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From Molecule to Market: A Comprehensive Review of the Drug Product Development Process

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ABATRACT:

New product development (NPD) is one of the many tactics used in today's competitive world to deal with the ever-changing environment. Nevertheless, nearly half of the funds that businesses invest in NPD go towards potentially unsuccessful innovations.

The pharmaceutical business is especially affected by this problem, mostly because to its lengthy development period, poor success rate, high capital needs, and unstable market. Through the analysis of 50 completed questionnaires structured using the Analytical Hierarchy Process (AHP) approach, this study determines the critical success factors of NPD based on pertinent literature and expert opinions in the Iranian pharmaceutical industry. These factors are then prioritised using the multiple criteria decision making (MCDM) methodology. Although the NPD success factors seem the same in both generic and bio-generic pharmaceutical businesses, the underlying determinants and related sub-factors indicate the varied importance in these two industries. However, this study reveals that, the "corporate capabilities" is the most critical element determining new product development performance in both pharmaceutical generic and bio-generic industries. The results of this study contribute to generate baseline information for pharmaceutical industry especially Iranian pharmaceutical companies to be more effective in budget allocation on increasing NPD success factors so that they may improve the success rate of NPD more effectively.

KEY WORDS: New product development, bio-generic industries, unstable market, multiple criteria decision making.

INTRODUCTION:

Successful new product introduction, which is essential to a company's growth and development, calls for technological know-how and the capacity to turn it into worthwhile new items. Furthermore, supplementary resources are needed to support such products' production, promotion, sales, and distribution (20). Using the Analytical Hierarchy Process (AHP) approach on 50 filled-out questionnaires, this study seeks to identify and rank the essential success criteria of NPD in the Iranian pharmaceutical business, including both generic and biogeneric pharmaceutical enterprises.
There are also significant distinctions between generic and bio-generic pharmaceutical companies in terms of NPD, including the time and money spent on product development. It takes a long time for a biologic product to meet the necessary standards to be introduced to the market since biogeneric firms have lengthier clinical phases and longer regulatory approval timeframes, whereas generic companies are exempt from these requirements.

CONCEPTUAL STRUCTURE:

Numerous studies address the success elements of developing new products. According to earlier research, some success variables include senior managers' dedication to the development of new products, skilled teams, appropriate internal and external connections and communications, an innovative culture, and appropriate marketing support.

Success factors for new product development:

- Human capital
- Intellectual capital
- Organisational capital
- Relation capital
- Organisation learning capability

Organisational capital comprises a company's capacity for launch, marketing, forecasting, and information gathering.

FACTORS PERTAINING TO THE COMPANY:

- According to the research, management commitment to NPD initiatives and managerial talents are two crucial company-related elements that contribute to NPD success.
  The research also discusses adaptability across disciplines and top managers' supportive approaches to innovation as NPD success factors.
- The next two company-related elements for NPD performance are tangible and intangible assets. Intangible assets are currently receiving increased attention as a crucial component of innovation success. Human capital, organisational capital, relational capital, and organisational learning are all considered forms of intangible capital. Employee behaviour, knowledge, and experience make up human capital and help businesses create new, profitable goods. Organisational culture and its capacity for creativity and output are indicated by organisational capital. It is created by combining and coordinating many resources, is rooted on organisational procedures, and often consists of marketing, manufacturing, and innovation skills. Many organisations have been focussing more on their social ties with their various stakeholder groups in recent years.
- The resource-based view of the company holds that the ability to generate products requires tangible assets. Thus, a substantial number of human resources, resource creation, testing, and launch are dedicated to NPD projects and their financial success. Furthermore, a company's ability to spend in project development has a significant impact on NPD.

FACTORS CONNECTED TO THE PRODUCT:

- Most products are created to meet the demands of consumers; but, in the case of medicines, stakeholders' interests in the health system should be taken into account rather than the needs of customers. As a result, one of the aspects associated to pharmaceuticals is the attribute of product health impact. Similarly, quality, a crucial component of any new product, is strictly managed in the pharmaceutical sector.

DRUG PRODUCT DEVELOPMENT:

Drug product development is a multi-step, intricate process that turns a promising novel medication into a product that is safe, effective, and commercially viable. It starts with discovery, in which researchers and experimenters find a possible new drug candidate.
After that, the candidate's pharmacokinetic and pharmacodynamic characteristics such as its absorption, distribution, metabolism, and excretion (ADME) are assessed. If the candidate has promise, it moves on to the Preclinical Development stage, when both in vitro and in vivo tests are conducted to evaluate its safety and effectiveness. After the candidate's development is reported to regulatory bodies like the FDA, an Investigational New Drug (IND) Application is filed to start human clinical trials.

There are three stages in the clinical development phase:

- **Phase 1** involves testing the drug's safety and tolerability in a small group of healthy volunteers
- **Phase 2** involves evaluating the drug's efficacy and side effects in a larger group of patients
- **Phase 3** involves confirming the drug's safety and efficacy in an even larger, more diverse population.

The drug's formulation, packaging, and Chemistry, Manufacturing, and Controls (CMC) are all finalised during clinical development. A New Drug Application (NDA) or Biologics License Application (BLA) is submitted for approval after regulatory bodies evaluate the data and determine that the medication is safe and effective.

DRUG PRODUCT DEVELOPMENT PROCESS:

Drug development frequently takes ten years.
It takes a very long time to develop novel, cutting-edge medications. The typical time from invention to market is 12 years, however it can take up to 30 years in more recent medical fields like gene therapy. Given the startling fact that only about 1 in 5000 novel compounds are accepted as pharmaceutical drugs by regulatory bodies such as the European Medicines Agency (EMA) in the EU or the Food and Drug Administration (FDA) in the US, many participants in the drug development industry would view the 12-year milestone as hopeful.

Drug development is divided into four stages:

- Market approval
- Clinical development
- Preclinical research
- Discovery.

DISCOVERY:

Duration: (2-5 years)
The journey begins with the discovery phase, where scientists identify a potential new medicine through target identification, high-throughput screening, and lead optimization. They use cutting-edge technologies like genomics, proteomics, and computer-aided design to select a candidate molecule with desirable properties.

Laboratory research and development is the first step in the discovery stage. Target molecules are identified by researchers as having the potential to cause or exacerbate a disease. Examples of these molecules include genes and proteins.

Following this, hundreds or even thousands of chemical or biological compounds are subjected to so-called in silico, or computer, testing to determine how well they interact with the target molecule or molecules and, consequently, the disease.

PRECLINICAL RESEARCH:

Duration: (2-3 years)

The pre-clinical research phase, which follows the discovery phase, involves testing the lead drugs in both in vitro and in vivo-experimental models that are as similar to human as possible. The most promising compounds become lead candidates after they have been thoroughly characterised.

Thorough safety testing is the most crucial component of preclinical research since it makes sure the candidate is safe before it can proceed with human clinical trials.

The preclinical and discovery phases together can take four to seven years. Developers will request approval to move forward with clinical, in-human, studies once the preclinical testing is over, if the findings support the researchers' hypotheses. Either a Clinical Trial Application (CTA) in the EU or an Investigational New Drug (IND) application in the US is used for this. After reviewing all of the information, the relevant regulatory body makes a decision regarding whether to authorise a move to the clinic.

CLINICAL DEVELOPMENT:

Duration:(6-8 years)

PHASE 1: SAFETY

The initial clinical study, a phase I study, which is the first study in humans, is started after regulatory and ethics committee approval. In order to ascertain if the candidate operates in the human body in the same manner as preclinical studies have suggested, the candidate is often evaluated on 20 to 80 healthy volunteers.

This time, the primary focus is on the substance's safety profile, or toxicity, in humans. Phase I involves testing the drug's absorption, duration of action in the body, and what a safe dosage is. It should be noted that women of childbearing age are typically excluded from phase I clinical trials for safety concerns. It can take up to a year to complete a phase I study.

PHASE 2: PROOF OF CONCEPT

Drug developers can request authorisation to proceed to phase II clinical development if phase I safety data are favourable. During this stage, the candidate is typically assessed on 100 to 300 individuals who have been diagnosed with the condition the candidate is meant to treat.

Here, safety and efficacy come together as the drug's minimum and maximum dosages are established for use in the following stage of development. Phase II can take up to two years on average.

PHASE 3: REGULATORY EVIDENCE:

Phase III is the following stage if phase II safety and effectiveness data are positive. This is the final stage of assessing a medication before asking pharmaceutical regulators for market approval. A phase III study typically enrols at least 1000 people, ensuring that sufficient data is collected to demonstrate the drug's safety for humans and expected therapeutic efficacy.

Any adverse effects that individuals may have been recorded and reported by researchers as part of the phase III trial. This implies that in order to ensure that those side effects are accurately evaluated, patients must be exposed to the medication for extended periods of time. Any adverse effects that are identified at this point are subsequently mentioned in the final product's package leaflet.

Phase III typically lasts between one and four years.

MARKET APPROVAL AND LAUNCH:

The procedure for registering drugs:

An application for market approval, known as a Marketing Authorisation Application (MAA) in the EU and a New Drug Application (NDA)/Biologics License Application (BLA) in the US, is filed if phases I–III show promising findings. These may consist of hundreds of thousands of pages of paperwork that summarise all the data gathered from the beginning of the discovery phase and in which the main investigator makes an argument for FDA and EMA approval.

Take note that certain new medications are classified as new molecular units (NMEs), which are active components that need an NME and NDA application and have not yet received FDA or other regulatory agency approval.

It may take many months to prepare the application materials, and it will take the authorities six to ten months to process the application.

The candidate, or drug as it is now known, is prepared for market release if the regulatory bodies accept an application. The principle and the prospective purchasers (government organisations or insurance firms, depending on the healthcare system) then start negotiating prices.

The procedure of negotiating prices might vary significantly between nations. In addition to adhering to certain EU regulations, EU member states may also have national regulations. The rules governing compensation are set at the national level in Sweden. Continue reading. In contrast, the United States does not involve the government in the price talks between private insurance companies and pharmaceutical corporations. Because of the system, medicine prices in the US are far higher than in Europe and Developed countries.

PHASE 4:MONITORING MARKETING AND SAFETY

Following a drug's approval for sale, regulatory bodies may want follow-up phase IV research. Data from clinical practice, or actual care units that treat patients, is gathered in order to accomplish this.

REGULATORY SUBMISSION AND APPROVAL PHASE:

Duration (1-2 years):
The sponsor submits a New Drug Application (NDA) or Marketing Authorisation Application (MAA) to regulatory bodies (such as the FDA and EMA) after Phase 3 trials are successfully completed. These organisations examine the submission to make sure the medication satisfies strict safety, efficacy, and quality requirements.

RECENT TRENDS IN DRUG PRODUCT DEVELOPMENT:

- **Personalised medicine** is becoming more and more significant as a result of technological and genetic research developments. This method entails customising care for each patient according to their own genetic profiles, surroundings, and prognoses.

- **Artificial Intelligence (AI):** By enhancing patient outcomes, expediting clinical trials, and optimising research, AI is transforming the drug development process. By 2025, the pharmaceutical sector is projected to invest $3 billion in AI-powered drug discovery.

- **Clinical Trials:** These are gaining popularity, particularly in the wake of the COVID-19 epidemic. This method offers real-time data, boosts patient engagement, and lessens the need for in-person site visits.

- **Digital Health Technologies:** Digital health technologies, such as wearable devices and mobile health apps, are transforming the way we approach healthcare. These technologies enable remote patient monitoring, improve patient outcomes, and enhance the drug development process.

- **Orphan Drugs for Rare Diseases:** There's a growing focus on developing orphan drugs for rare diseases. This trend is driven by advances in technology, increasing demand for personalized medicine, and government incentives.
- **Decentralized Clinical Trials:** Decentralized clinical trials are becoming more popular, allowing patients to participate in trials from the comfort of their own homes. This approach increases patient engagement, reduces costs, and provides more accurate data.

- **Globalization and Outsourcing:** The pharmaceutical industry is becoming increasingly global, with companies outsourcing manufacturing and development to contract research organizations (CROs) and contract development and manufacturing organizations (CDMOs).

- **Biopharmaceutical Market Expansion:** The biopharmaceutical market is expanding rapidly, driven by advances in biotechnology and increasing demand for personalized medicine. This trend is expected to continue, with the global biopharmaceutical market projected to grow significantly in the coming years.

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