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Categorization of drug development projects[1]

Abstract

The aim of the article is to develop a categorization of drug development projects based on the identified determinants of project management at different stages of the drug development process. The authors assumed that the factors influencing the success of drug development project management are diverse and depend on the level of advancement of research work. The concept of Technology Readiness Levels, which is well operationalized and applied in a wide range of industrial sectors, was used as a benchmark for assessing the maturity of projects. The complex, costly and multi-stage drug discovery and development process has been referred to Technology Readiness Levels. To define the determinants of drug development project management, empirical material collected through the observation of 140 meetings of teams implementing a total of 7 projects with different levels of development work was used. The presented research results can be used for the stratification of drug development projects, which – thanks to the use of appropriately selected project management methods – will enable better organization of the work of R&D centers in the biotechnology and pharmaceutical industries.

Keywords: drug development, technology readiness levels, research and development, project management, success factors, project categorization
JEL Classification: L23, M11, L65

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Introduction

Over the last 20 years, there has been an increase in spending on developing new therapies, but the number of drugs approved by regulatory agencies has remained steady [www.fda.gov; www.ema.europa.eu/en]. This decline in productivity within the pharmaceutical industry has prompted the analysis of factors influencing the process of medicine development and the identification of key success factors in drug discovery and development projects [Bode-Greuel et al., 2008, Bukowski et al., 2018]. Due to intense market competition, companies are reluctant to share knowledge and development methods, resulting in insufficient information in the literature regarding the productivity of drug development projects [Matthews et al., 2023]. Therefore, it is crucial to examine the factors that determine the productivity of project teams in the pharmaceutical industry in order to take appropriate actions that ensure the highest quality of healthcare system components, with a focus on patient well-being and the creation of safer medicines [Antonijevic, 2014].

Research and development (R&D) productivity can be defined as the relationship between the value generated by a drug, both commercially and medically, and the investments required to develop the medicine. In the literature, R&D productivity is described as the ability of research and development to transform investments, such as funding, human resources and know-how, into outcomes, such as the number of drugs approved or specific milestones [Paul et al., 2010].

The literature emphasizes the decrease in revenues resulting from patent expirations, which is associated with a decline in the number of truly innovative molecules recently approved by the regulatory agencies such as the Food and Drug Administration (FDA) or the European Medicines Agency (EMA) [Gonzales Pena et al., 2021]. On the one hand, an increase in regulatory requirements driven by safety and efficacy concerns has been observed, while on the other, issues related to data transparency and reproducibility have also emerged, leading to higher demands from regulatory agencies and increased costs of new medicines development. These two aspects are closely related and indicate a decline in the quality of reliable data within the drug discovery and development industry [Schuhmacher et al., 2022; Stadler, 2022].

The effectiveness of the realization and transition of projects to the next stages of the drug discovery and development process depends on the level of organization of the teams involved in research and implementation work, in particular on the configuration of the entire project management system – both at the level of a given organization and at the level of cooperation with its external partners [Kim et al., 2023; Teramae et al., 2020].

The aim of the article is to develop a categorization of drug development projects based on the identified determinants of project management at different stages of the drug development process. The authors imply that the factors influencing the success of drug development project management are diverse and their significance varies depending on the level of advancement

of the research work. The reference point for assessing the advancement of research work in this article is the concept of Technology Readiness Levels, which is well operationalized and applied in many industrial sectors.

A Technology Readiness Assessment (TRA) is a systematic and formalized process describing the maturity of developed technology or product. The implementation of TRA is a tool to weigh the maturity and mitigation of risks associated with technologies under development [Department of Defense United States of America, 2009]. Due to the nature of the drug discovery projects, its tremendous time and resource consumption, it seems reasonable to implement measurements allowing navigation of risks related to the projects under development to maintain data driven decisions on further funding and investment. TRA process refers to Technology Readiness Levels (TRLs) as a metric which can be used to navigate the speed of development of the asset and mitigate risks at each stage of the process. According to NASA, there are nine TRLs in general (www.nasa.gov).

The article defines 13 sets of factors that determine the effectiveness of drug development project management. The defined factors were related to the Technology Readiness Levels, which were then described from the perspective of the drug development process. A process-specific technology readiness system can be used to categorize projects in pharmaceutical R&D organizations and companies involved in the discovery, development and marketing of new medicines to adjust specific managerial and operational processes.

To meet the need of determining key productivity factors in project teams focused on drug discovery and development activities, authors conducted 140 observation of 7 projects in biotechnology company supported by the review of regulatory guidelines and standards. The aim of the study was to identify and analyse the areas of focus and practices to manage them, used in drug development to manage research projects at different levels of project advancement. Efforts were made to observe the key areas of work in research projects and their impact on the work of the project team. In addition, attempts were made to observe what factors, challenges and limitations are related to the drug development process and what factors are important for the success of such projects. The participants' behaviour, roles and levels of decision-making in the project, scientific and managerial competences, seniority, personality traits, organizational culture and the type and the form of project data were taken into account.

Drug development process

Innovative, new drugs which address unmet medical needs are the key value drivers of research-oriented companies of pharmaceutical industry [Schuhmacher et al., 2022]. Any drug research and development project can be considered as a long-lasting and highly complex process that requires the cooperation of multiple disciplines. The process typically consists of the four general stages [Chen, 2018; Ravina, 2011].

1. Basic research or pre-discovery (aimed at the new drug target identification and initial validation).
2. Drug discovery (focused on lead compound selection and optimization).
3. Preclinical development (to assess efficacy and safety in animal models).
4. Clinical trials (focused on assessment of safety and efficacy in humans) – all followed by the drug approval and marketing.

The process of discovering and developing a new drug is complex and the first step in the drug development process is usually target identification and validation. This is where drug development companies select a molecule (s), such as a gene or protein, to target with a drug. This is also where the drug developer confirms that the molecular target is actually involved with the disease in question. After testing multiple drug molecules, the drug development company chooses those that show promise. Target selection can be performed in several ways: internal characterization of the interesting molecule, collaboration with scientific units (outsourcing) and literature search [Chaguturu 2014].

After target selection, the next three steps of drug discovery and development take place – hit identification, hit confirmation and lead optimization. Hit identification is the stage where compounds which can reach the target are identified. This is the stage where big screening libraries are tested against the target or other approaches can be selected such as phenotypic screening or rational design. Hit confirmation (hit to lead, H2L) is related to the confirmation of the compounds found in various methods and ways to confirm that the company can work on the compounds. This process is time consuming and crucial due to its impact on the further discovery process [Fisher, et al., 2021].

Lead optimization is the final step before preclinical development, where the company works on few compounds which can potentially move into preclinical and clinical development. At this stage, compounds are tested in higher animal models to translate and confirm the results generated in vitro. If necessary, the chemical structures of lead compounds identified at this stage can be altered to improve their selectivity and specificity for a given target. For example, lead optimization in drug metabolism studies typically involves both in vitro and in vivo assays that assess the drug metabolism and pharmacokinetic (DMPK) properties. These studies are also used to identify potential safety concerns, and determine whether they need to be assessed in a higher throughput manner [Fisher et al., 2021].

Preclinical testing is work performed on the compound(s) selected as a potential clinical candidate(s). This means that all aspects related to chemical parameters of the active compound, as well as salts (formulations) which are used for administration, need to be tested. Here, most of biotech companies has to use external companies for the scale up production (differences between small and large scale in parameters and final compounds – purification, intermediates, solutions used, stability testing, etc.). Advanced in vitro and in vivo testing has to be performed as well. Tox studies in higher species such as dogs, rats or monkeys are particularly important, as studies, parameters and dosing regiments need to be translated into another species. In vitro testing examines the drug molecules' interactions in test tubes and

within the lab setting. In vivo testing involves testing the drug molecules in animal models and other living cell cultures. Although efficacy is beginning to be established here, safety is paramount, as no regulatory agency can let preclinical studies move into human trials without extensive safety data [Chaguturu, 2014].

The next step is to fill an investigational new drug application, which involves submitting an application to the FDA (Food and Drug Administration), before human clinical trials will begin. This is the point at which the regulatory agency examines the results of preclinical testing, looks at the side effects and other safety features of an experimental drug, examines the drug's chemical structure and how it's believed to work, and takes the first look at the manufacturing process of the drug. If the regulatory agency approves a drug developers' IND, the drug can move on to human trials. Clinical studies (human clinical testing) can be described as a four-phase process [Ng, 2015].

The first phase of clinical studies involves a relatively small group of healthy people, usually a dozen to a few dozen, and it is focused entirely on safety. During this stage of studies, it is checked how a drug is absorbed and eliminated from the body, what side effects it may cause and whether it brings the desired effect [Ng, 2015].

In the second phase of clinical studies, the number of patients increases from a few dozen to perhaps 100 or more patients, and the patients treated are no longer healthy volunteers but people with the disease in question. There is still a big focus on the safety, with short-term side effects closely monitored, however, an increasing emphasis is placed on whether the drug is working as expected and whether it improves the condition or not. The second phase of clinical studies also determines which dose (if several doses are tested, as is often the case) works best. If the experimental drug continues to look promising it moves on to late-stage studies [Chaguturu, 2014].

In the third phase, safety remains a priority, but efficacy starts to play a big role as well. Trials involve even more patients, perhaps from hundreds to thousands, and are by far the longest and the most expensive from the drug development process. This is also the stage at which drug developers start to think how they are going to ramp up production if the phase 3 results are promising. Assuming an experimental drug meets its primary endpoint and is demonstrated to be safe, the next step is to apply for its approval. The New Drug Application (NDA) document is prepared, containing all the research and safety data examined during each of previous steps. It is the basis for the regulatory agency to make a decision on the acceptance or rejection of the potential new drug to be used in human [Poduri, 2021].

After approval, the regulatory agency can request long-term safety studies to be conducted, whereby drug developers are required to submit regular reports detailing any adverse events associated with the drug. Even after approval, safety remains the top priority [Ng, 2015].

From start to finish, the entire drug development process usually takes about 10 to 15 years, leaving drug developers with around a decade or less of patent exclusivity for branded drugs once they make the way to market [Ng, 2015; Poduri, 2021].

Research method

The aim of the study is to gather information and define the factors influencing drug discovery and development project management at various stages of advancement. The organization, in which the research was conducted, has been engaged in research on new compounds with therapeutic potential for unmet medical needs for over 10 years and has experience in providing services to external entities. The company's activity focuses on projects developed individually or with the support or supervision of external partners. The company has its own R&D center located in a large city with extensive university facilities. Projects are carried out in a matrix structure. They are financed from internal resources, scientific cooperation with business and scientific institutions, as well as due to institutional grants. The organization is multicultural and multinational.

The method of participant observation was used to obtain empirical material. Participant observation provides an opportunity to learn more about the development of the phenomenon studied, decision-making and their motivations [Jemielniak, 2023]. Observation is a tool for many scientific studies, mainly those in which the main goal is to define characteristics, events, phenomena and facts in order to describe and interpret them [Cybulska, 2013; Sztumski, 2005; Szuchalska, 2020].

The observation was conducted openly, systematically and continuously from September 2021 to August 2022 through regular, passive participation in project meetings. Meetings were conducted in a stationary, remote or hybrid formula. During and after meetings, self-notes of observations were prepared. Notes taken by people directly involved in meetings were also used to collect data. A total of 140 meetings were held, related to the implementation of 7 projects. The data obtained from the observations were supplemented by the data contained in the documentation of analyzed projects.

Characteristics of the analyzed projects and teams

Table 2 presents the synthetic characteristics of the projects observed based on publicly available data. Projects concerned different phases of drug development. The table provides information on the technological readiness level (TRL) of projects studied, which is described in more detail in the next section of the article.

Table 2. Overview of the analyzed projects

Name of the project	No. of observations	Time from initiation of the project (in weeks)	TRL	No. of external competitive projects
A	24	84	2	8
B	16	133	2	12

Name of the project	No. of observations	Time from initiation of the project (in weeks)	TRL	No. of external competitive projects
C	10	309	4 or 5	>15
D	24	139	3	6
E	20	121	2	n/a
F	40	700	6 or 7	>10
G	6	121	1	n/a

Source: own elaboration.

A description of the projects for which the observation was conducted is presented below.

Project A: The molecular target of the project plays an important role in controlling DNA repair mechanisms. The project is at the stage of generating compounds that are active on a molecular target (hit compounds). The project is carrying out parallel basic research to determine the therapeutic potential of the molecular target and the development of molecules with therapeutic potential. The projects of competing companies are at a more advanced stage. Competing organizations include global pharmaceutical companies and biotechnology companies. The project is developed independently with the participation of commercial contractors.

Project B: The molecular target in this project simultaneously participates in the activation of the immune system and reduces the immunosuppressive microenvironment of the affected site. The project is developing molecules that stimulate the patient's immune system to self-diagnose the disease and sensitize the affected cells to immune attack. The project is developed independently with the participation of commercial contractors.

Project C: The molecular target of the project is involved in the body's innate immune response. It facilitates the recognition of patient-specific antigen, which should allow for the development of highly personalized therapy. The project uses two strategies – molecules for use alone and in combination with delivery technologies or other therapies. Competing projects are at more advanced levels of development – the most advanced competitor is at the stage of clinical trials. The level of advancement of competitive projects varies depending on the selected development strategy. The project is developed in cooperation with or at the request of partners with the participation of commercial contractors.

Project D: As part of the project, molecules exploiting the phenomenon of synthetic lethality are being developed. It refers to the simultaneous disruption of two or more genes, leading to the death of that cell or even the entire organism of which it is a part. The product of one of these genes is important for cell survival. Molecules are at the stage of lead compounds. The competitive environment includes early-stage clinical trials, pre-clinical and early development projects. The project is developed independently with the participation of commercial contractors.

Project E: The project is conducting fundamental work on a number of novel molecular targets in different therapeutic areas. The aim of the work is to verify and validate the work

on selected molecular targets from selected therapeutic areas viewpoint. Due to the very early stage of project development and the novelty of the approach, the competitive environment is varied or lacking in knowledge. The project is developed independently with the participation of commercial contractors and in scientific cooperation.

Project F: The project is in the phase of advanced clinical trials in various therapeutic areas. Translational work is also underway to determine the broader therapeutic potential of the molecule. The project is developed independently with the participation of commercial contractors and in scientific cooperation.

Project G: As part of the project, screening and scouting work is carried out in relation to the search for new projects from external entities that have development potential from the viewpoint of organization's scientific and business assumptions. The project is performed with internal resources.

Information on the projects described above was obtained during the meetings and based on publicly available data. In the project management system of the organization studied, four types of meetings are used in the work of drug development teams, i.e. core team meetings, research team management meetings, meetings as part of the so-called strategic project review and quarterly project meetings. As the observation took place during such meetings, a brief description of them is given below.

Core team meeting: a meeting of people directly involved in the research and tasks in the project. Meetings are held weekly or bi-weekly, depending on the project. Current activities in the project are discussed, short-term work is planned and results are reported. Meetings last about 90 minutes once a week for projects at the stage of leading relationships, and about 120 minutes once every two weeks for projects at the stage of hit relationships.

A meeting of the leadership of the research teams: the meeting takes place every 4–6 weeks and is consultative in nature. It is attended by department directors and those with the greatest research experience in drug development. It is used to discuss current challenges in the project andemerging results that have an impact on the scientific strategy of the project. The project team has a chance to discuss issues that are important for the success of the project with a more experienced body that is not involved in the day-to-day work on the project. Meetings last about 90 minutes every 5 weeks.

Strategic project review: the meeting is held every 2 weeks for projects in clinical trials and every 4 weeks for projects in earlier stages of development. It concerns strategic issues of the project that determine the further course of work on the project. The meeting is attended by selected senior executives, including board members, the scientific leader, the project manager, and representatives of the business development department. Meetings last 60 minutes for early stage projects and 120 minutes for clinical stage projects.

Quarterly project meetings: Meetings to summarize the progress of the project organized for all employees of the organization. During the meeting, the progress of the project, plans and challenges related to further development are discussed. During the meeting, participants have the opportunity to ask questions and share ideas. Meetings last about 60 minutes every quarter.

The information gathered during meetings described above and from publicly available sources, made it possible to identify the key areas of work in research projects and their impact on the effectiveness of project teams. In addition, the effort was made to identify factors, challenges and limitations associated with the drug development process and factors that are important for the success of such projects. The participants' behavior, their roles and levels of decision-making in the project, scientific and managerial competences, seniority, personality traits, organizational culture and the type and the form of project data were taken into account. During meetings, the attention was also paid to management practices applied at different levels of advancement of individual projects.

During project meetings, the type and the order of discussion of topics related to the project were noted. This made it possible to identify the leading and secondary topics that emerged during the design work. In addition, the way in which research results and information related to the project were presented was observed. It was observed who participates in the process of discussing the project and making decisions, how the process of planning, organizing, implementing and reviewing tasks related to the development of therapeutic compounds is carried out, which employees speak and how they communicate. In the course of the research, it was also recorded what tools and communication channels are used by the participants of meetings, what are the dynamics of project meetings, how long they last and whether the planned length of meetings is adequate to the needs of the project.

Analysis and summary

The data collected in the form of notes and reports from meetings of the project teams allowed to clarify the groups of factors that are important in management of drug development projects. There is no doubt that the implementation process and partial results of such projects are influenced by many interrelated factors. Therefore, after a preliminary analysis of all the data obtained, an attempt was made to re-categorize the material collected. In the course of analyses, 13 categories of factors that play a key role in the drug development process were identified andare synthetically described in Table 2.

Table 2. Determinants of drug development project management

Factors	Description
Economic	They concern the business aspects of the drug development, including the analysis of the profitability of launched research and development projects, the issue of selling rights to manufacture a drug, a drug entry to the market, marketing and competition.
Financial	They concern the preparation of the research budget, ensuring appropriate sources of financing for projects (the company's own funds, investors, grants) as well as financial risk analysis and cost control.
Organizational	They concern the division of roles, responsibilities and authorizations in project teams and communication processes between team members and other specialist units in the organization.
Managerial	They concern the skills, knowledge and competences of managers and project team members, in particular the ability of managers to support creativity and motivate employees.

cont. Table 2

Factors	Description
Legal	They concern obtaining licenses to work on biological material, licenses and approvals from bioethics agencies and other regulatory agencies, including the preparation of appropriate documentation.
Ethical	They concern ensuring the fairness and safety towards research participants, compliance with the regulations of bioethics committees and other guidelines, maintaining confidentiality and reliable presentation of research results.
Intellectual Property	They concern intellectual property rights, obtaining patents for new active substances, treatment methods or innovative technologies that enables commercialization, including the production and sale of products.
Infrastructure	They concern a complex system that includes laboratories, research centers, production facilities and academic institutions, as well as IT infrastructure and the provision of appropriate equipment.
Technical	They concern advanced methods used in molecular, genetic and drug chemistry research, which are necessary for the implementation of preclinical and clinical studies and production processes.
Technological	They concern know-how, i.e. skills and knowledge in drug development, the ability to identify potential therapeutic targets, drug design, analysis of molecular structures and understanding of biological mechanisms.
Collaborative	They concern commercial relations and cooperation with external partners with the use of various competences and resources, including undertaking joint initiatives and creating alliances with industry entities.
Scientific	They concern the exchange of knowledge between research institutions, in particular with academic centers, including the transfer of innovation technology from academic laboratories to the industrial sector.
Brand-related	They concern issues related to building a social trust and maintaining proper relations with investors, the scientific community, patients and other stakeholders.

Source: own elaboration.

Prepared categories of factors were then related to the Technology Readiness Levels. According to NASA, there are nine TRLs in general [www.nasa.gov].

TRL 1: basic principles observed and reported. The lowest level of technology readiness. Initial research work begins to be applied into development such as paper research studies on technology's basic properties.

TRL 2: technology concept and/or application formulated. At this stage basic scientific findings are collected and the first practical application can be invented. Data is speculative and may not be confirmed by any detailed analysis.

TRL 3: analytical and experimental critical function and/or characteristic proof of concept. Research and development activities are initiated, including laboratory studies, analytical work and studies to physically confirm analytical estimates. Work at this stage is not representative or integrated.

TRL 4: component and/or breadboard validation in a laboratory environment. Basic activities and components of the study are integrated and capable of working together, however, they are not defined as a potential work system for the project.

TRL 5: Component and/or breadboard validation in a relevant environment. The basic components of technology are integrated and can be tested in that form in a given environment.

TRL 6: System/subsystem model or prototype demonstration in a relevant environment. A representative model is tested in a relevant environment. Technology can be tested in a high fidelity simulated and well-defined operational environment.

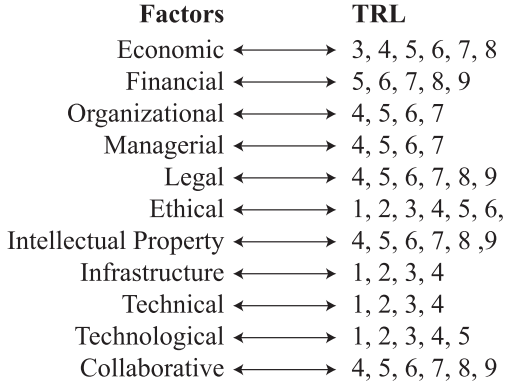
TRL 7: System prototype demonstration in an operational environment. Prototype close to, or at the planned operational system.

TRL 8: Actual system completed and qualified through testing and demonstration. The technology developed has been proven to work in its final form and under expected conditions.

TRL 9: Actual system proven through successful mission operations. Application of the technology in its final stage.

Groups of factors defined in Table 1 (determinants of drug development project management) play an important role at each technology readiness level. However, some of them are significantly critical at particular TRL levels. As the first step, an attempt was made to determine which Technology Readiness Levels are particularly related to the factors identified earlier. The results of the analysis are shown in Figure 1.

Figure 1. Linking determinants of drug development to technology readiness levels



Source: own elaboration.

Relationships presented in Figure 1 can be used to construct a system of indicators supporting the design of decision-making process at different stages of drug development. The identification of these relationships is also the basis for a more precise definition of different Technology Readiness Levels in relation to the drug development process.

Listed definitions provide a general understanding of TRL, therefore relevant parameters should be defined for each industry or a specific type of products. Substances and tools which are dedicated or related to any medical use require adjusted definitions of TRLs specific to the technology developed. In the medical field and drug development, the rate of risk reduction remains very low until very late.

The United States Army Medical Research and Materiel Command (USAMRMC) established appropriate definitions, descriptions, and processes in the context of military medical research and development that can be easily applied in the civil work in order to meet statutory and regulatory requirements ofthe Food and Drug administration (FDA) and the European Medicines Agency (EMA).

TRLs in a medical field outline a way to assess and communicate to the project management team the maturity level of developed technology. Biomedical TRL guidance has been provided by the U.S. Army Medical Research and Material Command and is based on practices

and generic definitions, regulations defined by regulatory agencies and common industry practices based on experience in R&D at all stages [Department of Defense United States of America, 2009; www.nasa.gov].

On the basis of the standards and guidelines presented above, as well as the results of own research, a nine-step categorization system for drug development projects has been developed, which directly refers to the well-described and widely used concept of Technology Readiness Levels. Different categories are described in Table 3.

Table 3. Categorization of drug development projects

Category	Characteristics of the project scope
1	Initial work focused on gaining the basic knowledge and overview of the scientific findings. At this stage scientific findings, including internally developed and external data, are reviewed and discussed for the characterization of a potential new technology. Publicly available data from scientific literature and publications are evaluated. Initial market analysis for potential use and application of the technology should be assessed. Activities can be performed by internal resources or by external qualified consultants or specialized companies. The novelty of the approach should be understood.
2	Intellectual work to generate research ideas and hypotheses for the topic to address related scientific issues. Work mainly performed to generate ideas and potentially applicable answers to the scientific issues. Initial hypotheses are defined and addressed by research plans and/or protocols developed, reviewed and approved by the team. Ongoing focused literature and competition reviews are conducted and followed by scientific discussions to adjust research plans and studies that identify potential opportunities for intervention. Initial supporting analyses are performed to deliver scientific data for further research proposals. Protocols and plans for the further work are approved. First targeted molecular profile (TMP) draft should be prepared.
3	Basic research activities and generation of data is ongoing, additional analysis begin to test previously defined hypothesis, navigate alternative concepts, and identify technologies or activities supporting drug development. At this stage, first compounds are synthetized and initial mechanism of action (MoA) as well as structure – activity relationship (SAR) are identified. To reach TRL 3 for the drug discovery project, initial proof-of-concept for generated compounds has to be documented in *in vitro* and *in vivo* research models (defined cell lines, animal models). Protocols and plans for further work are reviewed and approved. Intellectual property (IP) for key markets should be secured and freedom to operate (FTO) should be analyzed. Targeted molecular profile (TMP) should be defined.
4	Pre-clinical research studies performed at non-Good Laboratory Practice (non-GLP) level to learn about drug metabolism and drug interaction studies. At this stage, laboratory work is performed to improve hypothesis and identify adequate parametric data required for technological assessment in a strict experimental design to address the worst case scenario. To meet requirements of TRL 4, the potential drug candidate has to demonstrate proof-of-concept and safety in selected cell and animal model (s). The primary targeted patient population should be defined. Protocols and plans for the further work are reviewed and approved. Back up compounds and series for leading compounds should be obtained. IP and FTO monitoring is ongoing.
5	Non-clinical and pre-clinical research studies involving the collection and analysis of parametric data for pilot candidate(s). Results provide the basis for a manufacturing process in Good Manufacturing Practice (cGMP) – compliance. GLP safety and toxicity studies are conducted in animal models. Pharmacokinetic and pharmacodynamic parameters are defined for candidate drugs. Stability studies are initiated for a potential drug formulation. TRL 5 is reached when sufficient data on the drug candidate is collected and IND application is under preparation, including animal pharmacology and toxicology studies, proposed manufacturing information and protocol (s) for Phase 1 clinical testing. Protocols and plans for further work are reviewed and approved. IP and FTO monitoring is ongoing. Translational and/or combination studies should be initiated.
6	IND application is prepared and submitted. Phase 1 clinical trials are conducted in a small number of patients to demonstrate the safety of the drug candidate. TRL 6 decision criterion includes clinical safety requirements from Phase 1 and supports proceeding to Phase 2 clinical studies. In Phase 1, the potential drug has to demonstrate safety in a defined population. IP and FTO monitoring is ongoing. Translational work is being performed.
7	Phase 2 clinical trials are conducted to demonstrate the initial efficacy and to gather further safety and toxicity data. Final dose, dose range, administration route and schedule are established. Phase 2 clinical trials are completed and documentation needed for the initiation of Phase 3 is prepared. To achieve TRL 7, Phase 3 clinical study plan or surrogate test plan has to be approved by the selected regulatory agency. IP and FTO monitoring is ongoing. Translational work is being performed.

Category	Characteristics of the project scope
8	Implementation of expanded Phase 3 clinical trials or surrogate tests to gather information. Trials are conducted to evaluate the risk-benefit of administering the drug candidate and to provide an adequate drug labelling. Approval of the NDA by given regulatory agency is needed to reach TRL 8. IP and FTO monitoring is ongoing, extension strategies are …? and recognized. Translational work is being performed.
9	The pharmaceutical product, such as a drug or device, can be distributed and marketed. Phase 4 studies may be required and are designed in consultation with the regulatory agency. After drug approval, product reaches TRL. Continue surveillance is being conducted. IP and FTO monitoring is ongoing, market life extension strategies…are recognized. Translational work is being performed.

Source: own elaboration based on National Aeronautics and Space Administration Technology Readiness Level description (www.nasa.gov, as of January 6, 2024) and Euraxess (euraxess.ec.europa.eu, as of January 7, 2024).

Categories described in Table 3 refer directly to definitions recognized in the industry. They have been developed as a basis for the qualification of projects to improve the management system of drug development processes. These processes are carried out in commercial units and research centers and, by definition, are oriented towards the implementation of specific projects. Categorization not only allows for a better selection of project management tools [Wysocki, 2009], but also allows for a better configuration of the research project portfolio management system.

Based on the analysis of the research performed, shifts or needs in several key areas can be observed.

Firstly, there's a noticeable move away from solely prioritizing infrastructure development towards fostering cooperative efforts. Project teams focused on the development of new drugs are recognizing the value of partnerships and alliances with other companies, research institutions, and even governmental bodies to leverage expertise and resources more effectively. This approach not only promotes the collaborative nature of drug discovery, but also releases financing from infrastructure to other areas of project needs.

Moreover, with advancement of the project maturity, the focus is shifts from purely technological aspects to organizational and human aspects. While technological innovation remains crucial, there is a growing importance of optimizing internal processes, managing talent, and fostering a culture of creativity and collaboration within team members.

The shift towards cooperation and a more holistic approach to drug development reflects the industry's recognition of the interconnected nature of scientific, economic, and organizational factors. Embracing this shift not only enhances efficiency and innovation, but also holds the potential to bring positive outcomes for both companies and patients.

By scrutinizing factors influencing the management approach to the project at different levels of technology readiness, the authors build a ground for a more detailed and adjusted analysis of needs of drug discovery and development projects. The authors emphasize the importance of adjusting project management strategies to unique challenges encountered at different stages of technological readiness, ranging from early research and preclinical studies to clinical trials and regulatory approval. Through this approach, the article aims to improve the project management efficiency and mitigate risks inherent in drug development endeavors.

Ultimately, the proposed categorization framework offers valuable insights for pharmaceutical companies and stakeholders to streamline their project management practices, optimize resource allocation, and increase the likelihood of successful drug development outcomes.

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