validation protocol development:

This involves developing a validation protocol to validate the production process for further distribution.

8. Registration:

The criteria for registration of new drug formulas through ASEAN Harmonization will be used. The documents required for the registration of a new drug with an already existing original chemical drug consist of four parts as follows:

Part 1: Administration data and product information.

Part 2: Quality document.

Part 3: Safety (non-clinical document).

Part 4: Efficacy (clinical document).

These documents include the preparation of non-clinical study data and clinical study data for the registration application of the six previously approved active drug formulations (IMDs): (1) drugs with new formulations, (2) drugs with new drug delivery systems, (3) drugs with new dosing ports, (4) drugs with new indications, (5) new combinations of drug formulations, and (6) drugs with new potencies. The licensee can refer to clinical study recommendations and guidelines as per the Announcement of the Food and Drug Administration FDA Re: Recommendations and Guidelines for Non-Clinical Studies and Clinical Studies for the registration of new drug formulations developed from previously approved chemical drugs. The estimated cost of this process, obtained from expert interviews, is 0.1 million baht, and the duration is 12 months or longer, depending on the number of resolutions to be consulted and registered, including the government system.

9. Process validation batch:

After registering and obtaining a registration number from the Food and Drug Administration for the manufacture and sale of drugs, the drug can be produced in the production process for commercial batches. Process validation is conducted on three batches, and the results of the production process inspection are submitted to the Food and Drug Administration for consideration and permission to continue production and distribution. The estimated cost of this part, based on interviews with experts, is about

three times the cost of pilot batches, ranging from 28.5 to 69 million baht. The duration is 3 to 5 months, depending on the difficulty or ease of production.

The financial feasibility study for the development of a sustained-release formulation from the original drug is conducted using scenario analysis in two scenarios, according to the clinical study requirements for registration:

Scenario 1: Study only Phase I study.

In this scenario, non-clinical studies are not required, and information can be referenced from the reference product. The original data must be sufficient and consistent with currently accepted standards, and the total amount of drug absorbed by the body must not exceed that of the reference product. However, Phase I clinical studies are necessary to compare the pharmacokinetics of the new drug with the reference drug in healthy volunteers and/or patients with the indicated disease. For immediate-release formulations, the effects of food on bioavailability are studied. If the pharmacokinetic study of the new drug is not clinically significantly different from that of the reference drug, there is no need for Phase II-III clinical trials.

Scenario 2: Necessary to study Phase I-II study.

In this scenario, non-clinical studies are not required, and information can be referenced from the reference product, similar to scenario 1. The original data must be sufficient and consistent with currently accepted standards, and the total amount of drug absorbed by the body must not exceed that of the reference product. However, Phase I clinical studies are necessary to compare the pharmacokinetics of the new drug with the reference drug in healthy volunteers and/or patients with the indicated disease. For sustained-release formulations, the effects of food on bioavailability and dose dumping are studied. If the pharmacokinetic profile of the sustained-release formulation is clinically significantly different from that of the reference drug, clinical trials for Phase II-III are required.

Table 3 Cost list and annual expense distribution according to the IMDs research and development process (sustained release) in scenario 1

Time period	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7
Sourcing	0.6-0.7						
R&D lab scale		2.25-5.2					
Pilot scale			9.5-23				
Clinical study							
- Phase I				10			
Registration						0.1	
Process validation batch							28.5-69

Table 4 Cost list and annual expense distribution according to the IMDs research and development process (sustained release) in scenario 2

Time Period	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10	Year 11
Sourcing	0.6-0.7										
R&D lab scale		2.25-5.2									
Pilot scale			9.5-23								
Clinical study											
Phase I				10							
Phase II						150					
Phase III								450			
Registration										0.1	
Process validation batch											28.5-69

Table 5 Cost list according to the different phases of product research and development processes.

Process	Cost scenario 1 (Millions thb)	Cost scenario 2 (Millions thb)
Sourcing	0.6-0.7	0.6-0.7
R&D lab scale	2.25-5.2	2.25-5.2
Pilot scale	9.5-23	9.5-23
Clinical study		
-Phase I	10	10
-Phase II	-	150
-Phase III	-	450
Registration	0.1	0.1
Process validation batch	28.5-69	28.5-69
Total (million baht)	50.95-108	650.95-708

Based on the information in Tables 5 above, the research and development of new sustained-release forms of IMDs took approximately 7 years in the case of only Phase 1 clinical studies and 11 years for full clinical trials. This duration is longer compared to the development of new generic drugs, which ranged from 25 to 46 months(Liangrokapart et al., 2013). The longer duration can be attributed to the development of new formulas, higher failure rates, the need for more extensive analysis, and the inclusion of clinical studies since it involves a new drug.

In scenario 1, which focuses only on studying the effects of food on bio efficacy, the investment period and capital requirements do not differ significantly from the development of new generic drugs. The development of new sustained-release drugs from existing chemical entities incurs fixed costs ranging from 50.95 to 108 million baht. However, when compared to the cost of research and development of new generic drugs, which ranges from 6.5 to 39.5 million baht (Liangrokapart et al., 2013), the cost is much higher due to the aforementioned reasons. Most of the cost in scenario 1 is invested in process validation batches, the final step in research and development before commercialization, which requires significant capital and depends on the complexity of production.

In scenario 2, which requires studying Phase 1 to Phase 3 clinical trials to demonstrate efficacy and safety, the development of new drugs incurs fixed costs ranging from 650.95 to 708 million baht. When compared to the cost of research and development of new generic drugs, which ranges from 6.5 to 39.5 million baht(Liangrokapart et al., 2013),the cost is significantly higher. In scenario 2, a major portion of the cost and time is allocated to clinical trial studies, as they are crucial processes for proving efficacy and safety. Factors such as study type, processes, sample size, and drug type can influence the research and development costs.

It is evident that investment in the development of new drugs from existing chemical drugs entails high costs. The data used in the feasibility analysis represent the cost of drug formulation development and are expressed as the income entrepreneurs should be able to generate in order to reach the break-even point. The feasibility depends on investors' considerations regarding the payback period, the nature of the business group, the drugs being produced, and the research and development capabilities of the investors.

Results of a financial feasibility study on research and development of IMDs produced by the domestic pharmaceutical industry in the form of sustained release.

The feasibility study results of this study show in terms of income that investors should be able to achieve in order to achieve capital gains.

Base case

Payback period: 5 years

Year	**1**	**2**	**3**	**4**	**5**
Sales growth rate	**0**	100%	100%	50%	50%

Income that investors should be able to make in order to make back the capital invested.

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1 Time for research and development: 7 years Research and development: 50.95 million baht						
Income (millions baht)		6.99	13.99	27.97	41.96	62.94
Scenario 2 Time for research and development: 11 years. Research and development: 650.95 million baht						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		105.44	210.88	421.75	632.63	948.94

The income in both scenarios demonstrates a clear growth pattern over the 5-year period. In Scenario 1, the income gradually increases from 6.99 million baht in year 1 to 62.94 million baht in year 5. In contrast, Scenario 2, with its higher initial investment and longer research and development period, experiences more substantial income growth, ranging from 105.44 million baht in year 1 to 948.94 million baht in year 5.

Sensitivity analysis

1. Payback period of 10 years

Year	1	2	3	4	5	6	7	8	9	10
Sales growth rate	0	100%	100%	50%	50%	30%	25%	25%	25%	25%

Income that investors should be able to make in order to make back the capital invested.

Year	1	2	3	4	5	6	7	8	9	10
Scenario 1 Time for research and development: 7 years Research and development: 50.95 million baht										
Income (millions baht)	1.47	2.93	5.86	8.79	13.19	17.14	21.43	26.79	33.48	41.85
Scenario 2 Time for research and development: 11 years. Research and development: 650.95 million baht										
Income (millions baht)	21.90	43.80	87.59	131.39	197.08	256.21	320.26	400.32	500.40	625.50

When examining the payback period for investors, it has been noticed that extended payback periods typically result in a reduced capitalization point, leading operators to generate lesser annual income compared to shorter payback periods. In situations involving drugs that do not necessitate frequent updates due to stable disease conditions, such as chronic diseases, the acceptable payback period may be more extended.

2. Period of research and development

Scenario 1 Payback period of 5 years Research and development: 50.95 million baht						
Period of research and development being 5 years						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		6.45	12.91	25.82	38.73	58.09
Period of research and development being 10 years						
Income (millions baht)		9.07	18.15	36.30	54.45	81.67
Scenario 2 Payback period of 5 years Research and development: 650.95 million baht						
Period of research and development being 10 years						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		99.66	199.32	398.64	597.96	896.95
Period of research and development being 15 years						
Income (millions baht)		146.72	293.45	586.90	880.35	1,320.52

From the table above, it is evident that over a 10-year period in scenario 1 and a 15-year period in scenario 2 of research and development, the annual income required from investors will be higher compared to a shorter timeframe, indicating a higher investment requirement.

3. Research and development costs

Scenario 1 Time for research and development: 7 years Payback period of 5 years **Research and development: 108 million baht**						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		14.86	29.72	59.44	89.16	133.75
Scenario 2 Time for research and development: 11 years Payback period of 5 years **Research and development: 708 million baht**						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		114.78	229.57	459.14	688.71	1,033.06

In the case of formula development, complex analysis methods have a higher probability of failure, and numerous aspects need to be developed, including advanced clinical and manufacturing studies. Investing in research and development processes for this scenario may necessitate a larger capital investment. Consequently, investors must strive to generate higher profits to reach a higher capitalization point.

4. 4. Growth rate

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1 Time for research and development: 7 years Research and development: 50.95 million baht						
100% in year 2		6.99	13.99	27.97	41.96	62.94
200% in year 2		4.64	13.91	27.82	41.72	62.59
300% in year 2		3.17	12.68	25.36	38.04	57.07
50% in year 5		6.99	13.99	27.97	41.96	62.94
100% in year 5		5.67	11.34	22.68	34.03	68.05
150% in year 5		4.64	9.27	18.54	27.82	69.54
Scenario 2 Time for research and development: 11 years. Research and development: 650.95 million baht						
100% in year 2		105.44	210.88	421.75	632.63	948.94
200% in year 2		69.90	209.69	419.39	629.08	943.62
300% in year 2		47.80	191.20	382.39	573.59	860.39
50% in year 5		105.44	210.88	421.75	632.63	948.94
100% in year 5		39.96	159.83	319.66	479.49	958.98
150% in year 5		33.63	134.51	269.02	403.52	1008.81

If the growth rate increases by 100% in year 2, the income that investors should make in year 1 will decrease by around 1.5 times for both scenarios, and the remaining years thereafter seem to show slight differences. However, a 3-times increase in the growth rate in year 2 appears to have a relatively more substantial impact on decreasing income. Additionally, a 50% increase in the growth rate in year 5 tends to make the income in the first year extremely lower. However, the growth rate pattern depends on the drug category chosen by the investors as well as the drug market situation

Financial feasibility study of oro-dispersible tablet dosage form

The oro-dispersible tablets, also known as disintegrating tablets, mouth-dissolving tablets, rapid-dissolving tablets, fast-disintegrating tablets, or fast-dissolving tablets, are uncoated tablets that disintegrate and dissolve in the mouth within 3 minutes before swallowing. Unlike immediate release tablets, this dosage form requires the inclusion of a disintegrant in the formulation to facilitate rapid dissolution upon contact with saliva. Patients who have difficulty swallowing can benefit from this dosage form as it does not require water. Additionally, Oro dispersible tablets are easy to carry and offer precise dosing. Various techniques can be employed to produce Oro dispersible tablets based on their specific properties. Among these techniques, compaction is the most convenient and popular method.

Compaction can be achieved through different methods such as dry granulation, wet granulation, and direct compression. The crucial step involves mixing the active ingredient with a disintegrant, such as cross povidone, croscarmellose sodium, sodium alginate, or acrylic acid (Dey & Maiti, 2010)

The research and development process for Oro-dispersible tablets typically involves six phases: data and raw material sourcing, R&D lab scale, pilot scale, clinical study, registration, and process validation batch.

Table 6 Oro-dispersible tablet research and development processes and data source

Process	Information Source
Sourcing - drug selection - academic research - raw material sourcing - package material sourcing	Interview with experts
R&D lab scale - formulation development (FD) - lab scale production - analytical method development /validation - finished product specifications - preliminary stability study	Interview with experts
Pilot scale - pilot batch production - stability study	Interview with experts
Clinical study	
-Phase I	IMDS regulation guideline Interview with experts Literature review: What Are Clinical Trials and Studies? (National Institute on Aging, 2023)
-Phase II	IMDS regulation guideline (Thai food and drug administration, 2019) Interview with experts
-Phase III	
Registration	Interview with experts
Process validation batch	Interview with experts

The process of researching and developing oro-dispersible tablet dosage forms by the domestic pharmaceutical industry

1. New drugs launched:

Once new drugs from the originator are released to the market, they serve as important reference products for the development of new pharmaceutical products. These reference drugs must be approved by the Food and Drug Administration as new drugs.

2. Sourcing:

Local manufacturers interested in producing IMDs select the reference drug by considering various information such as marketing data, user needs, problems associated with drug use, sales figures, and patent information. They also consider the drug itself, the main raw materials, and suitable dosage forms for IMDs. The cost of this process, based on expert interviews, is approximately 0.6-0.7 million baht, and the duration is 9-15 months, depending on factors such as the availability of information and raw materials in the market.

3. R&D lab scale:

The research and development department conducts studies to develop suitable formulations for Oro-dispersible tablets at the lab scale. This includes the development of analytical methods specific to the drug form and the determination of finished product specifications (FPS). The cost of this process, obtained from expert interviews, is approximately 2.25-5.2 million baht. The duration ranges from 12 to 36 months and depends on various factors, such as the bitterness of the active ingredient, the drug's Biopharmaceutics Classification System (BCS) class, drug-excipient interactions, raw material prices, and the cost of analytical tools and labor.

4. Pilot batches production:

Upon successful research and development, pilot batches of the drug are produced, and stability studies, including shelf-life specifications, are conducted. The results are then reported to the Food and Drug Administration (FDA). The cost of this process, obtained from expert interviews, is about 9.5-17.5 million baht. The duration ranges from 12 to 36 months, depending on the availability and modification of equipment, as well as the increasing number of topics requiring analysis.

5. Non-clinical trial:

Oro-dispersible drugs, classified as new drug delivery systems, may not require additional non-clinical studies. Instead, data from the reference product can be referenced, provided that the original data is sufficient and consistent with currently accepted standards. Furthermore, the total amount of drug received by the body must not exceed the amount in the reference product.

6. Clinical trial:

Phase I

For oral dosage forms that cannot be swallowed as a whole, samples from the pilot batches are used to study the effect of food and unintentional swallowing on bio-efficacy through bioequivalence studies. The cost of this process, obtained from expert interviews and literature reviews, is approximately 3 million baht, with a duration of 12 months, depending on the sample size and recruitment time for the study.

Phase II and III

Phase II and III studies may not be necessary if reference product data is sufficient, unless there is a change in indication for a new group of patients. The cost of this process, obtained from expert interviews and literature reviews, is approximately 150-450 million baht. The duration is 24 months, depending on factors such as the number of participants, time required to gather the necessary sample size, the drug used in the study, and the type of study.

7. Process validation protocol development:

This process involves developing a validation protocol to validate the production process for subsequent distribution.

8. Registration:

The registration criteria for new drug formulas follow ASEAN Harmonization standards. The registration application for a new drug formulated using an existing original chemical drug consists of four parts: administration data and product information, quality document, safety (non-clinical) document, and efficacy (clinical) document. Non-clinical and clinical studies are prepared for the application, and the licensee can refer to clinical study recommendations and guidelines provided by the FDA. The cost of this process, obtained from expert interviews, is approximately 0.1 million baht, with a duration of 12 months or longer depending on the number of resolutions to be consulted and registered, including the government system.

9. Process validation batch:

After obtaining a registration number for the manufacture and sale of the drug from the FDA, the drug can be produced in commercial batches for sale, and process validation is performed on three batches. The results of the production process inspection are submitted to the FDA for consideration and permission to continue production and distribution. The cost of this process, based on expert interviews, is approximately three times the cost of pilot batches, ranging from 28.5 to 69 million baht. The duration is 3-5 months, depending on the difficulty or ease of production.

The financial feasibility study for the development of an oro-dispersible formulation from the original drug is conducted using scenario analysis in two scenarios based on the clinical study requirements for registration:

Scenario 1: Study Phase I Only

In this scenario, there is no need for non-clinical studies. Information can be referenced from the reference product as long as the original data is sufficient and consistent with currently accepted standards. The total amount of drug received by the body must not exceed the amount from the reference product. However, Phase I clinical studies are necessary to conduct bioequivalence studies for unintentional swallowing and to compare the effect of food on bioequivalence between the new drug and the reference drug. There is no need for Phase II-III clinical trials since the group of patients will not be altered.

Scenario 2: Necessary to Study Phase I-III

In this scenario, non-clinical studies are not required, and information can be referenced from the reference product similar to scenario 1. The original data must be sufficient and consistent with currently accepted standards, and the total amount of drug received by the body must not exceed the amount from the reference product. However, Phase I clinical studies are necessary to compare the bioavailability of the

new drug with the reference drug, including unintentional swallowing. In addition, Phase II-III clinical studies are required for this case to study the effects of the new drug in different populations, such as children or older individuals.

Table 7 Cost list and annual expense distribution according to the IMDs research and development process (Oro-dispersible tablet) in scenario 1

Time period	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**
Sourcing	0.6-0.7						
R&D lab scale		2.25-5.2					
Pilot scale			9.5-17.5				
Clinical study							
Phase I				3			
Registration						0.1	
Process validation batch							28.5-52.5

Table 8 Cost list and annual expense distribution according to the IMDs research and development process (Oro-dispersible tablet) in scenario 2

Time period	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	**Year 10**	**Year 11**
Sourcing	0.6-0.7										
R&D lab scale		2.25-5.2									
Pilot scale			9.5-17.5								
Clinical study											
Phase I				3							
Phase II						150					
Phase III								450			
Registration									0.1		
Process validation batch											28.5-52.5

Table 9 Cost list according to the different phases of product research and development processes

Process	Scenario 1 cost	Scenario 2 cost
Sourcing	0.6-0.7	0.6-0.7
R&D lab scale	2.25-5.2	52.25-5.2
Pilot scale	9.5-17.5	9.5-17.5
Clinical study		
-Phase I	3	3
-Phase II		150
-Phase III		450
Registration	0.1	0.1
Process validation batch	28.5-52.5	28.5-52.5
Total	43.95-79	643.95-679

Based on the information provided in Table 9, it was found that the research and development of IMDs oro-dispersible tablets took approximately 7 years in the case of only Phase 1 clinical trials and around 11 years to complete Phase 1-3 clinical studies. In comparison, the development of new generic drugs typically ranges from 25 to 46 months(Liangrokapart et al., 2013) . The extended duration in developing oro- dispersible tablets can be attributed to the formulation development needed to mask the bitterness of drugs and achieve appropriate disintegration time. Additionally, the sourcing of raw materials, which is crucial in clinical studies involving a new drug, adds to the duration. Furthermore, studying the effects of food and unintentional swallowing is necessary in these cases. Moreover, in scenario 2, there is a need to study the drug's effects in new populations, such as older people or children, which may require longer periods to complete all phases of clinical trials.

The development of IMDs in the form of oro-dispersible drugs incurs fixed costs ranging from 43.95 to 79 million baht for scenario 1 and 643.95 to 679 million baht for scenario 2, respectively. In comparison, the cost of research and development of new generic drugs ranges from 6.5 to 39.5 million baht(Liangrokapart et al., 2013). The higher costs of developing oro-dispersible drugs are mainly due to the reasons mentioned earlier. The majority of the cost in scenario 1 is invested in process validation batches, which is the final step before commercialization and requires three consecutive production cycles, resulting in high capital requirements depending on the complexities of production. Conversely, this process takes the shortest time as it occurs just before the drug's launch, and the manufacturing methods and related factors are more stable.

In scenario 2, the majority of the cost and time of drug development is allocated to clinical trial studies, which are essential for proving the efficacy and safety of the new drug in a new group of populations. Therefore, factors such as the type of study, processes studied, sample size, and the type of drug can all influence research and development costs. It is evident that investment in new drug development from existing chemical drugs incurs high costs. The data used in the feasibility analysis represent the cost of drug formulation development and are expressed as the income that entrepreneurs should be able to generate to achieve the capitalization point. The feasibility depends on investor considerations, such as the payback period, the nature of the business group, the drugs produced, and the research and development capabilities of the investors

Results of a financial feasibility study on research and development of IMDs produced by the domestic pharmaceutical industry in the form of oro-dispersible tablets.

The feasibility study results of this study show in terms of income that investors should be able to achieve in order to achieve capital gains.

Base case

Payback period: 5 years.

Year	**1**	**2**	**3**	**4**	**5**
Sales growth rate	**0**	100%	100%	50%	50%

Income that investors should be able to make in order to make back the capital invested.

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1 Time for research and development: 7 years Research and development: 43.95 million baht						
Income (millions baht)		6.05	12.09	24.18	36.28	54.42
Scenario 2 Time for research and development: 11 years. Research and development: 643.95 million baht						
Income (millions baht)		104.95	209.89	419.78	629.68	944.52

The income in both scenarios exhibits a noticeable upward trend over the 5-year timeframe. In Scenario 1, the income steadily rises from 6.05 million baht in year 1 to 54.42 million baht in year 5. Conversely, Scenario 2, characterized by a larger initial investment and an extended research and development period, demonstrates more significant income growth, ranging from 104.95 million baht in year 1 to 944.52 million baht in year 5.

Sensitivity analysis

1. Payback period of 10 years

Year	1	2	3	4	5	6	7	8	9	10
Sales growth rate	0	100%	100%	50%	50%	30%	25%	25%	25%	25%

Income that investors should be able to make in order to make back the capital invested.

Year	1	2	3	4	5	6	7	8	9	10
Scenario 1 Time for research and development: 7 years Research and development: 43.95 million baht										
Income (millions baht)	1.26	2.52	5.04	7.56	11.35	14.75	18.44	23.05	28.81	36.01
Scenario 2 Time for research and development: 11 years. Research and development: 643.95 million baht										
Income (millions baht)	21.67	43.34	86.67	130.01	195.01	253.51	316.89	396.12	495.15	618.93

When analyzing investors' payback period, it has been noted that longer payback periods often lead to a lower capitalization point. This means that the annual income required by operators to achieve the desired return on investment is reduced compared to shorter payback periods.

2. Period of research and development

Scenario 1 Payback period of 5 years Research and development: 43.95 million baht						
Period of research and development being 5 years						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		5.91	11.81	23.62	35.43	53.15
Period of research and development being 10 years						
Income (millions baht)		7.80	15.60	31.20	46.81	70.21
Scenario 2 Payback period of 5 years Research and development: 643.95 million baht						
Period of research and development being 10 years						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		98.55	197.09	394.18	591.28	886.92
Period of research and development being 15 years						
Income (millions baht)		144.88	289.76	579.52	869.27	1,303.91

Based on the information provided in the table above, it is clear that with a research and development duration of 10 years in scenario 1 and 15 years in scenario 2, the annual income required by investors will be higher compared to a shorter timeframe. This also implies a larger investment needed.

3. Research and development costs

Scenario 1 Time for research and development: 7 years Payback period of 5 years **Research and development: 79 million baht**						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		10.93	21.85	43.71	65.56	98.34
Scenario 2 Time for research and development: 11 years Payback period of 5 years **Research and development: 679 million baht**						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		110.19	220.39	440.77	661.16	991.74

When it comes to formula development, employing intricate analysis methods poses a significant risk of failure, and there are several aspects that demand additional development, such as complex clinical and manufacturing studies. Investing in research and development under these circumstances may require a larger capital investment. As a result, investors must generate adequate returns to achieve a higher capitalization point.

4. Growth rate

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1 Time for research and development: 7 years Research and development: 50.95 million baht						
100% in year 2		6.05	12.09	24.18	36.28	54.42
200% in year 2		4.01	12.02	24.05	36.07	54.11
300% in year 2		2.74	10.96	21.93	32.89	49.34
50% in year 5		6.05	12.09	24.18	36.28	54.42
100% in year 5		4.90	9.81	19.61	29.42	58.84
150% in year 5		4.01	8.02	16.03	24.05	60.12
Scenario 2 Time for research and development: 11 years. Research and development: 650.95 million baht						
100% in year 2		104.95	209.89	419.78	629.68	944.52
200% in year 2		69.57	208.72	417.43	626.15	939.22
300% in year 2		47.58	190.30	380.61	570.91	856.37
50% in year 5		104.95	209.89	419.78	629.68	944.52
100% in year 5		85.10	170.21	340.42	510.63	1021.26
150% in year 5		69.57	139.14	278.29	417.43	1043.58

If the growth rate increases by 100% in year 2, the income that investors should make in year 1 will decrease by approximately 1.5 times for both scenarios, and the following years seem to exhibit minor variations. However, a 3-times increase in the growth rate in year 2 has a more substantial impact on reducing income. Moreover, a 50% increase in the growth rate in year 5 significantly lowers the income in the first year in scenario 2 but only slightly alters it in scenario 1. Nevertheless, the growth rate pattern relies on the drug category selected by investors and the prevailing drug market conditions.

Financial feasibility study of nasal spray dosage form

Nasal spray is a solution or suspension product that contains a specific device for delivering drugs through the nasal cavity. This form is mostly found in drugs for nasal-related diseases, such as allergic rhinitis and stuffy nose, as well as other systemic diseases. The nasal delivery system not only allows rapid absorption but also provides a fast onset, benefiting drugs used for pain treatment. Moreover, nasal sprays can avoid gastric enzymes, making them suitable for delivering proteins or hormones to the body (Ehrick et al., 2013)

There are 7 phases in the research and development of nasal sprays, which include data and raw materials sourcing, R&D at a lab scale, pilot scale production, non-clinical studies, clinical studies, registration, and process validation batches.

Table 10 nasal spray research and development processes and data source

Process	Information Source
Sourcing - drug selection - academic research - raw material sourcing - package material sourcing	Interview with experts
R&D lab scale - formulation development (FD) - lab scale production - analytical method development /validation - performance test - finished product specifications - preliminary stability study	Interview with experts
Pilot scale - pilot batch production - stability study	Interview with experts
Non-clinical -Pharmacodynamic - Pharmacokinetics - Toxicity	IMDS regulation guideline (Thai food and drug administration, 2019) Interview with experts Literature review (Stergiopoulos et al., 2013)
Clinical study	
-Phase I	IMDS regulation guideline (Thai food and drug administration, 2019) Interview with experts
-Phase II	IMDS regulation guideline (Thai food and drug administration, 2019) Interview with experts Literature review: What Are Clinical Trials and Studies? (National Institute on Aging, 2023)
-Phase III	

Process	Information Source
	Estimated Costs of Pivotal Trials for Novel Therapeutic Agents Approved by the US Food and Drug Administration (Moore et al., 2018)
Registration	Interview with experts
Process validation batch	Interview with experts

The process of researching and developing nasal spray dosage forms by the domestic pharmaceutical industry

1. New drugs launched:

After the originator's new drugs have been released to the market, which are products containing important drugs used as references in the development of new pharmaceutical products, they must be important chemical drugs approved by the Food and Drug Administration for registration as new drugs.

2. Sourcing:

Local manufacturers wishing to produce IMDs select the reference drug by considering information such as marketing information, the needs of drug users, problems encountered from drug use, sales, and patent information. This applies to both the drug itself and the raw materials that are the main components of the drug, as well as the suitable dosage forms of IMDs. The cost of this process, obtained from interviews with experts, is about 0.6-0.7 million baht, and the duration is 9-15 months, depending on the difficulty of finding information, related wages, finding available raw materials and devices in the market, and the availability of existing information.

3. R&D lab scale:

The research and development department conducts studies to develop suitable formulations for nasal sprays at the lab scale production. This includes the development of an appropriate analytical method for the drug form and determining the specifications of the finished product. Additionally, an analytical method for the nasal spray device should be developed, as well as a performance test. The cost of developing a nasal spray is not different from developing a solution or suspension, but the challenge lies in generating an appropriate analytical method and performance test for the device to ensure consistency of droplets and the capability to deliver to the target site. Some parts of the analytical method will be sent abroad due to the lack of facilities in domestic labs. These factors influence the cost and duration. The cost of the performance test abroad, obtained from expert interviews, is approximately 0.15 million baht per process. However, if the industry invests in its own equipment, the cost will be approximately 20 million baht. The duration is 12-18 months and depends on the complexity of the formula and analytical process.

4. Pilot batch production:

When drug research and development is successful, pilot batch production begins, and stability studies, including shelf-life specifications, are conducted. The results are reported to the Food and Drug Administration (FDA). The duration is 18-24 months.

5. Non-clinical trial:

Nasal spray is classified as a new route of administration. Non-clinical studies, including pharmacokinetics and toxicity, are required. Pharmacological data from the reference product can be used as a reference. The cost of this process, obtained from literature review, is about 5.5-7.3 million baht, and the duration is 12 months, depending on the duration of toxicology studies, which may require chronic toxicity outcomes. These studies may not be conducted within domestic toxicology labs.

6. Clinical trial:

For drugs with a new route of administration, a full clinical trial must be conducted due to changes in pharmacological, pharmacokinetic, and toxicological outcomes. These studies can be waived if there is sufficient supporting data. The cost

of this process, obtained from expert interviews and literature reviews, is approximately 150-450 million baht, and it takes 24 months, depending on the sample size and the time it takes to recruit participants for the study, including the drugs being studied.

7. Process validation protocol development:

This is the process of developing a validation protocol to be used in validating the production process in subsequent production processes for further distribution.

8. Registration:

The criteria for registration of new drug formulas through ASEAN Harmonization will be used. The documents used in the application for the registration of a new drug with an existing original chemical drug consist of four parts: Administration data and product information, Quality document, Safety (non-clinical document), and Efficacy (clinical document). Non-clinical study data and clinical study preparation are required for the registration application of the six previously approved active drug formulations (IMDs), which include drugs with new formulations, drugs with new drug delivery systems, drugs with new dosing ports, drugs with new indications, drug formulations with new combinations, and drugs with new potency. The licensee can refer to clinical study recommendations and guidelines. The cost of this process, obtained from expert interviews, is 0.1 million baht, and the duration is 12 months or longer, depending on the number of consultations and registrations, including the government system.

9. Process validation batch:

After registering and obtaining a registration number for the manufacture and sale of drugs from the Food and Drug Administration, the drug can be produced in the commercial batch production process, and process validation is conducted for three batches. The results of the inspection of the production process are submitted to the Food and Drug Administration for consideration and permission to continue production and distribution. The cost of this part, obtained from expert interviews, is approximately three times the cost of pilot batches, 34.5 million baht, and the duration is 3-5 months, depending on the difficulty or ease of production.

The financial feasibility study for the development of a nasal spray formulation from the original drug is conducted using scenario analysis in two scenarios, based on the clinical study requirements for registration:

Scenario 1: Non-clinical and clinical studies are conducted, except for the pharmacology effect. In this scenario, there is no need for pharmacology non-clinical studies since the data can be referred to from the information of the reference product. However, the original data must be sufficient and consistent with currently accepted standards. It is important to ensure that the total amount of drug received by the body is not higher than the amount of drug from the reference product. Nevertheless, pharmacokinetics and toxicity studies are required because the route of administration has been changed.

Scenario 2: Non-clinical and clinical studies are required due to a change in route of administration and insufficient evidence support. In this scenario, both non-clinical and clinical studies need to be conducted. The change in route of administration necessitates these studies, and there is not enough existing evidence to support the registration of the nasal spray formulation.

Table 11 Cost list and annual expense distribution according to the IMDs research and development process (Nasal spray) in scenario 1

Time period	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	**Year 10**
Sourcing	5.75									
R&D lab scale		5.75								
Pilot scale			5.75							
Non-clinical study					5.5					
Clinical study										
Phase I						15	15			
Phase II								75	75	
Phase III										225
Registration										
Process validation batch										

Table 12 Cost list and annual expense distribution according to the IMDs research and development process (Nasal spray) in scenario 2

Time period	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**	**Year 6**	**Year 7**	**Year 8**	**Year 9**	**Year 10**
Sourcing	5.75									
R&D lab scale		5.75								
Pilot scale			5.75							
Non-clinical study					7.3					
Clinical study										
Phase I						15	15			
Phase II								75	75	
Phase III										225
Registration										
Process validation batch										

Table 13 Cost list according to the different phases of product research and development processes

Process	Scenario 1 cost	Scenario 2 cost
Sourcing	23	23
R&D lab scale		
Pilot scale		
Non-clinical study	5.5	7.3
Clinical study		
-Phase I	30	30
-Phase II	150	150
-Phase III	450	450
Registration	0.1	0.1
Process validation batch	34.5	34.5
Total	693.1	694.9

Based on the information provided in Tables 13 regarding the research and development of IMDs nasal spray, it was observed that the research and development process took approximately 13 years, whereas for new generic drugs, it ranged from 25 to 46 months(Liangrokapart et al., 2013). The longer duration in developing nasal spray formulations may be attributed to the need for developing new formulas and analytical methods for both the drugs and the delivery devices. Additionally, certain analytical methods may not be available in domestic laboratories, necessitating their development abroad, as mentioned earlier. This scenario highlights the need for conducting non-clinical and clinical studies to confirm the efficacy, safety, and precision of drug delivery to the target site.

The development of new drugs in the form of nasal sprays from existing chemical drugs incurs fixed costs of approximately 693.1-694.9 million baht, in comparison to the research and development costs of new generic drugs, which range from 6.5 to 39.5 million baht(Liangrokapart et al., 2013). Most of the cost and time involved in drug development, in both scenarios, is attributed to the clinical trial studies. This is primarily due to the change in route of administration, which can alter the pharmacological, pharmacokinetic, and toxicological effects of the previous products. Therefore, the complexity of the study, the processes involved, the sample size, and the type of drugs can significantly influence the research and development costs.

It is evident that investment in the development of new drugs from existing chemical drugs incurs high costs. The data used in the feasibility analysis represent the cost of drug formulation development and are expressed as the income that entrepreneurs should be able to generate in order to achieve the capitalization point. The feasibility of such investment depends on factors such as the investor's consideration of the payback period, the nature of the business group, the drugs being produced, and the research and development capabilities of the investors.

Results of a financial feasibility study on research and development of IMDs produced by the domestic pharmaceutical industry in the form of nasal spray.

The feasibility study results of this study show in terms of income that investors should be able to achieve in order to achieve capital gains.

Base case

Payback period: 5 years.

The feasibility study results of this study show in terms of income that investors should be able to achieve in order to achieve capital gains.

Base case

Payback period: 5 years.

Year	**1**	**2**	**3**	**4**	**5**
Sales growth rate	**0**	100%	100%	50%	50%

Income that investors should be able to make in order to make back the capital invested.

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1 Time for research and development: 13 years Research and development: 693.1 million baht						
Income (millions baht)		109.42	218.85	437.70	656.54	984.81
Scenario 2 Time for research and development: 13 years. Research and development: 694.9 million baht						
Income (millions baht)		109.60	219.20	438.39	657.59	986.38

Both scenarios involve the same research and development duration of 13 years, and the cost of research and development is also comparable. The income increases gradually from year 1 to year 5 in both cases. The income figures in both scenarios are very close to each other for each corresponding year, and the difference in income between the two scenarios is relatively small.

Sensitivity analysis

1. Payback period of 10 years

Year	1	2	3	4	5	6	7	8	9	10
Sales growth rate	0	100%	100%	50%	50%	30%	25%	25%	25%	25%

Income that investors should be able to make in order to make back the capital invested.

Year	1	2	3	4	5	6	7	8	9	10
Scenario 1 Time for research and development: 13 years Research and development: 693.1 million baht										
Income (millions baht)	24.82	49.64	99.27	148.91	223.37	290.37	362.97	453.71	567.14	708.92
Scenario 2 Time for research and development: 13 years. Research and development: 694.9 million baht										
Income (millions baht)	25.02	50.04	100.09	150.13	225.20	292.75	365.94	457.43	571.79	714.73

When examining the payback period for investors, it has been observed that longer payback periods typically result in a lower capitalization point. This implies that the annual income required by operators to achieve the desired return on investment is diminished compared to shorter payback periods.

2. Period of research and development

Scenario 1 Payback period of 5 years Research and development: 693.1 million baht						
Period of research and development being 10 years						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		106.98	213.97	427.94	641.90	962.86
Period of research and development being 15 years						
Income (millions baht)		142.11	284.22	568.44	852.66	1,278.99
Scenario 2 Payback period of 5 years Research and development: 694.9 million baht						
Period of research and development being 10 years						
Year	**0**	**1**	**2**	**3**	**4**	**5**
Income (millions baht)		107.46	214.92	429.85	644.77	967.15
Period of research and development being 15 years						
Income (millions baht)		142.66	285.33	570.66	855.99	1,283.98

From the table above, it is evident that for a 15-year research and development period, the annual income required for investors will be higher compared to a shorter period. This indicates a higher investment as well. Consequently, if entrepreneurs possess the ability to conduct research and develop drugs at a faster pace, they can save on their investment costs and increase the likelihood of successfully developing these drugs.

3. Growth rate

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1 Time for research and development: 7 years Research and development: 50.95 million baht						
100% in year 2		109.42	218.85	437.70	656.54	984.81
200% in year 2		72.54	217.62	435.24	652.86	979.29
300% in year 2		49.61	198.42	396.85	595.27	892.91
50% in year 5		109.42	218.85	437.70	656.54	984.81
100% in year 5		88.74	177.47	354.94	532.41	1064.83
150% in year 5		72.54	145.08	290.16	435.24	1088.10
Scenario 2 Time for research and development: 11 years. Research and development: 650.95 million baht						
100% in year 2		109.60	219.20	438.39	657.59	986.38
200% in year 2		72.66	217.97	435.93	653.90	980.85
300% in year 2		49.68	198.74	397.48	596.22	894.33
50% in year 5		109.60	219.20	438.39	657.59	986.38
100% in year 5		88.88	177.75	355.51	533.26	1066.52
150% in year 5		72.66	145.31	290.62	435.93	1089.83

If the growth rate in year 2 increases by 100%, it will lead to a decrease of around 1.5 times in the income that investors should expect to make in year 1 for both scenarios. Subsequently, the following years exhibit minor variations. However, if the growth rate in year 2 increases by 3 times, it will have a more substantial impact on reducing income. Additionally, a 50% increase in the growth rate in year 5 significantly decreases the income in the first year for both scenarios, but the change is only around 1.2 times. Nevertheless, it is important to note that the growth rate pattern depends on the drug category chosen by investors and the prevailing conditions of the drug market.

Table 14 comparing the cost and duration of investment between three dosage forms.

Process	Sustained release	Oro-dispersible tablet	Nasal spray
Sourcing	0.6-0.7	0.6-0.7	23
R&D lab scale	2.25-5.2	2.25-5.2	
Pilot scale	9.5-23	9.5-17.5	
Non-clinical study			5.5-7.3
Clinical study			
-Phase I	10	3	30
-Phase II	150	150	150
-Phase III	450	450	450
Registration	0.1	0.1	0.1
Process validation batch	28.5-69	28.5-52.5	34.5
Total	50.95-708	43.95-679	693.1-694.9

The cost and duration of investment for different dosage forms vary significantly, and this variation is influenced by various factors, including formulation complexity, manufacturing processes, and regulatory requirements. These factors play a crucial role in determining the overall investment needed and the time required for the development and production of each dosage form. As a result, each dosage form may present unique challenges and opportunities for investors, necessitating careful consideration of these factors before making investment decisions.

CHAPTER V
DISCUSSION AND CONCLUSION

This study took a unique approach in conducting a financial feasibility analysis, distinct from conventional financial models that rely on net present value, internal rate of return, or payback period. Instead, the study model centered around four pivotal constructs: the total cost for IMDs development, the expected payback period, the projected growth rate, and the potential revenue that investors could generate to reach the break-even point or achieve profitability.

Specifically, the analysis was conducted at the higher technology dosage form level, with a focus on sustained-release tablets, oro-dispersible tablets, and nasal sprays. These particular dosage forms were chosen based on their market preference, as indicated by a prediction market in a previous study. However, it's crucial to acknowledge that these dosage forms may vary in their active ingredients, which makes it challenging to estimate sales revenue and market growth without precise information about the specific active ingredient being developed for the studied drug form.

To maintain consistency in the analysis, certain variables associated with drug type, such as the cost of goods sold and operational expenses, were identified as constants and compared at the dosage form level. Nevertheless, it is important to recognize that these variables may differ based on the specific type of drug under development.

The chosen methodology in this study proves suitable for analyzing the financial aspects of new drugs or innovations despite limited data availability. To strengthen the reliability of the limited data, the triangulation method was employed, enhancing the validity and credibility of the findings.

New delivery system: Sustained release tablets and Oro dispersible

The results of each scenario show that the investment required for research and development of sustained release tablets and oro dispersible tablets is relatively high, and the duration of development is longer compared to new generic drugs(Liangrokapart et al., 2013).

The majority of this investment is attributed to conducting clinical studies for registration, drug selection, and ensuring the sufficiency of data to confirm efficacy and safety. If clinical studies are not sufficient, additional studies must be conducted.

In cases where only phase I clinical trials are required, a significant portion of the investment will be allocated to process validation batches, which involve larger production scales before the product is launched into the market, rather than towards clinical studies. Conversely, if a full clinical trial is necessary, the majority of the investment will be allocated to this phase. The investment amount can vary depending on factors such as the study method, duration, number of participants, and specific characteristics of the drug being developed.

When comparing the two scenarios, significant differences in capital requirements can be observed. Financial feasibility considerations may also depend on the entrepreneur's ability to invest and generate income.

New route of administration: Nasal spray

The analysis of investment in nasal spray also reveals higher costs and longer time periods compared to new generic drugs, as well as sustained release tablets and oro dispersible tablets in the context of IMDs(Liangrokapart et al., 2013). The majority of this investment is allocated to conducting non-clinical and clinical studies for registration, drug selection, and ensuring the sufficiency of data to confirm efficacy and safety. In scenario 1, where pharmacology studies are not required, the investment may be lower compared to scenario 2, which necessitates full non-clinical and clinical trials. Costs are influenced by various factors such as the study method, duration, number of participants, and specific characteristics of the drug. Comparing the two scenarios, there may be slight differences in capital requirements, particularly because non-clinical pharmacology studies involve relatively smaller investments compared to other processes. Financial feasibility considerations also depend on the entrepreneur's ability to invest and generate income.

The key findings of the financial and investment decision analysis of IMDs by the domestic pharmaceutical industry are as follows:

1. Clinical Study:

Clinical studies play a crucial role in drug development, but they also contribute significantly to its overall cost. Challenges, such as limited clinical data from reference products and complexities associated with different types of Incrementally Modified Drugs (IMDs), along with drug properties like pharmacodynamics, pharmacokinetics, and toxicity, can drive up the investment required for this phase. Consequently, this cost burden can impact investors' decisions and hinder the development of new drugs in the domestic pharmaceutical industry.

When it is not feasible to bridge clinical study data from a previous product to support the development of a new drug, conducting a clinical study becomes imperative. In such cases, an alternative strategy could involve considering clinical trials in countries with high overall country attractiveness indices, such as China, India, and Russia. By doing so, the aim is to expedite the drug's path to the market, ultimately accelerating the return on investment and potentially gaining a competitive edge over other market players.(Bailey et al.)

2. Duration of Research and Development, including Clinical Study and Registration Process:

The development of Incrementally Modified Drugs (IMDs) in the domestic industry is still relatively new, and this can result in longer development times, leading to increased costs. One key factor contributing to this extended duration is the limited knowledge and expertise within the domestic industry and related organizations. Additionally, the conduction of clinical trials and challenges in the registration system can also add to the overall time required for IMD development. To mitigate these challenges and shorten the development duration, it is essential to focus on building capacity among all stakeholders involved in the process. Strengthening expertise and knowledge within the domestic industry can expedite the development process and lead to more efficient outcomes.

Furthermore, it is crucial to recognize that the research and development process for IMDs should commence early during the originator branded product's lifecycle. Since IMDs development can be time-consuming, starting the R&D process early ensures that there is sufficient time for thorough research, testing, and regulatory processes.

3. Drug Selection:

The process of selecting suitable drugs for IMDs development involves a careful consideration of various factors, including financial aspects, patient needs, scientific and technological feasibility, as well as legal and registration feasibility. It is crucial to acknowledge that not every drug can be formulated into every dosage form, making the drug selection process a significant factor influencing investment decisions.

Several key elements come into play during the drug selection process. Existing competitors in the market and the expected payback period that the pharmaceutical industry can accept play crucial roles in determining the feasibility of a drug for IMD development. For instance, drugs like antibiotics may require shorter payback periods due to the potential emergence of drug resistance, while drugs used to treat chronic diseases or orphan drugs may allow for longer payback periods.In this context, selecting drugs with longer life cycles and those that already possess sufficient existing data for bridging can be more feasible investment choices. These drugs are more likely to have sustainable market demand and provide a higher chance of success in the development process.

4. Market Feasibility and Selling Opportunities:

Due to the high investment required to reach the capital breakeven point and generate profits, entrepreneurs need to consider the market feasibility and potential sales opportunities for IMDs. The presence of generic drugs and new generics as competitors in the market adds complexity. In order to promote the adoption of IMDs, government and associated organizations can play a role by proposing supportive policies. As well as supporting exportation policies. Collaborative efforts involving the public and private sectors are crucial for the sustainable development of the domestic pharmaceutical industry.

These common factors highlight the involvement of not only the domestic pharmaceutical industry but also other organizations in both the public and private sectors, which can contribute to the formulation of policies aimed at supporting the sustainable development of the domestic industry

Policy recommendation

As previously mentioned, the participation of not only the domestic pharmaceutical industry but also other organizations from both the public and private sectors can play a vital role in formulating policies to support the sustainable development of the domestic industry.

The study results clearly demonstrate that the extended period and high costs of research and development (R&D) significantly impact the revenue that investors should aim to generate. Consequently, the proposed policy recommendations aim to address and support these factors effectively:

1. Offer incentives and support for conducting clinical studies, particularly for IMDs, to alleviate the financial burden on pharmaceutical companies. These incentives may take the form of grants, tax benefits, or expedited regulatory processes.

2. Establish comprehensive capacity-building programs to enhance expertise within the domestic pharmaceutical industry and related organizations. These programs should focus on improving proficiency in research and development processes, conducting efficient clinical trials, and navigating regulatory procedures. By implementing such initiatives, the duration of IMDs development can be reduced, resulting in cost savings.

3. Facilitate collaboration between the public and private sectors to ensure investors can generate sufficient revenue to cover the capital investment. A key focus of this collaboration should be on promoting the exportation of IMDs, thereby expanding market opportunities and driving economic growth within the domestic pharmaceutical industry.

By adopting and implementing these policy recommendations, the government and associated organizations can establish an enabling environment for the development of IMDs, fostering innovation, reducing costs, and ensuring the long-term sustainability of the domestic pharmaceutical industry.

Limitations of study

1. Assumption:

The study's hypothesis is based on investing in new drug development for companies with existing business and technologies. It does not account for the initial investment required for research and development.

2. Costing method:

Since no IMDs has been successfully registered yet, there is no actual investment data available. The estimated costs in this study are categorized by function due to limited access to financial data.

Suggestion for future research

The study adopts an industrial perspective, aiming to encourage the pharmaceutical industry to invest more in IMDs to build competitive advantages. However, to comprehensively assess the development of IMDs and its societal impact, future research should consider a broader societal perspective.

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Appendix

Table 15 Base case analysis for sustained release dosage form scenario 1

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**6,993,247.39**	**13,986,494.79**	**27,972,989.57**	**41,959,484.36**	**62,939,226.53**
Gross profit		5,594,597.91	11,189,195.83	22,378,391.66	33,567,587.48	50,351,381.23
Profit Before Tax		3,996,141.37	7,992,282.73	15,984,565.47	23,976,848.20	35,965,272.31
Net Profit		3,330,117.81	6,660,235.61	13,320,471.22	19,980,706.84	29,971,060.25
Total PV Payback	**65,307,052.15**	3,233,124.08	6,277,910.84	12,190,118.14	17,752,599.23	25,853,299.85

Table 16 Base case analysis for sustained release dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**105,438,089.11**	**210,876,178.22**	**421,752,356.44**	**632,628,534.66**	**948,942,801.99**
Gross profit		84,350,471.29	168,700,942.58	337,401,885.15	506,102,827.73	759,154,241.59
ProfitBeforeTax		60,250,336.63	120,500,673.27	241,001,346.54	361,502,019.81	542,253,029.71
NetProfit		50,208,613.86	100,417,227.72	200,834,455.45	301,251,683.17	451,877,524.76
Total PV Payback	**984,642,812.90**	48,746,227.05	94,652,868.06	183,791,976.81	267,658,218.66	389,793,522.32

Table 17 10 years payback period analysis for sustained release dosage form scenario 1

Year	0	1	2	3	4	5	6	7	
Revenue		**1,465,170.19**	**2,930,340.38**	**5,860,680.75**	**8,791,021.13**	**13,186,531.69**	**17,142,491.20**	**21,428,114.00**	**26**
Gross profit		1,172,136.15	2,344,272.30	4,688,544.60	7,032,816.90	10,549,225.35	13,713,992.96	17,142,491.20	21
ProfitBeforeTax		837,240.11	1,674,480.21	3,348,960.43	5,023,440.64	7,535,160.97	9,795,709.26	12,244,636.57	15
NetProfit		697,700.09	1,395,400.18	2,790,800.36	4,186,200.54	6,279,300.80	8,163,091.05	10,203,863.81	12
Total PV Payback	**65,933,290.51**	677,378.73	1,315,298.50	2,553,977.67	3,719,384.96	5,416,580.03	6,836,460.24	8,296,675.04	10

Table 18 10 years payback period analysis for sustained release dosage form scenario 2

Year	0	1	2	3	4	5	6	7
Revenue		**21,898,008.74**	**43,796,017.49**	**87,592,034.98**	**131,388,052.46**	**197,082,078.70**	**256,206,702.31**	**320,258,377.88**
Gross profit		17,518,407.00	35,036,813.99	70,073,627.98	105,110,441.97	157,665,662.96	204,965,361.85	256,206,702.31
ProfitBeforeTax		12,513,147.85	25,026,295.71	50,052,591.42	75,078,887.12	112,618,330.68	146,403,829.89	183,004,787.36
NetProfit		10,427,623.21	20,855,246.42	41,710,492.85	62,565,739.27	93,848,608.90	122,003,191.57	152,503,989.47
Total PV Payback	**985,419,840.11**	10,123,906.03	19,658,069.96	38,171,009.64	55,588,848.98	80,954,634.44	102,175,752.21	123,999,699.28

Table 19 5 years of research and development analysis for sustained release dosage form scenario 1

Year	0	1	2	3	4	5
Revenue		**6,454,477.08**	**12,908,954.17**	**25,817,908.34**	**38,726,862.51**	**58,090,293.76**
Gross profit		5,163,581.67	10,327,163.33	20,654,326.67	30,981,490.00	46,472,235.01
ProfitBeforeTax		3,688,272.62	7,376,545.24	14,753,090.48	22,129,635.72	33,194,453.58
NetProfit		3,073,560.52	6,147,121.03	12,294,242.07	18,441,363.10	27,662,044.65
Total PV Payback	**60,275,698.52**	2,984,039.34	5,794,251.14	11,250,973.08	16,384,912.26	23,861,522.71
NPV	**5,789,817.03**					

Table 20 10 years of research and development analysis for sustained release dosage form scenario 1

Year	0	1	2	3	4	5
Revenue		**9,074,530.91**	**18,149,061.83**	**36,298,123.66**	**54,447,185.49**	**81,670,778.23**
Gross profit		7,259,624.73	14,519,249.46	29,038,498.93	43,557,748.39	65,336,622.58
ProfitBeforeTax		5,185,446.24	10,370,892.47	20,741,784.95	31,112,677.42	46,669,016.13
NetProfit		4,321,205.20	8,642,410.39	17,284,820.79	25,927,231.18	38,890,846.78
Total PV Payback	**84,743,300.27**	4,195,344.85	8,146,300.68	15,818,059.58	23,036,009.10	33,547,586.06
NPV	**8,140,066.65**					

Table 21 10 years of research and development analysis for sustained release dosage form scenario 2

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**99,660,637.76**	**199,321,275.52**	**398,642,551.04**	**597,963,826.57**	**896,945,739.85**
Gross profit		79,728,510.21	159,457,020.42	318,914,040.84	478,371,061.25	717,556,591.88
ProfitBeforeTax		56,948,935.86	113,897,871.73	227,795,743.45	341,693,615.18	512,540,422.77
NetProfit		47,457,446.55	94,914,893.11	189,829,786.21	284,744,679.32	427,117,018.98
Total PV Payback	**930,689,578.40**	46,075,190.83	89,466,389.96	173,721,145.55	252,991,959.54	368,434,892.53
NPV	**89,397,924.93**					

Table 22 15 years of research and development analysis for sustained release dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**146,724,480.67**	**293,448,961.34**	**586,897,922.68**	**880,346,884.02**	**1,320,520,326.04**
Gross profit		117,379,584.54	234,759,169.07	469,518,338.15	704,277,507.22	1,056,416,260.83
ProfitBeforeTax		83,842,560.38	167,685,120.77	335,370,241.53	503,055,362.30	754,583,043.45
NetProfit		69,868,800.32	139,737,600.64	279,475,201.28	419,212,801.92	628,819,202.87
Total PV Payback	**1,370,199,389.89**	67,833,786.72	131,716,090.71	255,759,399.44	372,465,144.82	542,424,968.19

Table 23 Research and development maximum cost analysis for sustained release dosage form scenario 1

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**14,860,650.71**	**29,721,301.42**	**59,442,602.84**	**89,163,904.26**	**133,745,856.39**
Gross profit		11,888,520.57	23,777,041.14	47,554,082.27	71,331,123.41	106,996,685.11
ProfitBeforeTax		8,491,800.41	16,983,600.81	33,967,201.62	50,950,802.43	76,426,203.65
NetProfit		7,076,500.34	14,153,000.68	28,306,001.35	42,459,002.03	63,688,503.04
Total PV Payback	**138,777,485.82**	6,870,388.68	13,340,560.54	25,904,001.05	37,724,273.37	54,938,262.19
NPV	**13,330,351.54**					

Table 24 Research and development maximum cost analysis for sustained release dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**114,784,855.95**	**229,569,711.90**	**459,139,423.81**	**688,709,135.71**	**1,033,063,703.56**
Gross profit		91,827,884.76	183,655,769.52	367,311,539.05	550,967,308.57	826,450,962.85
ProfitBeforeTax		65,591,346.26	131,182,692.52	262,365,385.03	393,548,077.55	590,322,116.32
NetProfit		54,659,455.22	109,318,910.43	218,637,820.86	327,956,731.29	491,935,096.94
Total PV Payback	**1,071,928,412.18**	53,067,432.25	103,043,557.76	200,084,578.18	291,385,308.03	424,347,535.96

Table 25 Growth rate sensitivity analysis of oro-dispersible tablet.

Year	0	1	2	3	4	5
Scenario 1						
100% in year 2		6,993,247.39	13,986,494.79	27,972,989.57	41,959,484.36	62,939,226.53
200% in year 2		4,636,022.50	13,908,067.49	27,816,134.98	41,724,202.47	62,586,303.70
300% in year 2		3,170,312.33	12,681,249.30	25,362,498.60	38,043,747.90	57,065,621.85
50% in year 5		6,993,247.39	13,986,494.79	27,972,989.57	41,959,484.36	62,939,226.53
100% in year 5		5,671,078.24	11,342,156.48	22,684,312.97	34,026,469.45	68,052,938.90
150% in year 5		4,636,022.50	9,272,044.99	18,544,089.99	27,816,134.98	69,540,337.45
Scenario 2						
100% in year 2		105,438,089.11	210,876,178.22	421,752,356.44	632,628,534.66	948,942,801.99
200% in year 2		69,897,906.60	209,693,719.81	419,387,439.62	629,081,159.43	943,621,739.15
300% in year 2		47,799,206.10	191,196,824.41	382,393,648.81	573,590,473.22	860,385,709.83
50% in year 5		105,438,089.11	210,876,178.22	421,752,356.44	632,628,534.66	948,942,801.99
100% in year 5		39,957,305.20	159,829,220.81	319,658,441.62	479,487,662.43	958,975,324.86
150% in year 5		33,626,926.94	134,507,707.76	269,015,415.52	403,523,123.28	1,008,807,808.21

Table 26 Base case analysis for oro-dispersible tablet dosage form scenario 1

Year	0	1	2	3	4	5

Revenue		**6,046,245.14**	**12,092,490.28**	**24,184,980.57**	**36,277,470.85**	**54,416,206.27**
Gross profit		4,836,996.11	9,673,992.23	19,347,984.45	29,021,976.68	43,532,965.02
ProfitBeforeTax		3,454,997.22	6,909,994.45	13,819,988.90	20,729,983.34	31,094,975.01
NetProfit		2,879,164.35	5,758,328.71	11,516,657.41	17,274,986.12	25,912,479.18
Payback Contribution	**(51,039,765.42)**	**2,879,164.35**	**5,758,328.71**	**11,516,657.41**	**17,274,986.12**	**25,912,479.18**

Table 27 Base case analysis for oro-dispersible tablet dosage form scenario 2

Year	**0**	**1**	**2**	**3**	**4**	**5**

Revenue		**104,946,154.01**	**209,892,308.03**	**419,784,616.05**	**629,676,924.08**	**944,515,386.12**
Gross profit		83,956,923.21	167,913,846.42	335,827,692.84	503,741,539.26	755,612,308.89
ProfitBeforeTax		59,969,230.86	119,938,461.73	239,876,923.46	359,815,385.19	539,723,077.78
NetProfit		49,974,359.05	99,948,718.11	199,897,436.22	299,846,154.32	449,769,231.48
Total PV Payback	**980,048,833.99**	48,518,795.20	94,211,252.81	182,934,471.48	266,409,424.48	387,974,890.02

Table 28 10 years payback period analysis for oro-dispersible tablet dosage form scenario 1

Year	0	1	2	3	4	5	6	7	
Revenue		**1,260,727.84**	**2,521,455.67**	**5,042,911.34**	**7,564,367.02**	**11,346,550.52**	**14,750,515.68**	**18,438,144.60**	**23,0**
Gross profit		1,008,582.27	2,017,164.54	4,034,329.08	6,051,493.61	9,077,240.42	11,800,412.54	14,750,515.68	18,4
ProfitBeforeTax		720,415.91	1,440,831.81	2,881,663.63	4,322,495.44	6,483,743.16	8,428,866.10	10,536,082.63	13,1
NetProfit		600,346.59	1,200,693.18	2,401,386.35	3,602,079.53	5,403,119.30	7,024,055.09	8,780,068.86	10,9
Total PV Payback	**56,733,296.49**	582,860.77	1,131,768.48	2,197,608.69	3,200,401.01	4,660,778.17	5,882,535.55	7,138,999.46	8,6

	0	1	2	3	4	5	6	7	8	9
		21,667,907.08	**43,335,814.15**	**86,671,628.30**	**130,007,442.46**	**195,011,163.68**	**253,514,512.79**	**316,893,140.99**	**396,116,426.23**	**495,145,532**
		17,334,325.66	34,668,651.32	69,337,302.64	104,005,953.97	156,008,930.95	202,811,610.23	253,514,512.79	316,893,140.99	396,116,426
ax		12,381,661.19	24,763,322.37	49,526,644.75	74,289,967.12	111,434,950.68	144,865,435.88	181,081,794.85	226,352,243.56	282,940,304
		10,318,050.99	20,636,101.98	41,272,203.95	61,908,305.93	92,862,458.90	120,721,196.57	150,901,495.71	188,626,869.64	235,783,587
	975,065,165.79	10,017,525.23	19,451,505.30	37,769,913.21	55,004,727.98	80,103,972.78	101,102,101.57	122,696,725.21	148,903,792.73	180,708,486

Table 29 10 years payback period analysis for oro-dispersible tablet dosage form scenario 2

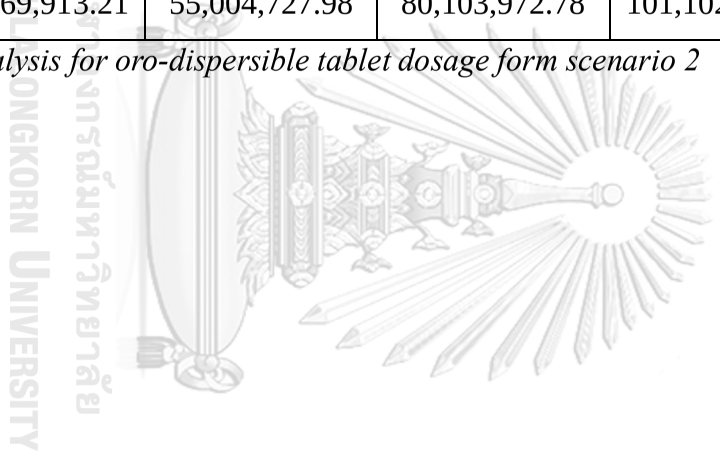

Table 30 5 years of research and development analysis of oro-dispersible tablet dosage form scenario 1

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**5,905,159.89**	**11,810,319.77**	**23,620,639.54**	**35,430,959.31**	**53,146,438.97**
Gross profit		4,724,127.91	9,448,255.82	18,896,511.63	28,344,767.45	42,517,151.18
ProfitBeforeTax		3,374,377.08	6,748,754.15	13,497,508.31	20,246,262.46	30,369,393.70
NetProfit		2,811,980.90	5,623,961.80	11,247,923.59	16,871,885.39	25,307,828.08
Total PV Payback	**55,145,851.84**	2,730,078.54	5,301,123.38	10,293,443.46	14,990,451.64	21,830,754.82

Table 3110 years of research and development analysis of oro-dispersible tablet dosage form scenario 1

Year	0	1	2	3	4	5
Revenue		**7,800,912.54**	**15,601,825.08**	**31,203,650.16**	**46,805,475.24**	**70,208,212.86**
Gross profit		6,240,730.03	12,481,460.06	24,962,920.13	37,444,380.19	56,166,570.29
ProfitBeforeTax		4,457,664.31	8,915,328.62	17,830,657.24	26,745,985.85	40,118,978.78
NetProfit		3,714,720.26	7,429,440.51	14,858,881.03	22,288,321.54	33,432,482.32
Total PV Payback	**72,849,503.74**	3,606,524.52	7,002,960.24	13,597,981.04	19,802,885.01	28,839,152.93

Table 32 10 years of research and development analysis of oro-dispersible tablet dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**98,546,221.68**	**197,092,443.37**	**394,184,886.74**	**591,277,330.10**	**886,915,995.15**
Gross profit		78,836,977.35	157,673,954.69	315,347,909.39	473,021,864.08	709,532,796.12
ProfitBeforeTax		56,312,126.68	112,624,253.35	225,248,506.71	337,872,760.06	506,809,140.09
NetProfit		46,926,772.23	93,853,544.46	187,707,088.92	281,560,633.38	422,340,950.07
Total PV Payback	**920,282,506.44**	45,559,973.04	88,465,967.07	171,778,576.83	250,162,975.96	364,315,013.54

Table 33 15 years of research and development analysis of oro-dispersible tablet dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**144,878,889.72**	**289,757,779.44**	**579,515,558.87**	**869,273,338.31**	**1,303,910,007.47**
Gross profit		115,903,111.77	231,806,223.55	463,612,447.10	695,418,670.65	1,043,128,005.97
ProfitBeforeTax		82,787,936.98	165,575,873.96	331,151,747.93	496,727,621.89	745,091,432.84
NetProfit		68,989,947.49	137,979,894.97	275,959,789.94	413,939,684.91	620,909,527.37
Total PV Payback	**1,352,964,177.44**	66,980,531.54	130,059,284.54	252,542,300.08	367,780,048.66	535,602,012.61

Table 34 Research and development maximum cost analysis of oro-dispersible tablet dosage form scenario 1

Year	0	1	2	3	4	5
Revenue		**10,926,949.05**	**21,853,898.10**	**43,707,796.20**	**65,561,694.31**	**98,342,541.46**
Gross profit		8,741,559.24	17,483,118.48	34,966,236.96	52,449,355.45	78,674,033.17
ProfitBeforeTax		6,243,970.89	12,487,941.77	24,975,883.55	37,463,825.32	56,195,737.98
NetProfit		5,203,309.07	10,406,618.14	20,813,236.29	31,219,854.43	46,829,781.65
Total PV Payback	**102,042,268.98**	5,051,756.38	9,809,235.69	19,047,059.59	27,738,436.30	40,395,781.02

Table 35 Research and development maximum cost analysis of oro-dispersible tablet dosage form scenario 2

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**110,193,461.71**	**220,386,923.43**	**440,773,846.85**	**661,160,770.28**	**991,741,155.42**
Gross profit		88,154,769.37	176,309,538.74	352,619,077.48	528,928,616.23	793,392,924.34
ProfitBeforeTax		62,967,692.41	125,935,384.82	251,870,769.63	377,806,154.45	566,709,231.67
NetProfit		52,473,077.01	104,946,154.01	209,892,308.03	314,838,462.04	472,257,693.06
Total PV Payback	**1,029,051,275.69**	50,944,734.96	98,921,815.45	192,081,195.05	279,729,895.71	407,373,634.53

Table 36 Growth rate sensitivity analysis of sustained released.

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1						
100% in year 2		6,046,245.14	12,092,490.28	24,184,980.57	36,277,470.85	54,416,206.27
200% in year 2		4,008,227.78	12,024,683.35	24,049,366.70	36,074,050.05	54,111,075.08
300% in year 2		2,740,999.20	10,963,996.79	21,927,993.58	32,891,990.37	49,337,985.56
50% in year 5		6,046,245.14	12,092,490.28	24,184,980.57	36,277,470.85	54,416,206.27
100% in year 5		4,903,119.73	9,806,239.46	19,612,478.92	29,418,718.38	58,837,436.75
150% in year 5		4,008,227.78	8,016,455.57	16,032,911.13	24,049,366.70	60,123,416.75
Scenario 2						
100% in year 2		104,946,154.01	209,892,308.03	419,784,616.05	629,676,924.08	944,515,386.12
200% in year 2		69,571,788.84	208,715,366.53	417,430,733.06	626,146,099.59	939,219,149.39
300% in year 2		47,576,192.70	190,304,770.79	380,609,541.59	570,914,312.38	856,371,468.57
50% in year 5		104,946,154.01	209,892,308.03	419,784,616.05	629,676,924.08	944,515,386.12
100% in year 5		85,104,646.97	170,209,293.94	340,418,587.88	510,627,881.82	1,021,255,763.65
150% in year 5		69,571,788.84	139,143,577.69	278,287,155.37	417,430,733.06	1,043,576,832.65

Table 37 Base case analysis of nasal spray dosage form scenario 1

Year	0	1	2	3	4	5
Revenue		**109,423,763.66**	**218,847,527.33**	**437,695,054.65**	**656,542,581.98**	**984,813,872.97**
Gross profit		87,539,010.93	175,078,021.86	350,156,043.72	525,234,065.58	787,851,098.37
ProfitBeforeTax		62,527,864.95	125,055,729.90	250,111,459.80	375,167,189.70	562,750,784.55
NetProfit		52,106,554.13	104,213,108.25	208,426,216.50	312,639,324.75	468,958,987.13
Total PV Payback	**1,021,863,383.16**	50,588,887.50	98,230,849.52	190,739,513.62	277,775,990.71	404,528,141.81

Table 38 Base case analysis of nasal spray dosage form scenario 2

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**109,597,728.31**	**219,195,456.62**	**438,390,913.24**	**657,586,369.87**	**986,379,554.80**
Gross profit		87,678,182.65	175,356,365.30	350,712,730.60	526,069,095.89	789,103,643.84
ProfitBeforeTax		62,627,273.32	125,254,546.64	250,509,093.28	375,763,639.92	563,645,459.89
NetProfit		52,189,394.43	104,378,788.87	208,757,577.74	313,136,366.60	469,704,549.91
Total PV Payback	**1,023,487,967.23**	50,669,314.98	98,387,019.39	191,042,756.09	278,217,605.96	405,171,270.81

Table 39 10 years payback period analysis of nasal spray dosage form scenario 1

Year	0	1	2	3	4	5	6	7	
Revenue		**24,818,344.06**	**49,636,688.13**	**99,273,376.26**	**148,910,064.39**	**223,365,096.58**	**290,374,625.55**	**362,968,281.94**	**4**
Gross profit		19,854,675.25	39,709,350.50	79,418,701.01	119,128,051.51	178,692,077.26	232,299,700.44	290,374,625.55	3
ProfitBeforeTax		14,181,910.89	28,363,821.79	56,727,643.58	85,091,465.36	127,637,198.05	165,928,357.46	207,410,446.82	2
NetProfit		11,818,259.08	23,636,518.16	47,273,036.31	70,909,554.47	106,364,331.70	138,273,631.22	172,842,039.02	2
Total PV Payback	**1,116,836,189.33**	11,474,037.94	22,279,685.32	43,261,524.89	63,002,220.72	91,750,806.87	115,801,989.26	140,536,394.73	1

Table 40 10 years payback period analysis of nasal spray dosage form scenario 2

Year	0	1	2	3	4	5	6	7	
Revenue		**25,021,773.11**	**50,043,546.23**	**100,087,092.46**	**150,130,638.68**	**225,195,958.03**	**292,754,745.44**	**365,943,431.79**	**4**
Gross profit		20,017,418.49	40,034,836.98	80,069,673.97	120,104,510.95	180,156,766.42	234,203,796.35	292,754,745.44	3
ProfitBeforeTax		14,298,156.07	28,596,312.13	57,192,624.26	85,788,936.39	128,683,404.59	167,288,425.96	209,110,532.45	2
NetProfit		11,915,130.05	23,830,260.11	47,660,520.22	71,490,780.33	107,236,170.49	139,407,021.64	174,258,777.04	2
Total PV Payback	**1,125,990,584.33**	11,568,087.43	22,462,305.69	43,616,127.56	63,518,632.37	92,502,862.67	116,751,185.89	141,688,332.39	1

Table 41 10 years of research and development analysis of nasal spray dosage form scenario 1

Year	**0**	**1**	**2**	**3**	**4**	**5**
Revenue		**106,983,943.41**	**213,967,886.82**	**427,935,773.65**	**641,903,660.47**	**962,855,490.70**
Gross profit		85,587,154.73	171,174,309.46	342,348,618.92	513,522,928.37	770,284,392.56
ProfitBeforeTax		61,133,681.95	122,267,363.90	244,534,727.80	366,802,091.70	550,203,137.54
NetProfit		50,944,734.96	101,889,469.92	203,778,939.83	305,668,409.75	458,502,614.62
Total PV Payback	**999,078,908.44**	49,460,907.73	96,040,597.53	186,486,597.14	271,582,423.02	395,508,383.03

Table 42 15 years of research and development analysis of nasal spray dosage form scenario 1

Year	0	1	2	3	4	5
Revenue		**142,110,503.29**	**284,221,006.58**	**568,442,013.16**	**852,663,019.75**	**1,278,994,529.62**
Gross profit		113,688,402.63	227,376,805.27	454,753,610.53	682,130,415.80	1,023,195,623.70
ProfitBeforeTax		81,206,001.88	162,412,003.76	324,824,007.52	487,236,011.28	730,854,016.93
NetProfit		67,671,668.23	135,343,336.47	270,686,672.94	406,030,009.40	609,045,014.10
Total PV Payback	**1,327,111,358.76**	65,700,648.77	127,574,075.28	247,716,651.03	360,752,404.42	525,367,579.25

Table 43 10 years of research and development analysis of nasal spray dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**107,461,550.30**	**214,923,100.60**	**429,846,201.21**	**644,769,301.81**	**967,153,952.71**
Gross profit		85,969,240.24	171,938,480.48	343,876,960.96	515,815,441.45	773,723,162.17
ProfitBeforeTax		61,406,600.17	122,813,200.34	245,626,400.69	368,439,601.03	552,659,401.55
NetProfit		51,172,166.81	102,344,333.62	204,688,667.24	307,033,000.86	460,549,501.29
Total PV Payback	**1,003,539,082.14**	49,681,715.35	96,469,350.19	187,319,126.59	272,794,844.55	397,274,045.46

Table 44 15 years of research and development analysis of nasal spray dosage form scenario 2

Year	0	1	2	3	4	5
Revenue		**142,664,180.58**	**285,328,361.15**	**570,656,722.31**	**855,985,083.46**	**1,283,977,625.19**
Gross profit		114,131,344.46	228,262,688.92	456,525,377.84	684,788,066.77	1,027,182,100.15
ProfitBeforeTax		81,522,388.90	163,044,777.80	326,089,555.60	489,134,333.41	733,701,500.11
NetProfit		67,935,324.08	135,870,648.17	271,741,296.34	407,611,944.50	611,417,916.76
Total PV Payback	**1,332,281,922.49**	65,956,625.32	128,071,117.13	248,681,780.84	362,157,933.27	527,414,465.92

Table 45 Growth rate sensitivity analysis of nasal spray

Year	**0**	**1**	**2**	**3**	**4**	**5**
Scenario 1						
100% in year 2		6,046,245.14	12,092,490.28	24,184,980.57	36,277,470.85	54,416,206.27
200% in year 2		4,008,227.78	12,024,683.35	24,049,366.70	36,074,050.05	54,111,075.08
300% in year 2		2,740,999.20	10,963,996.79	21,927,993.58	32,891,990.37	49,337,985.56
50% in year 5		6,046,245.14	12,092,490.28	24,184,980.57	36,277,470.85	54,416,206.27
100% in year 5		4,903,119.73	9,806,239.46	19,612,478.92	29,418,718.38	58,837,436.75
150% in year 5		4,008,227.78	8,016,455.57	16,032,911.13	24,049,366.70	60,123,416.75
Scenario 2						
100% in year 2		109,597,728.31	219,195,456.62	438,390,913.24	657,586,369.87	986,379,554.80
200% in year 2		72,655,449.68	217,966,349.03	435,932,698.07	653,899,047.10	980,848,570.65
300% in year 2		49,684,933.10	198,739,732.41	397,479,464.81	596,219,197.22	894,328,795.83
50% in year 5		109,597,728.31	219,195,456.62	438,390,913.24	657,586,369.87	986,379,554.80
100% in year 5		88,876,777.47	177,753,554.94	355,507,109.89	533,260,664.83	1,066,521,329.66
150% in year 5		72,655,449.68	145,310,899.36	290,621,798.71	435,932,698.07	1,089,831,745.17

REFERENCES

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