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LA GESTIÓN DE LA CADENA DE VALOR EN LAS CIENCIAS DE LA VIDA: PROPUESTA DE MODELO PARA ESTIMAR EL VALOR AÑADIDO DE LOS PROYECTOS DE BIOTECNOLOGÍA DE LA SALUD

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A ustedes seis, que están.

Y a ustedes, que aún no han llegado.

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ABSTRACT

The importance of biotechnology has been recognized and demonstrated in practice over the years. Specifically, applications in health biotechnology stand out for their impact on human life. But this treatment that reaches the hands of the needy had to undergo a long period of trials, failures, and improvements, which involved the disbursement of large sums of capital, the achievement of specific activities developed by different actors across the world, as well as the decision-making under extremely uncertain conditions. For these reasons, a crucial moment when to deciding whether to continue researching a drug candidate is its assessment.

The most used method to value health biotechnology projects is the binomial real options tree, based on statistics of similar projects. However, other qualitative and quantitative factors coexist and influence the value a drug candidate adds, beyond the cash flows it promises. Additionally, the efforts to obtain the financial funds that this type of innovation requires are not insignificant, especially in countries with less developed economies such as Cuba. Therefore, the valuation method must offer a holistic and long-term view of the project's effects.

The following research question is raised in this context: What components should a biotechnology project valuation model have to become a flexible and strategic tool in companies' decision-making? In this thesis, it is considered that the answer to this unknown is found in a model that captures the intrinsic attributes of the project under study, the characteristics of the company and the market, the long term as the preferred period for forecasting, the interdependencies between all the businesses linked while transforming a drug candidate into an established product, the uncertainty in factors or parameters, the project or company's side effects, as well as the conditions of the macro environment.

In this sense, the main aim of this research is to propose and implement a mathematical model to estimate the added value by all interconnected activities and companies along the value chain of a health biotechnology project. To achieve this purpose, the variables of value chain and valuation models applied to the health biotechnology sector were studied in the doctoral research process. As a result, in addition to several papers presented at international scientific conferences and two book chapters published in prestigious publishers, five papers have been

written for publication in scientific journals, four of which make up the core of this doctoral thesis.

This thesis demonstrates few published papers address the value chain management in health biotechnology products and projects. There are no research or researchers' networks, at least in the last 12 years. It is also confirmed that this topic needs to be investigated in developing countries.

To cover this last gap, as part of the doctoral research process, a study of innovation in the Cuban biotechnology sector is developed, proposing a Cuban National Innovation System whose center is the value chains of the products and projects resulting from the Cuban Biotechnology Industry. This proposal reveals all the actors involved in obtaining a drug candidate and the need to consider the funding efforts these innovations demand as a primary activity in the value chain.

Once the sector's intrinsics and the most used valuation methods in this field are known, the model proposal is placed, which consists of calculating a unique indicator including the economic, financial, and sustainability components. Through the application of fuzzy mathematics, specifically the use of triangular fuzzy numbers and confidence intervals, the project's value added is calculated, resulting in a range that elucidates the long-term effects of the drug candidate's production and commercialization, both in the worst and the most favorable conditions.

The model includes a proposal to estimate the sales price of a treatment, considering and weighing the factors influencing it. By applying the ANP technique, a fairer price is reached, valuing the qualitative and quantitative elements dictating the market value of a drug candidate. Additionally, the added value of the funding options used by the project is estimated after choosing them through the application of Integer Goal Programming, another contribution of this model proposal. In this case, the value of the flexibility the possible patent sale provides is included and calculated by applying the Black & Sholes model. Finally, the sustainability component values the projects' savings, especially from an environmental point of view, and the income received from other potential uses they may suppose in the future. The uncertain component of sustainability is addressed by employing confidence intervals to define triangular fuzzy numbers.

This doctoral research provides the first bibliometric study that analyzes publications in health biotechnology from the value chain perspective. The Cuban National Innovation System proposal is also untold, given that this holistic approach is not applied in this country. Thirdly, this is the first use of the Analytical Network Process technique based on value chain approach. Fourthly, for the first time, the mathematical valuation model's proposal summarizes, in a unique indicator, unusual assessments, or assessments made in isolation or non-quantified. Lastly, some recommendations are offered as future research lines, some in this thesis' specific subject and others with a broader scope.

The results above are presented in seven chapters. Chapter I explains the problem that gave rise to the research, the proposed objectives, the methodology and methods applied, and how the research has been disseminated. Chapter II presents the study of value chains in health biotechnology companies from a bibliometric perspective. Chapter III explains the Cuban National Innovation System proposal. Chapter IV consists of applying the Analytical Network Process (ANP) methodology to calculate the price of drug candidates, a singular point at the time of valuation. The model proposal is presented in Chapter V, in which a first application in a Cuban experimental treatment is also shown. Chapter VI discusses the research results, and Chapter VII presents the conclusions and main limitations of the study, as well as the next steps to continue the research.

RESUMEN

La importancia de la biotecnología ha sido reconocida y demostrada en la práctica a lo largo de los años. Específicamente las aplicaciones en la biotecnología de la salud resaltan por su impacto en la vida humana en particular. Pero ese tratamiento que llega a manos del necesitado tuvo que transcurrir un largo período de ensayos, fracasos y mejoras; que implicó el desembolso de grandes sumas de capital, la consecución de actividades específicas desarrolladas por diferentes actores en disímiles partes del mundo, así como la toma de decisiones en condiciones sumamente inciertas. Por tales motivos, un momento crucial cuando se trata de decidir si se prosigue con la investigación de un candidato a fármaco, es su valoración.

El método más empleado hasta la actualidad para valorar proyectos de biotecnología de la salud es el árbol binomial de opciones reales, basado en historiales estadísticos de proyectos similares. Pero coexisten e influyen otros factores, cualitativos y cuantitativos, en el valor que añade un candidato a fármaco, más allá de los flujos de caja que este promete. Adicionalmente, los esfuerzos en obtener los fondos financieros que este tipo de innovaciones requiere no son insignificantes, sobre todo en países con economías menos desarrolladas como Cuba. Por tanto, el método de valoración que se emplee debe ofrecer una visión holística y de largo plazo de los efectos del proyecto.

En este contexto se plantea la siguiente interrogante de investigación: ¿qué componentes debe tener un modelo de valoración de proyectos biotecnológicos para convertirse en una herramienta flexible y estratégica en la toma de decisiones de las empresas? En esta tesis se considera que la respuesta a esta incógnita se encuentra en un modelo que capte los atributos intrínsecos del proyecto en cuestión, las características propias de la empresa y el mercado, el largo plazo como período preferente para la previsión, las interdependencias entre todos los negocios vinculados durante la transformación de un candidato a fármaco en un producto establecido, la incertidumbre en factores o parámetros, los efectos secundarios provocados por el proyecto o empresa, así como las condiciones del macro entorno.

En tal sentido, el objetivo principal de esta investigación es proponer e implementar un modelo matemático para estimar el valor agregado por todas las actividades y empresas interconectadas a lo largo de la cadena de valor de cualquier proyecto de biotecnología de la

salud. Para arribar a este propósito, en el proceso de investigación doctoral desarrollado se estudian las variables cadena de valor y modelos de valoración, ambos aplicados al sector de la biotecnología de la salud. Como resultado, además de varias ponencias presentadas en congresos científicos internacionales y dos capítulos de libro publicados en editoriales de reconocido prestigio, se han elaborado cinco trabajos para su publicación en revistas científicas, de los cuales cuatro conforman el núcleo de esta tesis doctoral.

Esta tesis demuestra que no son muchas las publicaciones que abordan el tema de la gestión de la cadena de valor de productos y proyectos de la biotecnología de la salud. No se concretan redes de investigación ni de investigadores, al menos en los últimos 12 años. Se corrobora también que este tema no es investigado en los países en vías de desarrollo.

Para cubrir este último vacío, como parte del proceso de investigación doctoral se realiza un estudio de la innovación en el sector biotecnológico cubano, proponiendo un Sistema Nacional de Innovación en Cuba cuyo centro sean las cadenas de valor de los productos y proyectos resultantes de la Industria Biotecnológica Cubana. Esta propuesta desvela todos los actores involucrados en la obtención de un candidato a fármaco, así como la necesidad de considerar los esfuerzos por captar el financiamiento que demandan estas innovaciones como una actividad primaria en la cadena de valor.

Una vez conocidas las características intrínsecas del sector y los métodos de valoración más empleados en este campo, se procede a realizar la propuesta de modelo, que consiste en el cálculo de un indicador único que incluye los componentes económico, financiero y de sostenibilidad. Mediante la aplicación de la matemática borrosa, específicamente el uso de números borrosos triangulares e intervalos de confianza, se calcula el valor añadido por un proyecto resultando en un rango que permite dilucidar los efectos a largo plazo de la producción y comercialización del candidato a fármaco, tanto en las peores condiciones como en las más favorables.

El modelo incluye una propuesta para estimar el precio de venta de un tratamiento, considerando y ponderando los factores que influyen en él. Mediante la aplicación de la técnica del ANP, se arriba a un precio más justo que valora los elementos cualitativos y cuantitativos que dictan el valor de mercado de un candidato a fármaco. Adicionalmente se estima el valor añadido por las fuentes de financiamiento empleadas por el proyecto, previa

elección de estas mediante la aplicación de la Programación por Metas Entera, como otro aporte de esta propuesta de modelo. En este caso se incluye el valor de la flexibilidad aportado por la posible venta de la patente de proyectos biotecnológicos, calculado mediante la aplicación del modelo de Black & Sholes. Finalmente, el componente de sostenibilidad valora los ahorros generados por los proyectos, sobre todo desde el punto de vista medioambiental, así como los ingresos percibidos por los otros usos potenciales que en el futuro esos puedan acarrear. El componente incierto de la sostenibilidad se palia con el uso de intervalos de confianza para definir números borrosos triangulares.

Esta investigación doctoral arroja el primer estudio bibliométrico que analiza las publicaciones en biotecnología de la salud desde la perspectiva de la cadena de valor. Adicionalmente, la propuesta de Sistema Nacional de Innovación para Cuba es también inédita, dado que este enfoque integral no es aplicado en el país. Además, esta es la primera vez que la técnica del Proceso Analítico en Red se emplea tomando como base el enfoque de cadena de valor. En cuarto lugar, la propuesta de modelo matemático de valoración recoge por vez primera en un único indicador valuaciones que usualmente no se hacen, o se realizan aisladamente, o no se cuantifican. Por último, se ofrecen algunas recomendaciones de posibles líneas de investigación futuras, algunas en el campo específico que aborda esta tesis y otras con un corte más amplio.

Los mencionados resultados se presentan a través de siete capítulos. El Capítulo I se dedica a explicar el problema que da origen a la investigación, los objetivos planteados, la metodología y métodos aplicados, así como las formas en las que la investigación se ha diseminado. En el Capítulo II se presenta el estudio de las cadenas de valor en empresas de biotecnología de la salud desde la perspectiva bibliométrica. El Capítulo III explica la propuesta de Sistema Nacional de Innovación cubano. El Capítulo IV consiste en una aplicación de la metodología Proceso Analítico en Red (ANP por sus siglas en inglés) al cálculo del precio de candidatos a fármacos, punto singular al momento de la valoración. La propuesta de modelo se realiza en el Capítulo V, en el cual también se presenta una primera aplicación en un tratamiento experimental cubano. En el Capítulo VI se discuten los resultados de la investigación, y en el Capítulo VII se presentan las conclusiones y principales limitaciones del estudio, así como los pasos a seguir para dar continuidad a la investigación.

RESUM

La importància de la biotecnologia ha estat reconeguda i demostrada a la pràctica al llarg dels anys. Específicament les aplicacions a la biotecnologia de la salut ressalten pel seu impacte en la vida humana en particular. Però este tractament que arriba a les mans del necessitat va transcórrer un llarg període d'assajos, fracassos i millores que va implicar el desemborsament de grans sumes de capital, la consecució d'activitats específiques desenvolupades per diferents actors en dissímils parts del món, així com la presa de decisions en condicions summament incertes. Per aquests motius, un moment crucial quan es tracta de decidir si es prossegueix amb la investigació d'un candidat a fàrmac, n'és la valoració.

El mètode més usat fins ara per valorar projectes de biotecnologia de la salut és l'arbre binomial d'opcions reals, basat en historials estadístics de projectes similars. Però coexisteixen i influeixen altres factors, qualitatius i quantitatius, en el valor que afegeix un candidat a fàrmac, més enllà dels fluxos de caixa que este promet. Addicionalment, els esforços a obtenir els fons financers que requereix aquest tipus d'innovacions no són insignificants, sobretot en països amb economies menys desenvolupades com Cuba. Per tant, el mètode de valoració que es faci servir, ha d'oferir una visió holística i de llarg termini dels efectes del projecte.

En este context es planteja la interrogant de recerca següent: quins components ha de tenir un model de valoració de projectes biotecnològics per convertir-se en una eina flexible i estratègica en la presa de decisions de les empreses? En esta tesi es considera que la resposta a esta incògnita es troba en un model que capti els atributs intrínsecs del projecte en qüestió, les característiques pròpies de l'empresa i el mercat, el llarg termini com a període preferent per a la previsió, les interdependències entre tots els negocis vinculats durant la transformació d'un candidat a fàrmac en un producte establert, la incertesa en factors o paràmetres, els efectes secundaris provocats pel projecte o l'empresa, així com les condicions del macro entorn.

En este sentit, l'objectiu principal d'esta investigació és proposar i implementar un model matemàtic per estimar el valor agregat per a totes les activitats i les empreses interconnectades al llarg de la cadena de valor de qualsevol projecte de biotecnologia de la salut. Per arribar a este propòsit, en el procés de recerca doctoral desenvolupat, s'estudien les

variables de cadena de valor i models de valoració, tots dos aplicats al sector de la biotecnologia de la salut. Com a resultat, a més de diverses ponències presentades en congressos científics internacionals i dos capítols de llibre publicats a editorials de reconegut prestigi, s'han elaborat cinc treballs per publicar-los en revistes científiques, quatre dels quals conformen el nucli d'esta tesi doctoral.

Aquesta tesi demostra que no són molts els treballs publicats que aborden el tema de la gestió de la cadena de valor de productes i projectes de la biotecnologia de la salut. No es concreten xarxes de recerca ni d'investigadors, almenys en els darrers 12 anys. Es corrobora també que aquest tema no és investigat als països en vies de desenvolupament.

Per cobrir aquest últim buit, com a part del procés de recerca doctoral es realitza un estudi de la innovació al sector biotecnològic cubà, proposant un Sistema Nacional d'Innovació a Cuba el centre del qual siguin les cadenes de valor dels productes i projectes resultants de la Indústria Biotecnològica Cubana. Aquesta proposta revela tots els actors involucrats en l'obtenció d'un candidat a fàrmac, així com la necessitat de considerar els esforços per captar el finançament que demanen aquestes innovacions com una activitat primària a la cadena de valor.

Una vegada conegudes les característiques intrínseques del sector i els mètodes de valoració més usats en aquest camp, es fa la proposta de model, que consisteix en el càlcul d'un indicador únic que inclou els components econòmic, financer i de sostenibilitat. Mitjançant l'aplicació de la matemàtica borrosa, específicament l'ús de nombres borrosos triangulars i intervals de confiança, es calcula el valor afegit per un projecte resultant en un rang que permet dilucidar els efectes a llarg termini de la producció i comercialització del candidat a fàrmac, tant en les condicions pitjors com en les més favorables.

El model inclou una proposta per estimar el preu de venda d'un tractament, considerant i ponderant els factors que hi influeixen. Mitjançant l'aplicació de la tècnica de l'ANP, arriba a un preu més just que valora els elements qualitatius i quantitatius que dicten el valor de mercat d'un candidat a fàrmac. Addicionalment s'estima el valor afegit per les fonts de finançament emprades pel projecte, prèvia elecció d'aquestes mitjançant l'aplicació de la Programació Sencera per Objectius, com una altra aportació d'aquesta proposta de model. En aquest cas s'hi inclou el valor de la flexibilitat aportat per la possible venda de la patent de

projectes biotecnològics, calculat mitjançant l'aplicació del model de Black & Sholes. Finalment, el component de sostenibilitat valora els estalvis generats pels projectes, sobretot des del punt de vista mediambiental, així com els ingressos percebuts pels altres usos potencials que en el futur aquests puguin comportar. El component incert de la sostenibilitat es pal·lia amb l'ús dintervals de confiança per definir nombres borrosos triangulars.

Esta investigació doctoral presenta el primer estudi bibliomètric que analitza les publicacions en biotecnologia de la salut des de la perspectiva de la cadena de valor. Addicionalment, la proposta de Sistema Nacional d'Innovació per a Cuba és també inèdita, atès que aquest enfocament integral no és aplicat al país. A més, aquesta és la primera vegada que la tècnica del Procés Analític en Xarxa s'empra prenent com a base l'enfocament de cadena de valor. En quart lloc, la proposta de model matemàtic de valoració recull per primera vegada en un únic indicador valuacions que usualment no es fan, o es realitzen aïlladament, o no es quantifiquen. Finalment, s'ofereixen algunes recomanacions de possibles línies de recerca futures, algunes al camp específic que aborda aquesta tesi i d'altres amb un àmbit més ampli.

Els resultats abans esmentats es presenten a través de set capítols. El capítol I es dedica a explicar el problema que dóna origen a la investigació, els objectius plantejats, la metodologia i els mètodes aplicats, així com les formes en què la investigació s'ha disseminat. Al capítol II es presenta l'estudi de les cadenes de valor a empreses de biotecnologia de la salut des de la perspectiva bibliomètrica. El capítol III explica la proposta del Sistema Nacional d'Innovació Cubà. El capítol IV consisteix en una aplicació de la metodologia Procés Analític en Xarxa (ANP per les sigles en anglès) al càlcul del preu de candidats a fàrmacs, punt singular al moment de la valoració. La proposta del model es realitza al capítol V, on també es presenta una primera aplicació en un tractament experimental Cubà. Al capítol VI es discuteixen els resultats de la investigació, i al capítol VII es presenten les conclusions i principals limitacions de l'estudi, així com els passos a seguir per donar continuïtat a la investigació.

CONTENIDO

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CAPÍTULO I. INTRODUCTION

Since its inception in the 1970s, life science has significantly transformed its objectives. Initially focused on the generation of novel insights and advancements in comprehending biological and biochemical processes, the discipline has evolved towards contributing to the biotechnology (biotech hereafter) economy (Akhondzadeh, 2016; Apell & Eriksson, 2023; Huttner, 1999; Tibell & Rundgren, 2010). This transition reflects a paradigm shift wherein the emphasis has broadened from pure scientific inquiry to encompassing the practical application of knowledge for economic, financial (A. R. Castro et al., 2023), and societal benefit.

Entirely innovative in processes, procedures, technologies, inputs, outputs, and relationships, this sector became a business with high levels of risk and profitability (Pisano, 2010; Su & Wu, 2015). However, the scope of activities and market pursuits within health biotech firms varies significantly (Carden et al., 2010), contingent upon the specific stage within the biotechnological product life cycle that an enterprise targets. Some companies prefer to dedicate their efforts to existing treatments, but there are some others that accept the challenge of new drugs' research and development.

A medication or therapy is the result of an extensive and expensive period of tests and trials (CDER, 2022), after which starts its production and commercialization. Prior to receiving the marketing approval, a drug candidate may be referred to as a project or experimental treatment. In this stage, there is a huge uncertainty about the future outcomes and successes of the drug candidate; hence it is imperative for the most accurate project valuation.

According to the economic theory, a firm's value equals to the present value of the anticipated future cash flows the company expects (Damodaran, 2012). This concept is also fixed to project valuation in life science, in which specific fundamental principles are traditionally applied to. Carden et al. (2010) and Hitchner (2017) agree that the asset, income, and market approaches are the main harnessed in health care and life science companies. These approaches support the most broadly valuation methods employed by health biotech companies: the discounted cash flows (DCF hereafter) risk adjusted, the relative-value (a

comparison with a similar firm's value) technique, and the real options (Bogdan & Villiger, 2010; Chandra & Mazumdar, 2024).

The DCF risk adjusted is based on two main principles according to Brealey et al. (2011): a dollar today is worth more than a dollar tomorrow; and a safe dollar is worth more than a risky one. Its main purpose is to estimate the cash inflows and outflows that a project promises in the long term, considering the risk premiums prevailing in the market, to calculate the capital gain or loss expected from the project, expressed in today's money (Bogdan & Villiger, 2010; Brealey et al., 2011; Koller et al., 2010). According with De la O & Myers (2021), Fernández (2007), and French & Gabrielli (2005) the advantage of the DCF risk adjusted is that it makes the valuation an explicit process, by letting know the expectations about future rent, cost of management, depreciation, taxation, financing plans, etc. Brealey et al. (2011); Wang et al. (2023); and Zhang et al. (2022) point out that the accuracy of the results after applying this method will depend on the veracity of the supporting information, making them uncertain. Uncertainty is present in this process due to the lack of knowledge and poor information about all the inputs that can be used in the valuation (Byrne, 1996; French & Gabrielli, 2005).

The relative-value technique consists of finding the comparable enterprise equity value for comparison (Chandra & Mazumdar, 2024; Zhirui, 2023). It reflects the market view by assessing capital market players without many input variables (Chowdhury & Saima, 2023; Hendrawan et al., 2020). The need for more transparency in this method, as well as the possibility of a market firm's overestimation, are the main weaknesses noticed by Damodaran (2012).

The real option valuation method refers to current opportunities for which an investor may benefit, by valuing managerial flexibility (Gilson Dranka et al., 2020). The main models to assess real options according to Bogdan & Villiger (2010) and Fabrini (2011), are the Black & Sholes and the binomial tree. The most important advantage when using this method is the managerial flexibility, because managers can update projects and make decisions according to the uncertainty's evolution (Martínez-Ceseña & Mutale, 2011). Market

speculation can significantly impact this method, potentially affecting the future results of evaluated projects (Zhirui, 2023).

But do these methods capture all the value-adding components of a health biotech company or project? What are their value drivers? The explained methods (DCF risk adjusted, relative-value, and the real options) are mainly focused on the market expectations, and when focusing on a health biotech firm, strategic, organizational, monetary, executory, and external value drivers are present. The researchers' teams and the management team are crucial; they mark the short and long-term paths to follow and how the processes and procedures are executed. The company's age or stage of development likewise influences its reliability, technology portfolio, and resiliency. The country environment, government regulations, and integer settings to apply the therapies and medication also affect the regulatory agencies, competitors, and clients' perceptions of the firm and the experimental treatment. All these facts impact the company's visibility and ability to relate with those who could be its key partners, hence they need to be considered due to their incidence in the project or firm's value.

The established alliances when a drug candidate is under research and development and the effort to raise the market approval imply the disbursement of significant amounts of money. According to the information provided in Chandra & Mazumdar (2024) work, it is expected that not more than 12% of the projects complete the process until the marketing stage, and it costs on average $1.4 billion (in 2013 dollars). This justifies the continued funding requirements demanded by firms in this industry, even more if they are set up in developing economies.

The lack of funding for Cuban health biotech projects started this doctoral research, which initially intended to address the problem of the projects' funding strategy in the Cuban biotech industry. A deeper analysis of the problem's state and a better understanding of the sector in study, allowed to discover a more accurate cause inducing the effect of issues to find financial providers.

The impact of globalization in this sector generates cross-border interconnections and expansion of the industry's regulatory requirements to be accomplished. Additionally, the emergence of new competitors such as China and India (Salter et al., 2016; WHO, 2022) is pushing price down, which together with low ratio of projects' success and the lack of innovations making novel and effective therapies instead of a variation on existing drugs (Carden et al., 2010), is limiting the pricing flexibility. Furthermore, the agility of the worldwide changes prints a particular level of uncertainty in addition to what by nature this sector has. All these elements directly affect the sales grow projections, the profitability of the industry, and the attractiveness for investors and stakeholders.

Quantifiable factors and a broad spectrum of qualitative and intangible elements similarly affect the project and the firm's performance. The social impact of health innovations, the consumption trends, the cultural behavior and decisions of each individual, the relationships across companies inside and outside the region, the knowledge rounding the studied illness, the role of the commercial insurance companies, etc., are examples of non-quantifiable factors influencing the funding decisions.

The lecture on these facts seems more a wide valuation task than a simple funding strategy, hence the scientific problem in this research lies in the next question: What components should a biotech project valuation model have to become a flexible and strategic tool in companies' decision-making? To become flexible and strategic, the model proposal needs to take into consideration the intrinsic attributes of the project, company, and market; the long-term as a preferred period for forecasting; the interdependences among all the companies linked to transforming a drug candidate in an established product; the uncertainty in factors or parameters; and the side effects provoked by the project or company; as well as the macroenvironment conditions.

Considering intrinsic conditions of a project, company, and sector in valuation ensures accuracy, facilitates risk assessment, aligns with market perception, supports strategic planning, and enhances investor confidence (Ochuba et al., 2024). By analyzing regulatory, clinical, market, technological, economic, and ethical factors, with a long-term perspective

stakeholders can make informed decisions, mitigate risks (Marcus et al., 2024), capitalize on opportunities, and ultimately enhance the project's success in improving public health.

The links between the nodal biotech firm and its allies in obtaining a new drug can be revealed if each project is analyzed from the perspective of the value chain (VC hereafter). A VC encompasses a set of connected activities to create a product by separating those that directly produce, market, and deliver it and those that provide all the input requirements to successfully complete the main activities (Porter, 1985). This approach apportions a product (project in this case) into small pieces to reveal each actor or activity influencing the value creation. That is the main point in the valuation process.

The healthcare sector is intrinsically uncertain (Seoni et al., 2023). To manage the uncertainty in parameters, there exist three macro programming methods: based on probabilities theory, based on uncertainty theory, and based on fuzzy theory (Chen et al., 2023). Cheng et al. (2017) and Hazır & Ulusoy (2020) reveal that the first compute uncertainty by using possibility' measures with stochastic, reactive, proactive, and sensitivity approaches. The second defines three degrees of uncertainty in variables, in measures, and in distribution; all separately defined on uncertainty spaces (Liu, 2010). These two methods model the degree of human beliefs, facing the fuzzy theory that consider the degree of beliefs as a fuzzy set (Cheng et al., 2017; Gil-Lafuente et al., 2022; Kaufmann, 1990; Zadeh, 1965).

Considering the side effects provoked by a project or company is essential for patient safety, regulatory compliance, risk management, product labeling, market acceptance, reputation management, litigation risk mitigation, and investor confidence (Niv & Tal, 2023). By prioritizing safety and transparency, companies can build trust, mitigate risks, and ensure healthcare products' responsible development and commercialization.

Knowing the effects of macroenvironmental conditions is critical for businesses and projects to assess risks, navigate the competitive landscape (R. Wang, 2024), ensure regulatory compliance, optimize resource allocation, plan strategically, and manage stakeholder relations effectively. By incorporating macroenvironmental analysis into decision-making

processes, businesses can adapt to changing external conditions (Danishev, 2024) and achieve long-term success and sustainability.

Some of the model's components mentioned previously are considered when valuating health biotech projects, but it remains to put all together in a unique model as well as contemplate, score, and measure qualitative factors. This research is going to be focused on these gaps.

1.1 OBJECTIVES

The main objective of this research is to propose and implement a mathematical model to estimate the value added by all activities and companies interconnected along the VC of a health biotech project. The proposal should grant a holistic and flexible assessment by considering qualitative and quantitative factors and by applying scoring methods and fuzzy tools.

To address the main objective of this thesis, the following specific objectives are defined:

1. Assess the theoretical foundations of the VC approach supporting the model proposal, focusing the analysis in the biotech sector.
2. Evaluate the Cuban biotech sector as a goodness and development driven.
3. Study valuation methods and tools.
4. Explain the fundamentals of the mathematical model proposal.
5. Apply the model proposal to a Cuban health biotech project.

The achievement of this objectives' system will be conducted in the next four chapters. The specific objective number 1 is approached from chapters II to V, with more emphasis in chapters II and III. The specific objective number 2 is due in Chapter III. The specific objective number 3 is met in chapters IV and V. Finally, specific objectives 4 and 5 are achieved in Chapter V. The next research' stages allowed the accomplishment of this objectives' system.

i. The study of the roots of the VC approach, starting with its mother science: logistics.
ii. A bibliometric analysis of the VC approach in the field of health biotechnology.
iii. The study of the impacts of innovations in the Cuban Biotechnological Industry.

iv. A deepening of the impacts of the Cuban health biotech sector as a drive of the Cuban economy and society by implementing a National Innovation System.
v. The computation of the funding options' impacts in health biotech projects, specifically when selling patents.
vi. A proposal to estimate the value of externalities impacting any health biotech project.
vii. The proposition of a multicriteria model to estimate the price of any drug candidate, based on ranking factors.
viii. The conjugation of all value-adding elements into a single indicator.

All these stages were consolidated by presenting papers at 11 national and international conferences. Additionally, the research has been disseminated through the publication of two book chapters, five contributions to books of proceedings, and five papers in indexed journals. The chapter structure of this doctoral thesis is mainly determined by the four most relevant papers published, under review, and accepted for publication.

1.2 CHAPTER STRUCTURE

This is a seven-chapter thesis. To answer the research question, satisfy the main and specific objectives, fulfill the research' stages, and reach the expected results, this thesis goes from the general to the particular in studying the variables value chain and valuation models applied to the health biotechnology sector. Next, it will be explained the chapter structure supporting the research.

Capítulo I. Introducción. This section presents the origin of the research problem, the thesis' objectives, the chapter structure satisfying the proposed objectives' system, the pursued methodologies and methods, and how the research has been disseminated.

Capítulo II. The value chain approach in red biotechnology companies from a bibliometric perspective. This paper constitutes the first bibliometric analysis of the VC approach in the field of the health biotech. It shows the non-existence of an author network working on the health biotech sector from the VC management perspective. It raises some research gaps related to the lack of publications emphasizing the early stage of a project in health biotech, and the lack of a holistic analysis of the complex network that the VC of a health biotech

project represents. This paper also suggests a stop to study the VC of health biotech projects or products in less developed countries by applying methods to palliate the uncertainty and considering all the actors connected. This work accumulates one quotation in Google Scholar.

Capítulo III. A proposal for a National Innovation System supported by the Value Chain of the Cuban Biotechnological Industry. This paper shows the impacts of the Cuban biotech industry in the economy and the society of this country. By studying National Innovation Systems of developed and less developed countries and proposing one for Cuba, it allows to reveal all the connections the health biotech sector implies nationally and worldwide. This paper exposes the impacts of the national and international regulations for the health biotech projects, as well as technology and innovation policies. This research also offers some ideas about how to improve the financial system based on the biotech needs. It proposes to manage the biotech' business activities under the VC approach, and to consider the research and educational system as the initial stage of health biotech projects.

Capítulo IV. Multicriteria decision techniques applied to valuation in the life sciences. The study highlights the lack in incorporating appropriately weighted quantitative and qualitative factors in the pricing estimation of drug candidates. Starting with the definition of the VC of the health biotech project, and by applying the Analytic Network Process methodology to determine the relevance of the drug candidates' price determinants, this paper shows a methodology to estimate a most accurate price for experimental treatments, compared to the most used techniques in the sector until now. The proposed methodology reduces the risks in valuating health biotech projects, and enhances their presentation to investors, policymakers, and stakeholders.

Capítulo V. Estimating Value in Health Biotech Projects: Fuzzy Modelling, Funding, and Chain Management in a Cuban Case. This last paper proposes a mathematical model to estimate the value of any health biotech project, taking as a basis the identification and definition of the VC that it implies. To provide a holistic assessment, the model encompasses the impact of quantifiable and non-quantifiable factors and the uncertainty management, as well as the sustainability perspective. By applying scoring methods and fuzzy tools in estimating the discounted cash flows the project promises, the model output is an only

indicator that comprises the most relevant indicators when valuating health biotech projects, as well as the gaps revealed in previous research. One of the most relevant aspects of this proposal, is to use the Integer Goal Programming to suggest an order of funding options to apply for, and to include the value added when selling the patent of a health biotech project. In addition, the computation of objective and subjective elements to calculate the value created is also highlightable.

Capítulo VI. Discussion. In this section the main results of the research are presented, according to the papers that are the core of this thesis.

Capítulo VII. Conclusions. It collects the main conclusions of the study carried out, the existing limitations, as well as future studies that could be developed from the present work.

Appendixes. They provide data and information not included in the published papers. Appendix 1 reflects the characteristics and information sources of the studied National Innovation Systems. Appendix 2 presents some of the matrices resulting from applying the Analytic Network Process methodology. Appendix 3 collects the data when applying the model proposal in a Cuban case.

After achieving the objectives of the thesis and considering this author's opinion, the main contribution of this thesis is to propose a model resulting in a unique and holistic indicator that analyzes and quantifies the value of health biotech projects from the economic, financial, and sustainability perspectives by mixing well-known methods and methodologies. Also relevant is the fact of developing the first bibliometric study linking the VC approach and health biotech sector. Especially in the Cuban study case, it is likewise a contribution the NIS proposal, the application of Analytic Network Process methodology to determine the relevance of the drug candidates' price determinants, and the Integer Goal Programming with funding purposes.

1.3 METHODOLOGY AND METHODS

Qualitative and quantitative methodologies are used in this research. To delve into the characteristics of the sector, a qualitative methodology is essentially used. In addition, to determine the price determinants and their influences, as well as the components of the Cuban National Innovation System proposed, this is the approach used. Unstructured interviews, documentary review, and user testing are used as qualitative research methods in companies and projects where the model and its components are applied independently.

The quantitative methodology appears since the bibliometric study. Counting publications, studying research' trends, calculating and analyzing the indexes that measure the number of published papers with quality, developing the content analysis of the publications in this research topic are examples of applications of this methodology.

The estimation of the drug candidate' price is based on quantifying qualitative factors. The model proposal is founded on quantify measurable and unmeasurable factors impacting the project from the economic, financial, and sustainability point of view. As quantitative research methods, a survey of managers and scientists of the entities in which the research is applied is used, as well as controlled experiments regarding the sources of financing to apply for. Some applications of fuzzy logic are used as data analysis techniques.

The data undergoes a collaborative, integrated qualitative and quantitative analysis aimed at comprehensively elucidating the phenomenon and deriving accurate conclusions, proposed resolutions to the issue, and avenues for enhancement. This methodological framework is devised to foster innovation and knowledge generation, augmenting the original concept, and establishing a scalable model applicable beyond the confines of health biotech to encompass other enterprises.

In this research, theoretical and empirical methods are used. At first, a documentary analysis is carried out since the object of study requires prior knowledge. This method allows to create the theoretical framework of the research. Additionally, the analysis and synthesis method is used to decompose the research object into the different elements that make it up in order to integrate them later. This method allows to know how the object works. The historical-logical

method is also used, which makes it possible to know the different stages of the development of the object, its chronological evolution; in addition to providing the most important elements of the phenomenon, the object in its internal and essential connections.

Specifically, the consensus method was used to select the experts participating in the application of the Analytic Network Process methodology. In this same paper (Chapter IV) the brainstorming method is employed by the experts to elect the factors affecting the drug candidate's price estimation. These factors were refined by the same experts to eliminate repetitions. After that, a non-hierarchical clustering method (non-model-based) is used by one of the experts and the research authors to group factors affecting the drug candidate's price estimation.

Validity, reliability and setting criteria in the methods used for decision-making are relevant concepts to achieve good results (Canós et al., 2014; Canós & Liern, 2008). It is possible to distinguish between internal and external validity. The first occurs when the conclusions obtained from the research results are adequately supported by the data, that is, the data collected is accurate and reliable, the analysis are relevant to the type of data (von Solms, 2011) and the measurement of the data is representative because it includes the main elements of the construct under study, which can be evaluated through opinions of various stakeholders (Déry et al., 2020). External validity implies that the findings of a research are generalizable, as long as internal validity is met (Babbie, 2007). Both the internal and external validity of the AHP/ANP method have been defended in different papers, in which some of them described examples to support this fact, for example, Saaty (2010); Ishizaka & Labib (2009); Saaty et al. (2009); or Saaty (2005). To sum up, von Solms (2011) concludes that, in a real world with different stakeholders, where there is uncertainty, there are no known results, but where the values, preferences and subjective criteria of decision makers need to be included in a model, AHP and ANP are tools for which validity has been verified. The process involved in the implementation of these tools is stable, coherent, systematic, transparent and involves setting criteria, so there is reliability (Van Horenbeek & Pintelon, 2014).

The binomial real option tree was also employed as a method to manage uncertainty (Santa Cruz, 2023) and provide flexibility. This method divides the time to maturity in small stages or time steps, in which the market results can move up or down, with a certain probability (Bogdan & Villiger, 2010; Kamel et al., 2023; Tian et al., 2023). The binomial real option tree constitutes also a tool for strategic risk managing according to Savchuk (2023).

Fuzzy logic methods are applied in Chapter V to palliate uncertainty. Specifically, the triangular fuzzy numbers were employed to express parameters such as the percentage of diagnosis, access to the health system, the treatments' adherence rate, the cost of capital, and the probabilities of moving forward in the development process of a drug candidate to improve the Alzheimer desease. A triangular fuzzy number is a fuzzy number represented with three points, each one of those is interpreted as membership functions (Mallo et al., 2001; Oramas Santos, Anido, et al., 2022). The data was provided by the company leading the project, and the confidence intervals were constructed from information in published papers that address the same disease, which are Alzheimer's Association (2023); BrightFocus Foundation (2021); CEPDE (2014); Cubadebate (2014, 2023); Fariñas (2022); Llibre (2013); MINSAP (2022); Molina (2021); Noda (2022); ONEI (2023); Ortega Cerda et al. (2018); Rajan et al. (2021); Rennane et al. (2021); Scott et al. (2014); Tom et al. (2015); and Trabajadores (2023). In the fuzzification of a certain number, the same value was employed in the three points of the triangular fuzzy number, as Kaufmann (1990) suggests.

1.4 RESEARCH DISSEMINATION

Research dissemination refers to sharing research findings with various audiences, including other researchers, practitioners, policymakers, etc. (Parent-Johnson & Duncan, 2024). It involves communicating the results, implications, and significance of research in a way that is accessible and understandable to different target groups (Stewart et al., 2023). The dissemination of this research can be corroborated through the following list of published papers, either as papers in academic journals or book chapters, as well as with participation in conferences as a speaker.

Papers

1. Oramas Santos, O., Canós-Darós, L., Babiloni, E., & Ortiz Torres, M. (2023). De cadena de suministros a cadena de valor: Devenir y pertinencia de los conceptos. *Economia y Desarrollo*, *167*(1). http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0252-85842023000100012&lng=es&nrm=iso&tlng=es

2. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). The value chain approach in red biotechnology companies from a bibliometric perspective. *International Journal of Production Management and Engineering*, *11*(2), 187-196. https://doi.org/10.4995/ijpme.2023.19135

3. Oramas Santos, O., Canós-Darós, L., Ortiz Torres, M., & Babiloni, E. (2023). A proposal for a National Innovation System supported by the Value Chain of the Cuban Biotechnological Industry. *GECONTEC: Revista Internacional de Gestión Del Conocimiento y La Tecnología*, *11*(1), 69-78. https://doi.org/10.5281/zenodo.7927982

4. Oramas Santos, O., Ortiz Torres, M., Canós-Darós, L., & Babiloni, E. (2024). Multicriteria decision techniques applied to valuation in the life sciences. *European Research on Management and Business Economics*. (Submitted March 10th, 2024; Accepted for review March 18th, 2024)

5. Oramas Santos, O., Ortiz Torres, M., Canós-Darós, L., & Babiloni, E. (2024). Estimating Value in Health Biotech Projects: Fuzzy Modelling, Funding, and Chain Management in a Cuban Case. *Journal of Economic Literature*. (Submitted October 26th, 2023; Accepted for review December 8th, 2023; Accepted for publication March 3rd, 2024)

Papers from 2 to 5 constitute the core of this thesis and will be presented in as chapters II, III, IV, and IV.

Book Chapters

1. Oramas Santos, O., Anido, L. S., & Torres, M. O. (2022). *Investment Evaluation Proposal with Fuzzy Tools: Case Molecular Immunology Center*. https://doi.org/10.1007/978-3-030-93787-4_5

2. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). Value Chain Approach in Biotechnology Companies: A Bibliometric Analysis. En *IoT and Data Science in Engineering Management. CIO 2022. Lecture Notes on Data Engineering and Communications Technologies*. Vol. 160, p. 527. Springer, Cham. https://doi.org/10.1007/978-3-031-27915-7_59

Proceedings' Books Chapters

1. Oramas Santos, O., Canós-Darós, L., Babiloni, E., & Ortiz Torres, M. (2022). La logística y el enfoque de cadenas. *Simposium de Investigadores Predoctorales en Organización de Empresas*, *1*, 161.

2. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2022). The value chain of the Cuban biotechnological industry in the core of the national innovation system. *I International Conference of Entrepreneurship, Education and Digital Transformation. Book of Proceedings*, *1*, 185.

3. Oramas Santos, O., Canós-Darós, L., Ortiz Torres, M., & Babiloni, E. (2022). La innovación en la Industria Biotecnológica Cubana. *10th International Conference on Innovation, Documentation and Education*. INNODOCT/22, València, España. https://doi.org/10.4995/INN2022.2022.15738

4. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). Valoración de un producto biotecnológico cubano a partir de su cadena de valor. *II Simposium Predoctoral de Organización de Empresas*, p. 108-113. http://hdl.handle.net/10251/196663

5. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2024). Valuation in biotech: estimation of value added by externalities. *III Simposium Predoctoral de Organización de Empresas*. (in publication process)

Conferences

1. Oramas Santos, O., Souto Anido, L. (2021). Cadena de valor de un producto biotecnológico. *I Congreso Internacional de Investigación en Contabilidad*. Barcelona, España.
2. Oramas Santos, O. (2021). El enfoque de la cadena de valor: aplicación práctica a un producto biotecnológico cubano. *Encuentro Internacional de Investigación en Ciencias Económicas, Administrativas y Contables*. Cartagena de Indias, Colombia.
3. Oramas Santos, O. (2021). La cadena de valor como parte de la cadena de suministro: Caso práctico CIGB500. *Conferencia Internacional de ADMINISTRACIÓN DE NEGOCIOS*. Cajamarca, Perú.
4. Oramas Santos, O., Canós-Darós, L., Babiloni, E., & Ortiz Torres, M. (2022). La logística y el enfoque de cadenas. *Simposium de Investigadores Predoctorales en Organización de Empresas*. València, España.
5. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2022). The value chain of the Cuban biotechnological industry in the core of the national innovation system. *I International Conference of Entrepreneurship, Education and Digital Transformation.* Costa Rica.
6. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). Value Chain Approach in Biotechnology Companies: A Bibliometric Analysis. En *IoT and Data Science in Engineering Management. CIO 2022. Lecture Notes on Data Engineering and Communications Technologies*. Toledo, España.
7. Oramas Santos, O., Canós-Darós, L., Ortiz Torres, M., & Babiloni, E. (2022). La innovación en la Industria Biotecnológica Cubana. *10th International Conference on Innovation, Documentation and Education*. INNODOCT/22, València, España.

8. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). Valoración de un producto biotecnológico cubano a partir de su cadena de valor. *II Simposium Predoctoral de Organización de Empresas*. València, España.

9. Oramas Santos, O., Ortiz Torres, M. (2023). La cadena de valor como herramienta previa a la aplicación de métodos de valoración: el caso de un proyecto biotecnológico cubano. *Congreso Internacional de Economía, Contabilidad y Administración, ECAD 2023*. La Habana, Cuba.

10. Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2024). Valuation in biotech: estimation of value added by externalities. *III Simposium Predoctoral de Organización de Empresas*. València, España.

11. Oramas Santos, O., Babiloni, E., Canós-Darós, L., Ortiz Torres, M., & Canós-Darós, M. J. (2024). Aplicación de ANP a la estimación de precios. *XV Reunión de GEDM*. Oviedo, España.

Even if the disseminated knowledge in each paper, book chapter, or conference paper stands alone, they are all aligned with the main objective of this research. Specially the papers constituting the core of this doctoral thesis are interconnected allowing to follow a logical thread in its reading. By analyzing the VC approach in Chapter II, particularly in the biotech sector, it was possible to show that the interaction between this field and the VC approach is not widely studied from a business perspective, especially in developing countries. It also reveals some of the actors that have been considered in the NIS and model proposals, including governments, universities, and the society. Studying the biotech health sector under the VC umbrella extends the range of possibilities to identify the value-drives in this field, which allows a more accurate projects valuation.

The study case of Cuba as a developing country appears in Chapter III. By imbibing from international experiences summarized in appendix 1, the NIS proposal strengthens the actors identified in the bibliometric analysis. It shows others also affecting valuation in biotech health projects, including investors, international regulations, technology and innovation policies, and the specific business activities. These factors have been considered when

determining the variables affecting the price of a drug candidate and when clustering in Chapter IV, as well as when identifying the funding options to apply for in Chapter V.

Chapter IV is a subset of Chapter V. It proposes applying the ANP methodology to drug candidates' price estimation using the information revealed in chapters II and III. The proposal is due to the ANP allows to include unquantifiable factors in the analysis and the relative importance they have regarding others, as well as it perfectly links with the VC approach.

The relationship between firms and organizations along the VC, the particularities of the health biotech industry, and the proposal for price estimation purposes (step 3 when computing the net present value risk adjusted), are considered in the model explained in Chapter V. The employed methodologies have been well applied in many published papers such as Byrne (1996); Chrysafis & Papadopoulos (2021); de Andrés-Sánchez (2023); French & Gabrielli (2005); Huang et al. (2020); Kahraman et al. (2023); León et al. (2002); Mahata & Mahata (2020); Oramas Santos et al. (2022); Sergi & Sari (2021); and S.-Y. Wang & Lee (2021). The Cuban study case developed in this chapter, which is the same in Chapter IV, allowed to demonstrate the applicability and benefits of the proposed model. This chapter proposal also includes the sustainability value, which, in the opinion of Santana et al. (2015), enlarge the vision of the health biotech project by enhancing it.

CAPÍTULO II. THE VALUE CHAIN APPROACH IN RED BIOTECHNOLOGY COMPANIES FROM A BIBLIOMETRIC PERSPECTIVE

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). The value chain approach in red biotechnology companies from a bibliometric perspective. *International Journal of Production Management and Engineering*, *11*(2), 187-196. https://doi.org/10.4995/ijpme.2023.19135

The value chain approach in red biotechnology companies from a bibliometric perspective

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ABSTRACT

This paper analyzes the value chain approach in the red biotechnology sector from the point of view of bibliometrics, using Scopus and Web of Science databases from 2011 to 2021. The 82 papers covering this topic were analyzed with VOSviewer and R studio. The primary results show increased scientific interest with a positive trend in publication for the period considered. However, there is no author network in both databases. Furthermore, the main reason for using the value chain approach in the red biotechnology sector is that it highlights government involvement in the industry due to its social impact. As a research gap, it is advisable to study the impacts of Industry 4.0 on the red biotechnology value chain approach.

Keywords: Value Chain Approach; Red Biotechnology; Bibliometric Analysis.

2.1 INTRODUCTION

The academic community has discussed value theory in several scientific conferences, journals (Benington & Moore, 2011), and research fields. From an economic point of view, value is considered as the willingness of customers to pay for a good provided by a company. This value is entered into the company's income statement by multiplying the quantity sold and the price of a particular product. However, Porter (1991) recognizes value theory as a tool for strategic competitive analysis.

Porter (1991) provides the seminal definition of a Value Chain (hereafter, VC). This author defines a VC as a tool for configuring and linking a company's activities to create a product or service. To source and supply products to customers, a company is not alone but must

develop relationships with other companies and their value chains. This network is called Value System.

Kaplinsky & Morris (2000) points out that there is considerable overlap between Porter's definition and similar definitions used in other contexts, which becomes a problem of terminology confusion.

The *filière* concept, for instance, was developed in the 1960s in France to describe the flow of inputs and services involved in producing a final product and is entirely in line with Porter's Value System definition. On the other hand, Gereffi (1994) talks about global commodity chains focusing on the power relations embedded in VC in a globalized ecosystem. A similar idea is provided by Womack & Jones (1996), who use the phrase value stream to refer to VC.

The modern VC analysis shows it as a tool that includes both, internal and external activities, to obtain and realize a product, from producers to consumers, including post-sale actions.

Ricciotti (2020) confirms that over the years, the definition of VC has been expanded, improved, and innovated with concepts such as Virtual VC, Added VC, Reverse VC, Sustainable VC, etc. However, in this study, the authors will only work with the concept of VC because from their point of view, other related concepts are attributes or characteristics of VC and not a different approach to VC.

A VC consists of a set of value-creating activities that are planned, coordinated, controlled, and continuously improved. All these activities occur to obtain a product or provide a service, along the flow channel, from the initial source to the destination.

In addition to tasks directly related to the production of goods, its distribution and sale, a VC includes those activities of research, development, patenting, search for and obtaining financing, waste treatment, recycling, and disposing of the final product after it is no longer in use.

VC performance is characterized by flexibility and cooperation between the different actors or decision makers. On this path, the main goal is to maximize the chain's margins, profitability, and value, to gain or maintain a competitive advantage.

The VC approach aligns with the new industrial policy's goal (Kaplinsky & Morris, 2000) to create global competitiveness, value-adding, and innovative industries to generate more productive jobs and reduce poverty towards shared prosperity (Terzi et al., 2022).

Nowadays, one of the five most innovative sectors is the biotechnology (hereafter, biotech) industry (Ideascale, 2017), which is considered one of the critical technologies of the XXI century to produce knowledge, goods, and services (Uecke, 2012). Biotech applications are classified using a color index as shown in Table 1.

Table 1. Biotech activities by colors.

Biotech Activity	Color sector
Health, Medical, Diagnostics	Red
Food Biotechnology, Nutrition Science	Yellow
Aquaculture, Coastal, and Marine Biotech	Blue
Agricultural, Environmental Biotechnology-Biofuels, Biofertilizers, Bioremediation, Geomicrobiology, Food Production	Green
Arid Zone and Desert Biotechnology	Brown
Bioterrorism, Biowarfare, Biocrimes, and Anticrop warfare	Dark
Patents, Publications, Inventions, IPRs	Purple
Gene-based Bioindustries	White
Bioinformatics, Nanobiotechnology	Gold
Classical Fermentation and Bioprocess Technology	Grey

Source. Adapted from De la Vega et al. (2015).

Companies that develop medical applications are also referred to as red biotechnology companies, as shown in Table 1. Uecke (2012) shows that the number of biotech companies active in health (51%, followed by 19% for companies in agriculture and food), as well as the R&D spending on red biotech internationally (87% of total expenditures in this sector) and the share of healthcare-related biotech products (80% of the industry's total sales), demonstrate that the red sector is the largest of all biotech sectors. Ten years later, Martin et al. (2021) reveals a global growth rate of 1.3% from 2015 to 2020, and claims that there will be more in-vestment in R&D worldwide within the next five years.

From a VC perspective, this study selects red biotech for several reasons. First, products or therapies are derived from research aimed at improving a patient's quality of life and are evaluated for added value. Researchers are constantly creating new knowledge in this field, and their contributions to science are measured by the value of this knowledge or its social impact. Third, this is a science-intensive field where innovation and cutting-edge technology are essential to their success.

Published works addressing the value chain in the red biotechnology sector seem to focus more on medical and technological issues. This does not appear to be an area that is sufficiently studied from a management standpoint.

Given this defined gap, the research questions posed in this study are: (1) What are the trends and citation networks of VC publications in red biotechnology? (2) Who are the most influential and productive authors, affiliates, countries, and years? (3) What are the most relevant reasons to use the VC approach in red biotech? (4) What are the research gaps in this field?

To answer the research questions, this study aims to analyze the VC approach in the field of red biotechnology from the bibliometric point of view.

To fill it, its authors use Scopus and Web of Science (WoS) databases as well as VOSviewer and R studio software to display the results and highlight findings and conclusions. This is the first bibliometric study to address this topic to the best of the authors' knowledge.

2.2 METHODOLOGY

Bibliometric analysis is increasingly popular in the scientific community (Choudhri et al., 2015; Dhiaf et al., 2021; Holgado de Frutos et al., 2020; Movahedipour et al., 2016). It is employed to analyze bibliographic literature from a quantitative perspective and to evaluate the activity of the scientific community in a particular area of knowledge (Dhiaf et al., 2021; Merigó et al., 2015).

The methodology pursued in this manuscript is shown in Fig. 1 and developed following Carrizo & Moller (2018)and Choudhri et al. (2015) propositions.

To complete step 1, it is necessary first to demonstrate the relevance of the study. The next step is to define a specific and measurable research goal. To achieve meaningful research, specific keywords and inclusion and exclusion criteria must be identified, and these are the follow-up actions. Search execution consists of consulting the Scopus and the WoS databases to collect the published papers on red biotech VC approach, following the criteria defined in step 1. The final step is intended to display, analyze, and discuss the results provided by the database and processed by the authors using Microsoft Excel, VOSviewer, and R studio software.

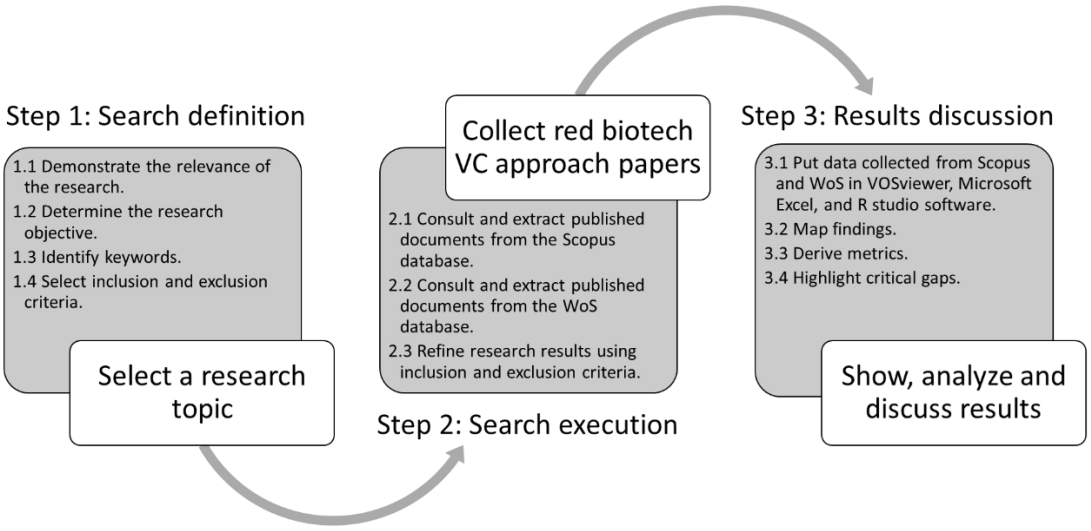

Fig. 1. The methodological research process of this study. Source. Self-made.

According to the research field, the keywords identified and selected are: “value chain”; “biotechnology”; “health biotechnology”; “disease biotechnology”; “medical biotechnology”; “red biotechnology”; “biopharmaceutical”; and “biopharmacy”.

Selected inclusion and exclusion criteria were keyword combination, period analysis, document type and communication language. In this sense, the first decision focused on determining the keyword combination to be researched, resulting in articles containing in their titles, abstracts, and keywords combinations of the following keywords: “value chain” AND “biotechnology” AND “health”.

The research period is from 2011 to 2021 which is justified according to Carrizo & Moller (2018), Gómez-Cedeño et al. (2014), and Codina (2019) recommendations. Additionally, the publications before 2011 are not significant either in number or citations. The final date of data collection is February 15, 2022.

Selection criteria for the document type included the choice of journals and articles, excluding conference papers, books, and book chapters. The journal editorial board has the knowledge and experience to identify relevant articles (often previously presented at conferences), to be used as the first filter. Another reason is that usually most book chapters used to be an article published by an academic journal.

After eliminating duplicate papers, the results from the first step are 30 and 52 papers from Scopus and WoS, respectively.

2.3 RESULTS AND DISCUSSION

This section specifically: (1) identifies the most influential authors, their affiliations, and the most productive publication's year and countries; (2) reveals current research trends; (3) highlights the main reason to adopt the biotech VC approach, and (4) maps and summarizes results.

2.3.1 Value chain approach on the selected databases

Amador & Di Mauro (2015) argues that the VC approach has become at the heart of the competitiveness debate and that by studying publications in different databases, researchers can compare this. Since 1928, the Scopus and WoS databases have collected 22.285 and 14.327 VC publications, respectively. The first documents related to the VC approach to appear in the Scopus and WoS databases were "CXLVIII. - On the oxidation of n-hexane", and "The role of global procurement in the value chain of Japanese steel".

Regarding the VC approach, the most cited paper, with 398 citations between 2011 and 2021, is "The governance of global value chains", published by Gereffi et al. (2005) in the Review of International Political Economy. Likewise, in more than 70 authors, all publications

following the VC approach are concentrated. Table 2 summarizes the most productive authors in the two databases.

Even if Table 2 shows that only Ponte, S. and Rich, K.M. have a publication in both databases, during the period 2011-2021, Gereffi, G.; Lee, J.; Bush, S.R.; Rushton, J.; Donovan, J.; Samsatli, S.; Alarcon, P.; Minten, B.; Mudambi, R.; Reardon, T.; Bijman, J.; Morris, M.; and Sieber, S. are frequent repeat authors in Scopus and WoS, but they are not listed in Table 2 because they are not in the top 20.

Table 2. Top 20 more productive authors in Scopus and WoS databases relative to the VC approach over the years.

Scopus		**WoS**	
Author	**Number of publications**	**Author**	**Number of publications**
Gereffi, G.	42	Ammann, M.J.	42
Ponte, S.	31	Wang, L.	38
Rich, K.M.	26	Cooke, D.R.	37
Minten, B.	23	Labaste, P.	32
Samsatli, S.	23	Webber, C.M.	32
Bijman, J.	22	Liu, Y.	30
Bush, S.R.	22	Li, Y.	28
Donovan, J.	22	Rich, K.M.	25
Morris, M.	22	Skreiberg, O.	25
Swinnen, J.	22	Dunshea, F.R.	24
Pietrobelli, C.	21	Wang, Y.	24
Reardon, T.	21	Ponte, S.	23
Rushton, J.	21	Fuentes, S.	22
Demont, M.	20	Grace, D.	22
Ingram, V.	20	Chen, Y.	21
Barrientos, S.	19	Farrell, R.	21
Dannenberg, P.	19	Viejo, C.G.	21
Häsler, B.	19	Zhang, J.	21
Nadvi, K.	19	Li, J.	20
Di Maria, E.	18	Torrico, D.D.	20

Source. Self-made.

Related to the most influential affiliations, Wageningen University & Research highlights a more prolific membership in the Scopus database, and the Consultative Group on International Agricultural Research (CGIAR) prevails in the WoS database. On the other hand, in both databases, USA, Germany, England, China, and Italy emerged as the most productive countries in VC research.

2.3.2 Biotechnology on the selected databases

Biotechnology "is considered to be one of the key technologies of the 21st century […], is the application of science and technology to living organisms, as well as parts, […] for the production of knowledge, goods, and services" (Uecke, 2012, p. 84). The first publication related to this topic in Scopus and WoS databases was dated 1933 and was provided by Nature Journal. From this year until 2021, the Scopus database shows 179.054 papers, while the WoS database collected 469.057 in the same period.

Especially health studies in biotech publications represent 7.9% in the Scopus database from 1961 to 2021 and 11.1% in the period 1982-2021 for the WoS database (1961 and 1982 represents the first publication year in red biotech registered in Scopus and WoS databases, respectively). The first publication in Scopus and WoS databases related to red biotech using the VC approach is "Disruptive technologies, stakeholders and the innovation value-added chain: a framework for evaluating radical technology development". Until today, it is the most cited paper in Scopus and WoS databases, with more than 100 total citations in each.

2.3.3 Temporal activity in red biotech VC approach: volume and impact of authors and publications

Fig. 2 summarizes the number of publications in Scopus and WoS, where a positive trend can be appreciated clearly. However, it is not an intensive research topic studied by authors in Scopus, who commonly have published only one publication over the period analyzed. Authors in WoS evidence a more stable behavior about year publications.

Table 3 summarizes the authors' publications related to the research topic in both databases and all their published and registered papers in these databases. Using all records (column of All Publications) in Scopus and WoS, H-index and M-index have been calculated separately. H-index measures quantity (number of papers) with quality (number of citations) of published research, is a metric to assess the entire body of scholarly output by an author and means how many papers have at least H citations. M-index is like an average of the H-index while it is calculated by dividing the H-index by the number of years since the first published paper, represented in the PY_Start column in Table 3.

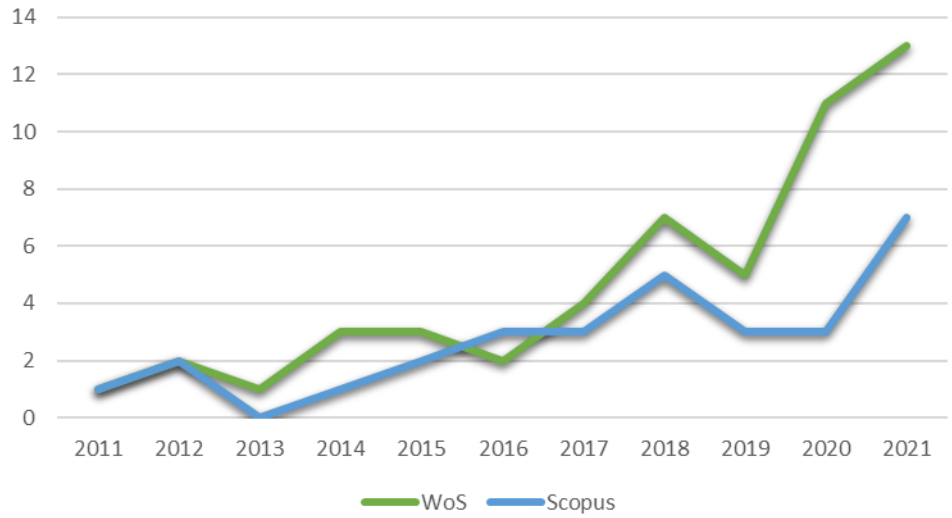

Fig. 2. Red biotech VC approach's publications between 2011 and 2021. Source. Self-made.

According to Scopus records, Van Montagu, M. ranks first in productivity with the highest H-index, followed by Giacca, M. and Singer, P.A. Fevre, E.M. ranks first in WoS with eleven published papers about red biotech VC, seconded by Alarcon, P., and Rushton, J. Analyzing M-index, Van Montagu, M. and Antun, R. rank first as more productive researchers as average per year in Scopus and WoS respectively.

These metrics present the inconvenience that authors in different databases are incomparable because the indexes depend on where you get the publication and citation data. In addition, even if the M-index is a time correction of the H-index, it depends on the H-index, which favors authors with more experience as far publishing years are concerned.

Table 4 presents five major publications on the topic of the study. G-index is calculated by ranking articles by the number of citations received in Scopus and WoS, in descending order. The next step is to number the positions. Finally, the G-index represents the number of documents that have accumulated at least g^2 citations (Hirsch, 2005), resulting in 5 papers for the two databases.

Table 3. Top 15 authors in publications and citations.

Scopus						WoS					
Authors	**Topic's Publications**	**All Publications**	**H-Index**	**PY_Start**	**M-Index**	**Authors**	**Topic's Publications**	**All Publications**	**H-Index**	**PY_Start**	**M-Index**
Van Montagu, M.	1	709	129	1993	4,61	**Fevre, E.M.**	11	161	38	1977	0,86
Giacca, M.	1	512	70	1993	2,50	**Alarcon, P.**	10	20	11	2011	1,10
Singer, P.A.	1	408	76	1993	2,71	**Rushton, J.**	10	135	22	1990	0,71
Wittmann, C.	1	312	46	1993	1,64	**Muinde, P.**	8	14	7	2016	1,40
Wieland, T.	1	240	58	1994	2,15	**Akoko, J.**	6	18	6	2016	1,20
Daar, A.S.	1	219	64	1994	2,37	**Atun, R.**	5	394	58	2000	2,76
Becker, J.	1	87	31	1991	1,03	**Fitchett, J.R.**	5	79	23	1994	0,85
McGahan, A.M.	1	87	21	1992	0,72	**Hasler, B.**	5	88	16	1997	0,67
Philp, J.	1	68	26	1991	0,87	**Head, M.G.**	5	42	12	2007	0,86
Kannt, A.	1	63	24	1996	0,96	**Murungi, M.K.**	5	9	5	2017	1,25
Pietrobelli, C.	1	59	33	2005	2,06	**Cooke, M.K.**	3	21	11	1967	0,20
Rao, N.H.	1	44	18	1993	0,64	**Hayward, A.C.**	3	121	37	1990	1,19
Heijde, M.	1	40	9	1989	0,28	**Kiambi, S.**	3	14	8	2017	2,00
McCarthy, B.	1	24	10	2000	0,48	**Momanyi, K.**	3	7	4	2018	1,33
Katz, J.	1	22	10	1997	0,42	**Wurie, F.B.**	3	24	10	2013	1,25

Source. Self-made.

Table 4. Top five cited papers.

	Scopus			WoS		
	Paper's Title	**Time Cited**	**G-index**	**Paper's Title**	**Time Cited**	**G-index**
1	Becker & Wittmann (2019). A field of dreams: Lignin valorization into chemicals, materials, fuels, and health-care products. *Microbial Engineering Biotechnologies, 37*(6), 107360	113	1	Becker & Wittmann (2019). A field of dreams: Lignin valorization into chemicals, materials, fuels, and health-care products. *Microbial Engineering Biotechnologies, 37*(6), 107360	113	1
2	Lokko et al. (2018). Biotechnology and the bioeconomy—Towards inclusive and sustainable industrial development. *Bioeconomy, 40*, 5-10	52	4	Head et al. (2013). UK investments in global infectious disease research 1997–2010: A case study. *The Lancet Infectious Diseases, 13*(1), 55-64	55	4
3	Philp (2018). The bioeconomy, the challenge of the century for policymakers. *Bioeconomy, 40*, 11-19	52	9	Kalpana Sastry et al. (2011). Nanotechnology for enhancing food security in India. *Food Policy, 36*(3), 391-400	44	9
4	Kalpana Sastry et al. (2011). Nanotechnology for enhancing food security in India. *Food Policy, 36*(3), 391-400	53	16	McCarthy et al. (2016). Innovations in the agro-food system. *British Food Journal, 118*(6), 1334-1349	32	16
5	McCarthy et al. (2016). Innovations in the agro-food system. *British Food Journal, 118*(6), 1334-1349	33	25	Alarcon et al. (2017). Mapping of beef, sheep and goat food systems in Nairobi—A framework for policy making and the identification of structural vulnerabilities and deficiencies. *Agricultural Systems, 152*, 1-17	31	25

Source. Self-made.

Network and content analysis

For network analysis (co-authorship, co-citation analysis, and bibliographic coupling), the VOSviewer software was used. Scopus authors are not connected, but Fig. 3 shows the author's network in WoS.

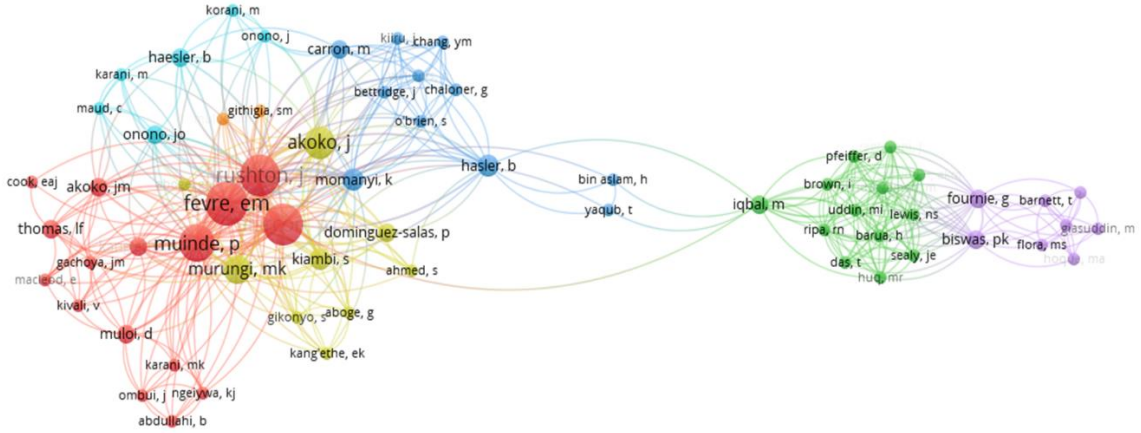

Fig. 3. Co-authorship network visualization in WoS. Source. VOSviewer report.

Authors in the WoS conform 65 links in 7 clusters. Therefore, a weak network of authors investigating VC in the red biotech sector exists. Fevre, E.M. is a vital author that connects other researchers, mainly due to his productivity.

The authors of the sample of papers in both databases come from a few countries: USA, UK, France, and Netherlands. In the same way, the authors' affiliations are also not extensive.

A co-citation source map for papers in both databases is inexistent. According to the co-citation reference map, the situation with Scopus is the same, and only two articles in the WoS form a network: Alarcon et al. (2017) and Gereffi et al. (2005). This result is in line with the dispersion of authors and the few quantities of clusters.

The content analysis provides an overview of the nature of the topic studied in this research. R studio software was used to plot the word cloud based on the author' keywords in Fig. 4.

Fig. 4 shows that in papers from the WoS (Fig. 4a.) and the Scopus (Fig. 4b.) databases, the most common keywords and therefore the most researched topics are: (1) value chain as a strategic tool, (2) innovation in the value chain, (3) impact and application of the VC

approach in the bioeconomy and biotech industry, (4) sustainability of VC, (5) risks in the pharmaceutical sector, (6) VC governance, (7) VC mapping, and (8) social health impacts.

Fig. 4a. WoS' words cloud

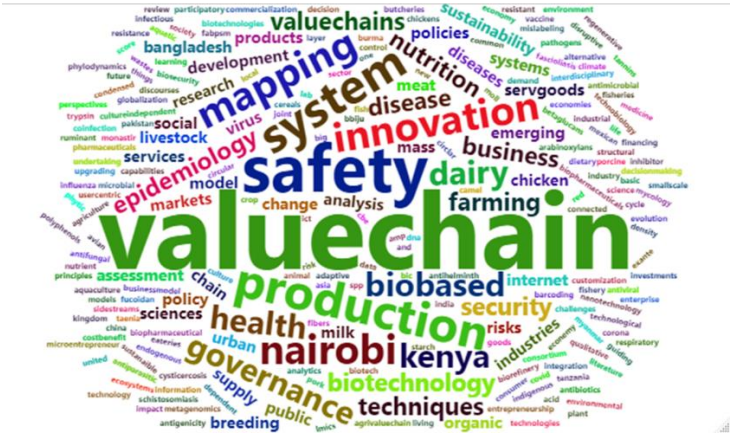

Fig. 4b. Scopus´ words cloud

Fig. 4. Authors' keywords word cloud in Scopus and WoS. Source. R studio report.

2.4 CONCLUSIONS AND HIGHLIGHTS

This study provides the first bibliometric analysis of the value chain approach in the field of the red biotechnology. It was developed to answer the four original research questions, presented in Section 1, and follows a three-step methodology with data collected from the Scopus and the WoS databases. The five most relevant findings are summarized as follows:

(1) After examining the performance of the VC publications on red biotechnology, and its current trends, it can be said that this is not a broad area of research (only 82 papers have

been reviewed, published in the last ten years). Publications have increased over the years, but the low number of publications per author proves that publications on red biotechnology focus on health topics rather than industry. Network does not connect much research. Co-citation analysis of articles is not possible because the articles do not make up the network.

(2) According to Scopus productivity, Van Montagu, M. is the most productive author, while Fevre, E.M. featured in WoS. Prominent institutions are Wageningen University and the University of Liverpool. The most productive years and countries are 2021 and the USA respectively. H-index and G-index were calculated, but these metrics were inconclusive because the authors in different databases could not be compared. After all, the indexes depend on where research get the publication and citation data.

(3) The most relevant reasons to use the VC approach in this industry are the effects of government, due to its social impact, and the ability to link activities in the technology and global environment.

(4) This study demonstrates the existence of certain gaps that shape the future agenda. First, the modern concept of VC, which analyzes a company's complex network, including international relationships, is not widely studied, and applied in the field of red biotechnology. Second, and regarding red biotechnology and its business model, there are no published works that analyze the early stages of a biotechnology product, i.e. when the product is a project. The value created in this process is just as important as the impact of the product in the future, if not more, because if the project cannot make it past this stage, it will never become a product. Third, research indicates that current topics such as the impact of Industry 4.0 on red biotech VC have yet to be thoroughly studied. Industry 4.0 applications such as Blockchain technology and the Internet of Things (Dhiaf et al., 2021; Khan et al., 2021; Meseguer-Sánchez et al., 2021; M. Wang et al., 2020; Wiedmer & Griffis, 2021; Zhang & Chen, 2020) can boost business performance and deliver better economic, social, and environmental outcomes.

(5) Finally, future research can be directed toward mapping VCs for products in less developed countries, applying techniques to reduce the uncertainty and risks these regions.

All actors must be considered, including governments, funding organizations, universities, and regulatory agencies.

REFERENCES

Alarcon, P., Fèvre, E. M., Murungi, M. K., Muinde, P., Akoko, J., Dominguez-Salas, P., Kiambi, S., Ahmed, S., Häsler, B., & Rushton, J. (2017). Mapping of beef, sheep and goat food systems in Nairobi—A framework for policy making and the identification of structural vulnerabilities and deficiencies. Agricultural Systems, 152, 1-17. https://doi.org/10.1016/j.agsy.2016.12.005

Amador, J., & Di Mauro, F. (Eds.). (2015). The Age of Global Value Chains: Maps and Policy Issues. Centre for Economic Policy Research.

Becker, J., & Wittmann, C. (2019). A field of dreams: Lignin valorization into chemicals, materials, fuels, and health-care products. Microbial Engineering Biotechnologies, 37(6), 107360. https://doi.org/10.1016/j.biotechadv.2019.02.016

Benington, J., & Moore, M. (Eds.). (2011). Public Value: Theory and Practice. Bloomsbury Publishing.

Carrizo, D., & Moller, C. (2018). Estructuras metodológicas de revisiones sistemáticas de literatura en Ingeniería de Software: Un estudio de mapeo sistemático. Ingeniare. Revista chilena de ingeniería, 26, 45-54. https://doi.org/10.4067/S0718-33052018000500045

Choudhri, A. F., Siddiqui, A., Khan, N. R., & Cohen, H. L. (2015). Understanding Bibliometric Parameters and Analysis. RadioGraphics, 35(3), 736-746. https://doi.org/10.1148/rg.2015140036

Codina, L. (2019). Taller de bases de datos académicas Scopus, WoS y Mendeley. 91.

De la Vega, I., Requena, J., & Fernández-Gómez, R. (2015). The colors of biotechnology in Venezuela: A bibliometric analysis. Technology in Society, 42, 123-134. https://doi.org/10.1016/j.techsoc.2015.03.007

Dhiaf, M. M., Atayah, O. F., Nasrallah, N., & Frederico, G. F. (2021). Thirteen years of Operations Management Research (OMR) journal: A bibliometric analysis and future research directions. Operations Management Research, 14, 235-255. https://doi.org/10.1007/s12063-021-00199-8

Gereffi, G. (1994). The Organization of Buyer-Driven Global Commodity Chains: How U. S. Retailers Shape Overseas Production Networks (Korzeniewicz & Gereffi, Eds.). Praeger.

Gereffi, G., Humphrey, J., & Sturgeon, T. (2005). The Governance of Global Value Chains. Review of International Political Economy, 12, 78-104. https://doi.org/10.1080/09692290500049805

Gómez-Cedeño, M., Castán, J. M. a, & Guitart-Tarrés, L. (2014). La importancia de los recursos humanos en la cadena de suministro. Dirección y Organización, 54, 13-25.

Head, M. G., Fitchett, J. R., Cooke, M. K., Wurie, F. B., Hayward, A. C., & Atun, R. (2013). UK investments in global infectious disease research 1997–2010: A case study. The Lancet Infectious Diseases, 13(1), 55-64. https://doi.org/10.1016/S1473-3099(12)70261-X

Hirsch, J. (2005). An index to quantify an individual's scientific research output. Proc Natl Acad Sci U S A, 102(46), 16569-16572. https://doi.org/10.1073/pnas.0507655102

Holgado de Frutos, E., Trapero, J. R., & Ramos, F. (2020). A literature review on operational decisions applied to collaborative supply chains. PLoS ONE, 15(3), e0230152. https://doi.org/10.1371/journal.pone.0230152

Ideascale. (2017). 5 Industries with the Most Innovative Companies. InnovationManagement. https://innovationmanagement.se/2017/03/30/5-industries-with-the-most-innovative-companies/

Kalpana Sastry, R., Rashmi, H. B., & Rao, N. H. (2011). Nanotechnology for enhancing food security in India. Food Policy, 36(3), 391-400. https://doi.org/10.1016/j.foodpol.2010.10.012

Kaplinsky, R., & Morris, M. (2000). A Handbook for Value Chain Research, (Vol. 113). Brighton: University of Sussex, Institute of Development Studies.

Khan, S. A. R., Godil, D. I., Jabbour, C. J. C., Shujaat, S., Razzaq, A., & Yu, Z. (2021). Green data analytics, blockchain technology for sustainable development, and sustainable supply chain practices: Evidence from small and medium enterprises. Annals of Operations Research. https://doi.org/10.1007/s10479-021-04275-x

Lokko, Y., Heijde, M., Schebesta, K., Scholtès, P., Van Montagu, M., & Giacca, M. (2018). Biotechnology and the bioeconomy—Towards inclusive and sustainable industrial development. Bioeconomy, 40, 5-10. https://doi.org/10.1016/j.nbt.2017.06.005

Martin, D. K., Vicente, O., Beccari, T., Kellermayer, M., Koller, M., Lal, R., Marks, R. S., Marova, I., Mechler, A., Tapaloaga, D., Žnidaršič-Plazl, P., & Dundar, M. (2021). A brief overview of global biotechnology. Biotechnology & Biotechnological Equipment, 35(sup1), S5-S14. https://doi.org/10.1080/13102818.2021.1878933

McCarthy, B., Liu, H.-B., & Chen, T. (2016). Innovations in the agro-food system. British Food Journal, 118(6), 1334-1349. https://doi.org/10.1108/BFJ-10-2015-0375

Merigó, J. M., Gil-Lafuente, A. M., & Yager, R. R. (2015). An overview of fuzzy research with bibliometric indicators. Applied Soft Computing, 27, 420-433.

Meseguer-Sánchez, V., Gálvez-Sánchez, F. J., López-Martínez, G., & Molina-Moreno, V. (2021). Corporate social responsibility and sustainability. A bibliometric analysis of their interrelations. Sustainability (Switzerland), 13(4), 1-18. https://doi.org/10.3390/ su13041636

Movahedipour, M., Yang, M., Zeng, J., Wu, X., & Salam, S. (2016). Optimization in supply chain management, the current state and future directions: A systematic review and bibliometric analysis. Journal of Industrial Engineering and Management, 9(4), 933-963. http://dx.doi.org/10.3926/jiem.2035

Philp, J. (2018). The bioeconomy, the challenge of the century for policy makers. Bioeconomy, 40, 11-19. https://doi.org/10.1016/j.nbt.2017.04.004

Porter, M. E. (1991). Towards a dynamic theory of strategy. Strategic Management Journal, 12(S2), 95-117. https://doi.org/10.1002/smj.4250121008

Ricciotti, F. (2020). From value chain to value network: A systematic literature review. Management Review Quarterly, 70(2), 191-212. https://doi.org/10.1007/s11301-019-00164-7

Terzi, A., Singh, A., & Sherwood, M. (2022). Industrial Policy for the 21st Century: Lessons from the Past. European Economy Discussion Papers, 157. http://data.europa.eu/doi/10.2765/xxxxx

Uecke, O. (2012). How to Commercialise Research in Biotechnology? Springer Gabler. https://doi.org/10.1007/978-3-8349-4134-3

Wang, M., Wu, Y., Chen, B., & Evans, M. (2020). Blockchain and Supply Chain Management: A New Paradigm for Supply Chain Integration and Collaboration. Operations and Supply Chain Management: An International Journal, 14(1), 111-122. https://doi.org/10.31387/oscm0440290

Wiedmer, R., & Griffis, S. E. (2021). Structural characteristics of complex supply chain networks. Journal of Business Logistics, 42(2), 264-290. https://doi.org/10.1111/jbl.12283

Womack, J. P., & Jones, D. T. (1996). Lean Thinking: Banish Waste and Create Wealth in Your Corporation. Simon & Schuster.

Zhang, C., & Chen, Y. (2020). A review of research relevant to the emerging industry trends: Industry 4.0, iot, blockchain, and business analytics. Journal of Industrial Integration and Management, 5(1), 165-180. https://doi.org/10.1142/S2424862219500192

CAPÍTULO III. A PROPOSAL FOR A NATIONAL INNOVATION SYSTEM SUPPORTED BY THE VALUE CHAIN OF THE CUBAN BIOTECHNOLOGICAL INDUSTRY

Oramas Santos, O., Canós-Darós, L., Ortiz Torres, M., & Babiloni, E. (2023). A proposal for a National Innovation System supported by the Value Chain of the Cuban Biotechnological Industry. *GECONTEC: Revista Internacional de Gestión Del Conocimiento y La Tecnología*, *11*(1), 69-78. https://doi.org/10.5281/zenodo.7927982

A proposal for a National Innovation System supported by the Value Chain of the Cuban Biotechnological Industry

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ABSTRACT

A National Innovation System (NIS) supposes updated, continuous, and collaborative work between different agents, so the value chain approach fits perfectly with this NIS conception. The sector selected to illustrate our proposal is the biotechnological industry because of its structure in technology-based companies and its contributions to de Cuban GDP. This is the first research that works in a proposition of NIS for Cuba. The objective of this paper is to suggest a NIS for Cuba based on the value chain of its biotechnological industry. We follow a benchmarking methodology. First, we analyze nine international NIS experiences from developed and developing countries. Then, we highlight several items to be applied to the Cuban proposed NIS by analyzing five indicators: regulations, technology and innovation policies, financial systems, business activities, and research and education systems. The proposed NIS shows links between funding, production, service, and scientific sectors based on the biotechnological industry. It is considered beneficial for the three most important actors in a nation (companies, government, and society) because it allows a profitable and durable solution for economic and social troubles.

Keywords: Biotechnology; Cuba; National Innovation System; Value Chain.

3.1 INTRODUCTION

The 90s witnessed the birth of a large body of research on the interrelationships of the companies' level of exploration and exploitation of knowledge and external knowledge providers, with the critical role of governments and policy in shaping these dynamics. In this

way, the National Innovation System (NIS further on) concept becomes a popular analytical tool for researchers who want to get a firmer grasp of what determines the performance of such interaction. However, adopting the innovation system approach to developing countries is a relatively recent phenomenon (Fagerberg & Srholec, 2008; Pietrobelli & Rabellotti, 2011).

In developing countries like Cuba, building dynamic and innovative interactions between business actors, knowledge and technology providers, and the government is crucial to improve local businesses' ability to deal with the risk in their market operations. A NIS conception linked to the value chains generated by the business system stimulates efficiency, resilience, and business responsiveness according to society's requirements.

In Cuba, the State places in the foreground the role of science, technology, and innovation in all instances. Nowadays, links between all the activities or sectors are fuzzy. Likewise, national policies promote the development and sustainability of the biotechnological industry, given its nature as a producer of goods and services with high added value, ensuring its interaction with the rest of the academic, productive, technological, service sectors, etc. (PCC, 2019). According to these priorities for the Cuban government and given the lack of a global managerial tool to improve business and social benefits, our research question is: how could improve Cuban society and economy with the innovation as a driven?

In this research, we want to offer ideas for a NIS based on the value chain of the Cuban Biotechnological Industry (CBI). We choose CBI because it is the industry with the most Technology-Based Companies (TBC) in Cuba. Its contributions to GDP approximately represented 10% in 2019, being the industry with the highest contribution according to the Spain' Secretary of State and Commerce (2021).

This paper is divided into six sections to achieve our main objective. Section one introduced the research field. Section two discusses the concept of innovation, NIS, and the value chain approach; also, in this section, we offer some general characteristics of the biotechnological companies. In section three, we explain the followed research method. Section four summarizes the common points of nine NIS studied, and then we present our proposal of NIS for Cuba, based on the value chain of the CBI. In section five, we explain all components

of our proposal for the Cuban NIS. The conclusion section summarizes the benefits of our proposal for Cuban industry and society.

3.2 BRIEF THEORETICAL FRAMEWORK

According to Schumpeter (1961), innovation means introducing new products, processes, organizational changes, etc., in an ongoing way oriented to the user. It is a process that starts with a new opportunity to achieve the invention's commercial success through designing, production, and marketing activities (OECD, 2010). Rodríguez Batista & Núñez Jover (2021) remark that innovation is more than technology and the market; it results from interactive processes in which companies use their own and others' resources through cooperation and coordination with other environmental actors. Open innovation, allowing internal and external knowledge flows, is promoted to extract the most outstanding value from the innovative potential, with a clear human nature component (Chesbrough, 2006).

Networks of actors in public and private sectors, whose activities and interactions initiate, import, modify, and disseminate new technologies and knowledge inside the borders of a nation-state, compose a NIS (Lundvall, 1992). According to Balzat & Hanusch (2004), a NIS also encompasses research and development efforts by companies and public actors (non-linear and multidisciplinary innovation processes) and innovation issues such as learning processes, incentive mechanisms, and availability of skilled labor. These authors affirm that NIS theory has been studied from a policy-oriented (benchmarking to reveal technology policy implications, innovation policy designs, incentive mechanisms for innovative action, etc.) and research-driven (descriptive frameworks and analytical models) points of view.

A NIS model has a variety of analysis' units (Balzat & Hanusch, 2004; E. Castro & Fernández, 2001; Kurpayanidi, 2021; Samara et al., 2012; Watkins et al., 2014) shown in Fig 5. Fig. 5 shows the main actors in a NIS: Governments, regulatory agencies, funding institutions, firms (which generate commercial innovations), and universities. In a continuous and open innovation process, these agents interact under determinate market conditions and in a specific institutional, cultural, and legal environment. Those links become a competitive advantage if innovative product creation and development are based on a value

chain perspective (Mollenhauer & Hormazábal, 2012; Pietrobelli & Rabellotti, 2011). Information flows from an agent to another as a data-driven innovation system (Yu et al., 2022).

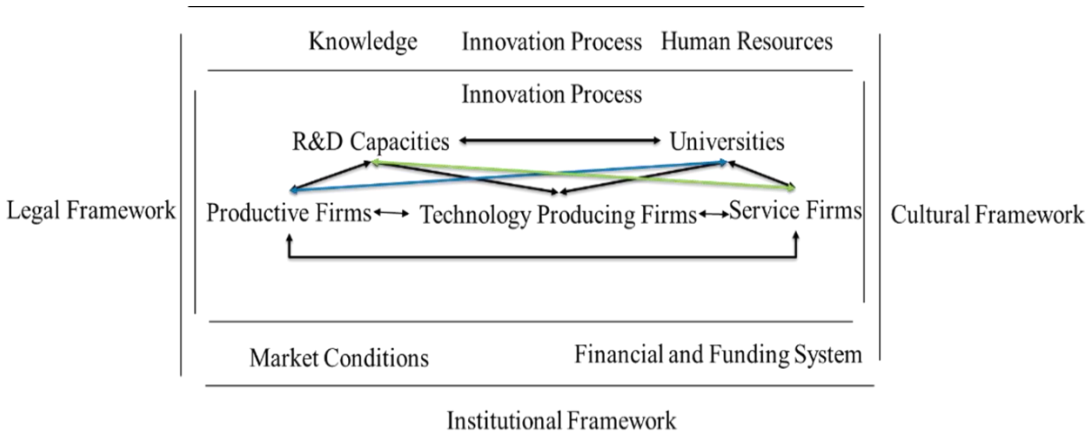

Fig. 5. A generic structure of a NIS model. Source. Self-made.

On the other hand, a value chain identifies the strategic activities that provide a competitive advantage for the company and other activities that support the previous ones (Porter, 1985). Kaplinsky & Morris (2000) note that the value chain describes those actions required to carry out a product or service from its conception, through the intermediate phases of production, until its delivery to the final consumers. Pietrobelli & Rabellotti (2011) suggest that a value chain evaluates how companies and producers can interact and modernize while participating in these chains, positively affecting the development of companies, regions, and countries. The nature of the value chain approach is systemic and comprehensive, with the ability to generate valuable sources of information for decision-making processes regarding industrial policy, value aggregation, and intersectoral and territorial linkages aimed at reducing social and territorial asymmetries (Padilla, 2014; Yin et al., 2021).

We can say that both NIS and value chain are complementary approaches that benefit from each other. Padilla & Oddone (2016) point out that the functioning of NIS and the availability of infrastructure are factors to consider for scaling up to global value chains. García et al. (2018) note that the value chain approach becomes a crucial tool to model and analyze the needed interactions between companies, governments, communities, and other actors to ensure adequate production and distribution of goods, services, and knowledge.

In this context, one of the most innovative industries is the biotechnological industry (Uecke, 2012). OECD (2010) defines biotechnology as applying science and technology to alive organisms and parts to produce goods, services, and knowledge. It is possible to characterize the biotechnology industry in terms of the units providing it value-added, which Link & Siegel (2007) summarize in three: universities and research institutes, biotechnology companies, and commercializing companies. Biotechnology applications can be found in various sectors, such as the healthcare sector (also called red biotechnology or medical biotechnology). The main areas of application of red biotechnology are therapeutics, diagnostics, and pharmacogenetics (Uecke, 2012). It is usual in this industry to find TBC, which are independently owned entities based on exploiting an invention or technological innovation involving the assumption of substantial risks (Little, 1991; Peces Prieto & Trillo Holgado, 2019).

As an emerging science-based industry, biotechnology makes new demands on the institutional environment of a NIS (Cornelissen et al., 2021; Kaiser & Prange, 2004). The production of innovative products demands cooperation and coordination between universities and firms. It is because of the high and increasing cost of those activities, the meaning of interdisciplinarity, the closer relationship between basic research and industrial application, and between producers and customers of innovations. Therefore, those industries require new institutional arrangements, alliances, etc., for funding innovations, technology transfer, and the coordination of R&D activities. The correct interaction between the industry, value chains, and a NIS becomes significant to allow the growth of the biotechnological sector and its spill effect on the national economy and society.

3.3 METHODS

We develop qualitative research. This paper follows the benchmarking method. Hassan et al. (2022) consider three dimensions of benchmarking: (1) identification of international practices, (2) comparison, and (3) implementation and improvements.

After these steps, this paper identifies relevant NIS actors from developed and developing countries in the first place. The studied countries are Germany, US, Greece, Taiwan,

Singapore, Brazil, India, Chile, and Costa Rica. We note that the concept of NIS was born in developed countries and was later applied to developing countries, a category in which Cuba is classified.

In step two, we extract some concurrences for the analysis in step one. Finally, these relevant results are extrapolated to our proposal of a NIS for Cuba.

3.4 RESULTS

Step 1: Identification of international practices

Examining NIS in different countries, it's possible to affirm that their drivers are not the same in developed and developing countries. The notion of NIS has been developed from the background of advanced economies (Kayal, 2008). Then, according to Shulin (1999), the primary factor of NIS in developed countries is the ability to focus strategic management in companies to update their economic, social, and political matters.

Studying NIS in developed countries such as Germany, US, Greece, Taiwan, and Singapore, in contrast with experiences in developing countries such as Brazil, India, Chile, and Costa Rica, we can conclude that its conceptions have been developed around five indicators: regulations, technology and innovation policies, financial systems, business activities, and research and education systems. We highlight these five indicators once we explore the paper's content. The experts suggested some items that conform different NIS, and we make clusters of items to reach the five general indicators.

Kaiser & Prange (2004) propose in Germany a multi-level approach, which directs the dynamic reconfiguration of NIS toward the sub-national and international levels. In contrast, Atkinson (2014) describes the broad elements of the NIS in US organized around the innovation success triangle: Business environment, regulatory environment, and innovation environment. Samara et al. (2012) analyze three subsystems and their independent variables for Greece, conducting six simulation experiments. In Taiwan, NIS supports the reverse value chain, and in Singapore, it emphasizes the government facilitation of technological learning from multi-national corporations (Kayal, 2008).

On the other hand, NIS in Brazil and India are studied by Nassif (2007). Brazil adopted a NIS in which three priorities for public policies were established: (i) Improvement and expansion of the infrastructure system; (ii) Increase in efficiency of the productive sectors, notably of tradeable goods; and (iii) Boost of the innovative capacity of firms with significant export orientation. In India, NIS is based on creating schemes to support the absorption of imported technologies by industry and develop, implement, and commercialize indigenous innovations. Its drives have been fiscal incentives for R&D and the development of medium and high technologies such as the pharmaceutical and information technology industries. Chile exposes the Design-driven Innovation System (DIS) through four elements: A model for innovation, actors, actions, and projects as good practices for innovation (Mollenhauer & Hormazábal, 2012). Finally, in Costa Rica, Herrera-González & Quesada (2013) proposed a value chain index. According to the Costa Rican NIS structure, the proposition identifies relevant value chain variables and innovation management in the metalworking sector.

Step 2: Comparison of international practices

According to regulations, a multilevel framework exists in the selected NIS to promote and evaluate the NIS performance. Technology and innovation policies aim to encourage and facilitate the improvement of innovations, but an access problem for the small and medium businesses keeps going, given their size and the volume of their activities. Related to the financial system, it prevails venture capital and the national funds for innovation activity. Business activities look for cooperation inside the company activities and other national or international firm activities in the value chain, aiming to create a product with social value. All these examined experiences recognize the significance of an efficient research and education system focused on the business demands, in which its international exposition must learn and develop the NIS.

Studying four experiences of NIS in developing countries (Brazil, India, Chile, and Costa Rica), we conclude that the perception of Shulin (1999) persists. In developing countries: (1) NIS, understood as enhanced learning, is established for a specific development level and not for the desired level, (2) Links between organizations are weak and short-term, and (3) Promotion of innovative learning persists in a second place, while the search for investment

is the main objective in policies and linkages. Identifying the lack or weak development of such improvement factors can be valuable to enhance innovation processes on a national level (Balzat & Hanusch, 2004).

Step 3: Implementation and improvements of international practices

For the Cuban government, innovation at the national and regional level is essential because of its benefits from an economic and social perspective. In this sense, in this paper, we offer ideas about a model of NIS for Cuba based on CBI. TBC forms this industry with a certain level of development within contributions to the national economy to capture foreign currency incomes.

Fig. 6 shows the proposed NIS for Cuba. It includes the national and the international community in an open exchange under reliable and secure conditions. The driving of this NIS is the creation of value for Cuban society. Value creation comes to the CBI's current and future projects, products, or services. This industry demands highly qualified and productive workers, raw materials, services, advanced technology, and financial resources. These are the associations or alliances in the value chain, which are carried out by respecting norms, policies, and elements that form the national and international culture and idiosyncrasy.

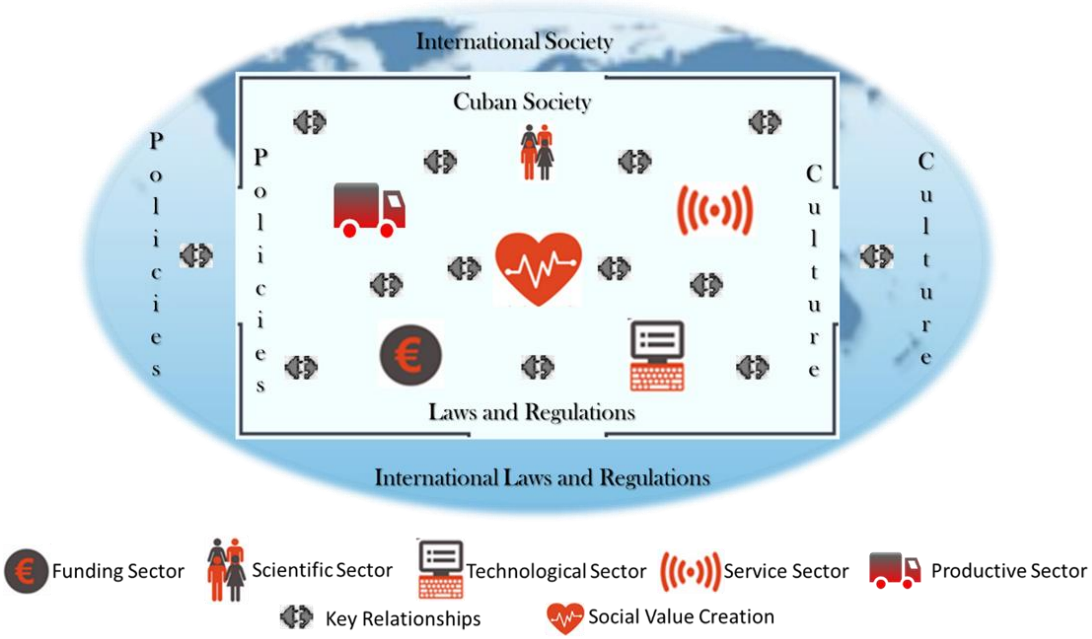

Fig. 6. NIS model based on the CBI. Source. Self-made.

3.5 DISCUSSION

This section extrapolates the interactions between the indicators identified in the previous section (regulations, technology and innovation policies, financial systems, business activities, and research and education systems) to our proposition of NIS for Cuba.

Starting with the regulations, the State is present throughout the system, directing rules and laws. Government institutions such as the CITMA, BioCubaFarma OSDE, MINSAP, and MINDUS determine national policies in CBI and warranty the national framework for working in the value chain approach. Given that it is an open system, Cuban NIS must fulfill international regulations to produce and commercialize its products. So, a multilevel regulation framework is also present in the Cuban case. In this context, the interactions between national and international actors will be driven by the conception of the global value chain and by considering the governance characteristics in these chains.

According to technology and innovations policies, in 2020, the Cuban Minister Council recognized its existence in Cuba of TBC (Consejo de Ministros, 2020). Since this year, innovation and technology policies have been weakly established. We propose working on vertical policy coordination arrangements, regional innovation policies, and the promotion of R&D in biotechnology. In the value chain, these are relevant relationships that act as supporting activities and increase the margin and value for society.

The third indicator is the financial system. Cuban TBC have supported its activity with State contributions. Still, the current reality is different; the country's decision-makers have indicated its inability to fund all the projects that CBI develops. In turn, the profits generated by the centers and institutes of this sector are insufficient to support research and the production of medicines. In addition, this type of investment is not attractive for the domestic financial industry (national banks), given that they present an uncertain return (in the long term, they are high risk considered). The articulation of a NIS that contemplates relationships with the rest of the world should improve the current situation of the CBI. Usually, funding activities are classified as support activities in the value chain approach. We propose considering them as a primary activity because it is essential to maintain and extend CBI results. In this regard, internal changes will be necessary to improve. Additionally, a study is

required to show the profitability of government contributions in each industry to eliminate inefficient businesses. Those funds can be redistributed to other initiatives that can capitalize on the investment and contribute to society. We also propose to create public or private financial entities whose money can come from the profits of different sectors (for example, the tourism sector) in the form of business angels, seed capital, or venture capital. International partners can offer varied funding options such as risk capital, joint ventures, subsidiaries, monetization of Cuban property, stock market, project financing, and international cooperation.

Business activities in the production sector must be developed under the conception of the value chain, working with the idea of insertion into global value chains. Links in the value chains must cover at least 80% of the inputs demanded by CBI: transportation towards medicines productive centers or research centers, and, in the case of the final products, to the health centers and points of sale. In this way, the sustainability of a sector whose productions will always be in demand, a source of employment inside and outside the industry, and coverage of the National Health System (NHS) needs are guaranteed. CBI must create nationally and internationally demanded products, studying the already known ailments and identifying possible future conditions based on current conditions and their cure (disruptive innovation in global value chains). The novel products or projects must be accompanied by a correct presentation that includes their social value, the critical associations that this would imply, and their economic profitability. In addition, ensuring that innovation management in CBI companies should be more than a benchmarking exercise between companies is also a significant challenge.

About the research and education sector, it is vital because it guarantees the quality of the personnel that works in the CBI, which requires a high professional level. We propose the initial stages of R&D&I of the projects to be developed in the university laboratories or research centers, reducing costs and risks to the business sector. These are primary activities in value chain conception, indeed. In addition, we propose that Cuban universities offer academic programs in biotechnology and cooperation with international universities or knowledge providers. The global environment provides excellent and new practices that can and should be incorporated in the CBI, about qualified human capital willing to share

knowledge and advanced technology that humanizes the processes and procedures and allows the realization of new and better activities more efficiently in most cases. Fostering the interest of young people in this specific industry, and developing the necessary skills in them, is an element that guarantees the sector's sustainability, quality, and profitability. It also implies teaching them to innovate instead of replicating, which could be a pending task for the Cuban educational system.

3.6 CONCLUSIONS

Once we examined the common and disruptive points of the studied NIS, we conclude that the correct definition of the value chain integrating regulations, technology and innovation policies, financial systems, business activities, and research and education systems as key indicators; should bring social and economic benefits in the medium and long term.

Firstly, from a practical point of view, it contributes to the sustainability of an industry whose productions guarantee the subsistence of the NHS. Secondly, income generation from the industry will increase its contribution to the State budget, intended to cover or subsidize certain products, services, or social projects. Finally, advances will boost other sectors, such as agriculture, and the environment, giving stability to the Cuban economy.

Theoretically, the proposed NIS is oriented to the common good. It considers a collaborative process in which the different actors of society and the Cuban and foreign economies intervene. It implies progress because it is viewed as a sustainable solution. It means an effective transformation in social behaviors and practices at the micro, meso, and macro levels. It also offers the possibility of insertion of Cuban companies into global value chains.

We agree with Bartels et al. (2012) when they affirm that while the structural dynamics of knowledge management, decision-making, government-business relations, and the market are crucial to NIS behavior, overall innovation is dominated by market forces; which implies that developing economies should establish an institutional environment that supports needs and market transactions, supporting domestic NIS and economic growth, all that under the value chain approach.

The following step is to validate our Cuban NIS proposal by implementing it to confirm if the identified theoretic benefits are true in practice. The main limitation in this study consists of the delay between the Government approval and the existence of the necessary economic conditions to apply it, given the negative impacts of covid-19. Moreover, another limitation is the nonexistence of a previous model of NIS for Cuba.

REFERENCES

Atkinson, R. D. (2014). Understanding the U.S. National Innovation System (ID 3079822; p. 27). Information Technology and Innovation Foundation. https://doi.org/10.2139/ssrn.3079822

Balzat, M., & Hanusch, H. (2004). Recent trends in the research on national innovation sys-tems. Journal of Evolutionary Economics, 14(2), 197-210. https://doi.org/10.1007/s00191-004-0187-y

Bartels, F. L., Voss, H., Lederer, S., & Bachtrog, C. (2012). Determinants of National Inno-vation Systems: Policy implications for developing countries. Innovation, 14(1), 2-18. https://doi.org/10.5172/impp.2012.14.1.2

Castro, E., & Fernández, I. (2001). Innovación y Sistemas de Innovación. https://www.coursehero.com/file/56306932/Sistemas-de-Innovacionpdf/

Chesbrough, H. (2006). Open Innovation: A New Paradigm for Understanding Industrial. En Open innovation: Researching a new paradigm (Chesbrough HW, Vanhaverbeke W, West J). Oxford University Press.

Consejo de Ministros. (2020). De las Empresas de Alta Tecnología. Gaceta Oficial, 156(O16), 433-437.

Cornelissen, M., Małyska, A., Nanda, A. K., Lankhorst, R. K., Parry, M. A. J., Saltenis, V. R., Pribil, M., Nacry, P., Inzé, D., & Baekelandt, A. (2021). Biotechnology for Tomor-row's World: Scenarios to Guide Directions for Future Innovation. Trends in Biotech-nology, 39(5), 438-444. https://doi.org/10.1016/j.tibtech.2020.09.006

Fagerberg, J., & Srholec, M. (2008). National innovation systems, capabilities and economic development. Research Policy, 37(9), 1417-1435. https://doi.org/10.1016/j.respol.2008.06.003

García, F., Domínguez, A. L., & Galván, A. (2018). Sistema de innovación y cadena de valor de la soya en el noroeste de México. Editorial Fomento.

Hassan, M. ghozali, Akanmu, D., Mohamad, A., Melan, M., Prapinit, P., Netsangsee, R., & Boonyarit, P. (2022). Development of Framework for Achieving Sustainability through Benchmarking. CENTRAL ASIA AND THE CAUCASUS English Edi-tion, 22(5), 524-540. https://doi.org/10.37178/ca-c.21.5.046

Herrera-González, R., & Quesada, A. (2013). Determinantes de la cadena de valor y la ges-tión de la innovación en el sector metalmecánico en Costa Rica. Revista Dirección y Organización, 51, 18-32.

Kaiser, R., & Prange, H. (2004). The reconfiguration of National Innovation Systems—The example of German biotechnology. Research Policy, 33(3), 395-408. https://doi.org/10.1016/j.respol.2003.09.001

Kaplinsky, R., & Morris, M. (2000). A Handbook for Value Chain Research, (Vol. 113). Bright-on: University of Sussex, Institute of Development Studies.

Kayal, A. (2008). National innovation systems a proposed framework for developing coun-tries. International Journal of Entrepreneurship and Innovation Management, 8(1), 74-86. https://doi.org/10.1504/IJEIM.2008.018615

Kurpayanidi, K. (2021). National innovation system as a key factor in the sustainable devel-opment of the economy of Uzbekistan. E3S Web of Conferences, 258(05026), 1-13. https://doi.org/10.1051/e3sconf/202125805026

Link, A. N., & Siegel, D. S. (2007). Innovation, Entrepreneurship, and Technological Change. OUP Oxford. Google-Books-ID: iw9REAAAQBAJ

Little, A. D. (1991). Logistics in Service Industries. Council of Logistics Management.

Lundvall, B.-Å. (1992). National Systems of Innovation: Towards a Theory of Innovation and Interac-tive Learning. Pinter Publishers.

Mollenhauer, K., & Hormazábal, J. (2012). Sistema de innovation basado en La red de valor. Revista Chilena de Diseño, 2, 15-35.

Nassif, A. (2007). National Innovation System And Macroeconomic Policies: Brazil And India In Comparative Perspective. En UNCTAD Discussion Papers (N.o 184; UNCTAD Discussion Papers). United Nations Conference on Trade and Develop-ment. https://ideas.repec.org/p/unc/dispap/184.html

OECD. (2010). The changing consumer and market landscape. Consumer policy toolkit. En Consumer Policy Toolkit (p. 15). https://read.oecd-ilibrary.org/governance/consumer-policy-toolkit/the-economics-of-consumer-policy_9789264079663-4-en#page1

Padilla, R. (Ed.). (2014). Fortalecimiento de las Cadenas de Valor como Instrumento de la Política Industrial: Metodología y Experiencia de la CEPAL en Centroamérica. Publicaciones de las Naciones Unidas. https://doi.org/10.18356/65e17760-es

Padilla, R., & Oddone, N. (2016). Manual para el fortalecimiento de cadenas de valor. Repo-sitorio CEPAL, 114.

PCC. (2019). Lineamientos de la política económica y social del Partido y la Revolución. Gaceta Ofi-cial. https://www.tsp.gob.cu/documentos/lineamientos-de-la-politica-economica-y-social-del-partido-y-la-revolucion

Peces Prieto, M. C., & Trillo Holgado, M. A. (2019). The influence of relational capital and networking on the internationalization of the university spin-off. Intangible Capital, 15(1), 22-37. https://doi.org/10.3926/ic.1186

Pietrobelli, C., & Rabellotti, R. (2011). Global value chains meet innovation systems: Are there learning opportunities for developing countries? World Development, 39(7), 1261-1269.

Porter, M. E. (1985). Competitive advantage: Creating and sustaining superior performance. The Free Press.

Rodríguez Batista, A., & Núñez Jover, J. R. (2021). El sistema de ciencia, tecnología e inno-vación y la actualización del modelo de desarrollo económico de Cuba. Revista Uni-versidad y Sociedad, 13, 7-19.

Samara, E., Georgiadis, P., & Bakouros, I. (2012). The impact of innovation policies on the performance of national innovation systems: A system dynamics analysis. Technova-tion, 32(11), 624-638. https://doi.org/10.1016/j.technovation.2012.06.002

Secretary of State and Commerce. (2021). Informe económico y comercial Cuba (p. 44). Oficina Económica y Comercial de España. https://www.icex.es/icex/es/navegacion-principal/todos-nuestros-servicios/informacion-de-mercados/paises/navegacion-principal/el-pais/informacion-economica-y-comercial/estructura-de-la-oferta/index.html?idPais=CU

Shulin, G. (1999). Implications of National Innovation Systems for Developing Countries: Managing Change and Complexity in Economic Development. United Nations University, Institute for New Technologies. https://www.researchgate.net/publication/4777136_Implications_Of_National_Innovation_Systems_For_Developing_Countries_Managing_Change_And_Complexity_In_Economic_Development?enrichId=rgreq-32dbe9409ac5f60c8418c31c8967319f-XXX&enrichSource=Y292ZXJQYWdlOzQ3NzcxMzY7QVM6MTgyMDk3MTYzNTk1Nzc2QDE0MjA0MjY3NTUwMTc%3D&el=1_x_2&_esc=publicationCoverPdf

Uecke, O. (2012). How to Commercialise Research in Biotechnology? Springer Gabler. https://doi.org/10.1007/978-3-8349-4134-3

Watkins, A., Papaioannou, T., Mugwagwa, J., & Kale, D. (2014). National innovation sys-tems, developing countries, and the role of intermediaries: A critical review of the literature. 15th International Conference of the (ISS), 25.

Yin, S., Zhang, N., Li, B., & Dong, H. (2021). Enhancing the effectiveness of multi-agent cooperation for green manufacturing: Dynamic co-evolution mechanism of a green technology innovation system based on the innovation value chain. Environmental Impact Assessment Review, 86, 106475. https://doi.org/10.1016/j.eiar.2020.106475

Yu, Z., Liang, Z., & Xue, L. (2022). A data-driven global innovation system approach and the rise of China's artificial intelligence industry. Regional Studies, 56(4), 619-629. https://doi.org/10.1080/00343404.2021.1954610

CAPÍTULO IV. MULTICRITERIA DECISION TECHNIQUES APPLIED TO VALUATION IN THE LIFE SCIENCES

Oramas Santos, O., Ortiz Torres, M., Canós-Darós, L., & Babiloni, E. (2024). Multicriteria decision techniques applied to valuation in the life sciences. *European Research on Management and Business Economics*. (Submitted March 10th, 2024; Accepted for review March 18th, 2024)

Multicriteria decision techniques applied to valuation in the life sciences

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ABSTRACT

This study addresses the topic of valuation in the life sciences, filling the gap of not considering the significance of one factor to another in determining the price of drug candidates. It introduces a multicriteria model for estimating drug candidates' prices, utilizing the Analytic Network Process (ANP) to determine priority among factors and incorporating the value chain (VC) of the study case to identify criteria and alternatives influencing pricing. This model enhances price estimation accuracy, which is validated by calculating Manhattan's distances. It reveals, for the first time, the comprehensive applicability of the ANP methodology to drug candidates' price estimation, accommodating qualitative and quantitative factors and considering interconnections between networked companies along the VC. The proposed approach mitigates risk in the valuation process, ensuring a more precise project assessment for presentation to investors, policymakers, and stakeholders.

Keywords: ANP, life sciences, price estimation, valuation, value chain.

JEL Classification: C63, G12, I15, M10

4.1 INTRODUCTION

The life sciences, encompassing disciplines such as biology, genetics, and biochemistry, have garnered widespread recognition due to their transformative effects on the health of both humans and animals. Most scholarly publications within this domain revolve around discoveries aimed at enhancing the quality of human life or the adept application of cutting-edge technologies to living organisms (Oramas Santos et al., 2023a). Nevertheless, authors

such as Agarwal et al. (2023), Gantait et al. (2021), Ifiok (2024), Sharma et al. (2022), and Van Looy et al. (2024) recognize the multifaceted nature of this industry.

Within the research landscape, publications in this field shed light on its far-reaching implications and categorically examine its three principal components in the opinion of Bogdan & Villiger (2010): Academia, biotechnology firms, and pharmaceutical entities. However, through elucidating pivotal factors, including innovation, research, and development (R&D), and market dynamics, this paper acknowledges the salience of financial considerations within the realm of biotechnology companies, particularly those involved in medical biotechnology and drug discovery.

Before to reach the market, a drug or treatment candidate must survive to a long and expensive development process divided into five main stages as Fig. 7 shows. Authors such as Deore et al. (2019), Kim et al. (2018), Mak & Pichika (2019), Ting (2006), and the US Food and Drug Administration in the CDER (2022) report, explain this process by categorizing it into two primary phases: Non-clinical (stages I and II in Fig. 7) and Clinical research (stages III, IV and V in Fig. 7).

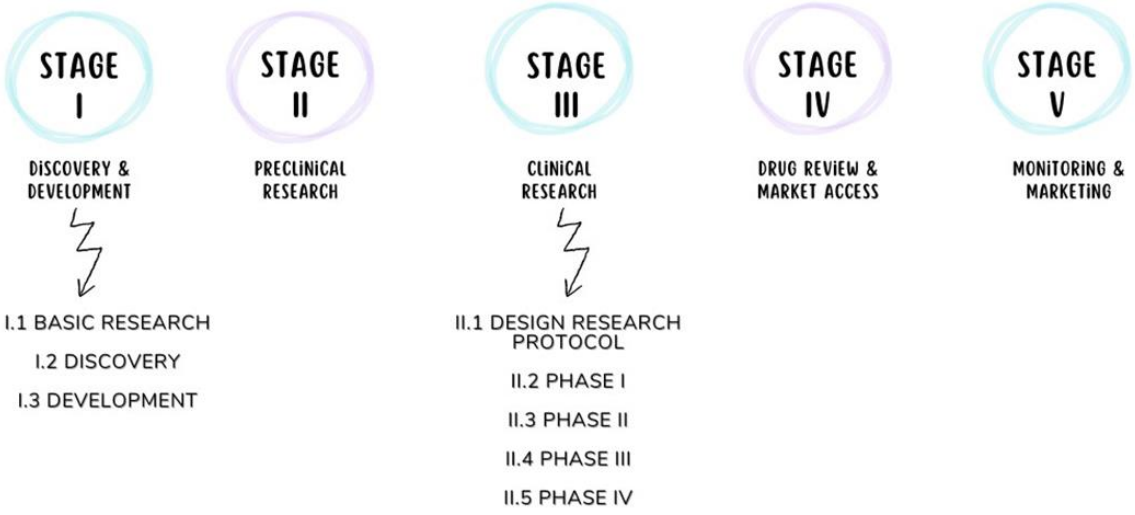

Fig. 7. Stages in the development process of a drug candidate. Source. Self-made.

Fig. 7 shows that, once found, the compound obtained in stage I is tested on non-human organisms as part of the stage II or preclinical research. After that, the stage III clinical trials starts, which means that the compound is tested in humans in four phases. These phases differ

in sample size, sample composition, and pursued goals: from description in phase I to analysis and statistics in phase II, the recommendation on the drug dosage in phase III, and the final follow-up and adjustments in phase IV. After data collection and application submission at the end of phase III and before the beginning of phase IV clinical trials, this information is forwarded to each region's new drug regulatory authority for approval as a new drug (stage IV). If the results are favorable, after 12-15 years of R&D and an average spend of over US$1335.9 million (CDER, 2022, 2023), stage V will begin along with the fourth phase of clinical trials which has an even larger sample, aiming to increase the potential market for the new drug by demonstrating an improvement in the quality of life of the patients who use it and by securing its economic value.

The sequence of stages showed in Fig. 7 requires the involvement of a network of entities outside the therapy researcher or developer, extending beyond input providers (Oramas Santos et al., 2023a). These organizations play a pivotal role in facilitating the seamless progression from one stage to another in the pursuit of novel drugs. Together, these interconnected entities form the value chain (VC) of the experimental treatment.

The real uncertainty leading drug candidate obtainment process, as well as its expensiveness, make it high risky, which is why both researchers and investors need a factual project valuation. The most widely spread valuation method in the life sciences is the mix between the Discounted Cash Flow (DCF) and the decision tree (Bogdan & Villiger, 2010; Viganò & Vella, 2022). Depending on the DCF promised by the project, it will be advanced to the next stages or stopped.

A critical factor in estimating the cash flows is the sales peak, which depends on the sold quantity and the sales price. To calculate the price of a treatment, some methods relate its cost to the effectiveness, benefits, and use value it generates. According to Polentinos (2015), two of the most widely used are the calculation of the Quality Adjusted Life Year (QALY) method and the comparative method. The first measures and compares the outcomes on the longevity and quality of health technologies (Weinstein et al., 2009). The second is based on establishing comparisons with other products currently on the market that target the same

disease and have a similar degree of effectiveness in saving lives and improving patients' quality of life (Peñalver, 2018).

In practical scenarios where both methods are employed, decisions are often made by drawing parallels between treatments without necessarily considering the interplay or significance of one factor to another when determining drug candidates' prices. This gap supports the research question posted in this paper: which methodology can be employed to appropriately consider the influence of qualitative and quantitative factors on the price of a drug candidate?

According to the research question, the main objective of this paper is to present a multicriteria model to estimate the price of any drug candidate, based on ranking factors. To achieve this goal, in the determination of the priority among factors, this paper proposes to use the Analytic Network Process (ANP) multi-criteria decision-making methodology explained in Saaty (1996), as a VC implies relationships between organizations, in addition to the subjective and nonquantifiable criteria that interfere on the price-decision. This method can provide a more nuanced health biotech project's valuation, ensuring that each factor's relevance is appropriately considered in the pricing determination for a treatment. Although ANP is a widely used technique and also in the health field (Büyüközkan & Çifçi, 2012; Freeborn et al., 2023; Lai et al., 2021; Magableh & Mistarihi, 2022; Mitincu et al., 2023; Nazari-Shirkouhi et al., 2023; Senturk et al., 2016; Valipour et al., 2015; Xu et al., 2022; Yontar, 2023; Zarbakhshnia et al., 2023), to the best of the authors' knowledge, this is the first time that it has been applied to set the price of drug candidates under the VC umbrella.

The project used as a study case consists in a novel treatment against a degenerative disease developed by a medium size Cuban health company. The drug candidate started the phase III of clinical trial on January 2023. Its main objective is to reduce the progression rate of cognitive impairment and improve functional activity in people with the disease.

This paper is structured into four sections. The initial section serves to acquaint the reader with the research subject and provides an overview of the operational dynamics within the studied sector. Section 2 elucidates the ANP methodology in the context of its application to

a study case. Section 3 delineates the research findings, while the fourth section captures the primary conclusions derived upon the culmination of the research endeavor.

4.2 METHODOLOGY

The ANP represents a methodology employed for the examination, synthesis, and rationale of intricate decisions, as outlined by Saaty (1996). This approach encompasses factors and criteria conducive to effective decision-making, incorporating considerations of interactions, interdependencies, and network-wide feedback, as expounded by Lai et al. (2021). The methodology involves a structured sequence of six steps, as depicted in Fig. 8.

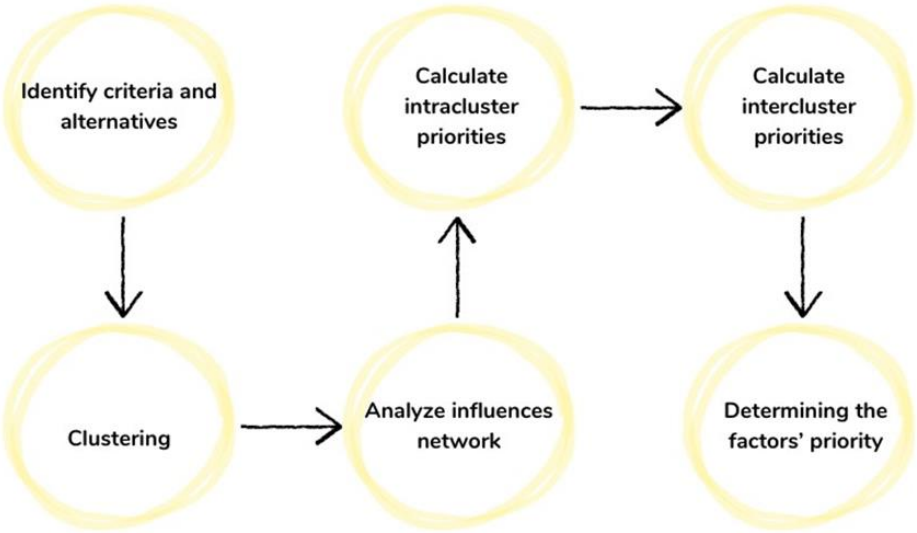

Fig. 8. Procedure to calculate the factors' priority by the ANP methodology. Source. Self-made.

Step 1. Identify criteria and alternatives

When determining the factors' priorities, the first step includes identifying the elements in the network: the explanatory factors of the drug candidate's price and the possible comparable treatments (Saaty & Vargas, 2013). VC design is the basis for identifying the explanatory variables. Then, it is necessary to develop market research to identify potential competitors.

The actors mostly involved in the Cuban project are the Research Company; the medical providers where the clinical trials are going to be developed; the inputs' suppliers; the

patients; the Cuban Center for State Control of Medicines, Equipment and Medical Devices; the Cuban Health Ministry; the Cuban Ministry of Science, Technology and Environment; the Cuban Ministry of Foreign Trade and Foreign Investment; and also the international regulatory agencies that indicate general procedures and rules and best practices to be followed to produce and market a medical biotech product. These are the main VC nodes.

Even if all the activities developed by each node are essential, some of those are more significant for valuation and price estimation. In this research, the three Cuban main researchers of the drug candidate, also directly linked to the drug candidate development process, identified fourteen explanatory variables that encompass primary and supporting VC activities, macro and microenvironment variables, and product specifications, as well as the closest comparable treatments. These activities are listed in Fig. 9.

Step 2. Clustering

The explanatory factors and comparable treatments identified in step 1 are grouped into clusters to determine their dependencies and relative weights in and between them (Aznar & Guijarro, 2012). Once defined the elements in the Cuban biotech project's network, the authors of this paper, together with the researcher in charge of the clinical trial, grouped them into three clusters as Fig. 9 shows.

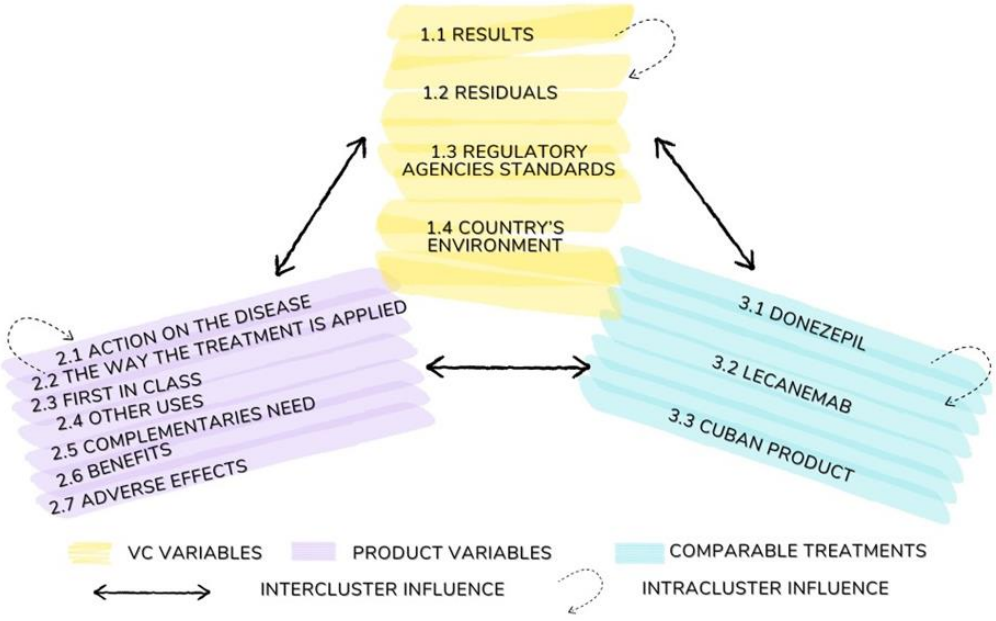

Fig. 9. Clustering of explanatory variables. Source. Self-made.

Cluster 1 includes VC explanatory factors (1.1) veracity and visibility of results, (1.2) waste generation and disposal, (1.3) compliance with the standards of national and international regulatory agencies, and (1.4) country environment factors that determine the access to funding options, technology, etc. Cluster 2 links the product's intrinsic specifications (2.1) if the treatment cures, slows down, or predicts the disease; (2.2) the method of application: self-applied or in healthcare facilities, (2.3) if the drug candidate is a first in its class, (2.4) if the treatment is applicable for more than one ailment, (2.5) if the treatment requires complementary medications, (2.6) if the drug produces benefits in memory, thinking and daily life; and (2.7) the nature of the adverse effect it induces: none, mild, or severe. Finally, cluster 3 is the comparable treatments cluster composed by two medications in the market (Donezepil and Lucanemab) in addition to the Cuban project been evaluated.

Step 3. Analyze the influences' network

The influence network analysis is performed to verify if there is a relationship or influence of the variables for themselves and the comparable treatments, and vice versa (Lai et al., 2021; Mohanty et al., 2005). For this purpose, an Interfactors' Dominance Matrix is constructed (see Fig. 10).

		C1				C2							C3		
		v11	v12	v13	v14	v21	v22	v23	v24	v25	v26	v27	v31	v32	v33
C1	v11	0	0	1	1	1	1	1	1	1	1	1	1	1	1
	v12	1	0	1	1	1	1	1	1	1	1	1	1	1	1
	v13	1	1	0	1	1	1	1	1	1	1	1	1	1	1
	v14	1	1	1	0	1	1	1	1	1	1	1	1	1	1
C2	v21	1	0	0	0	0	1	1	1	1	1	1	1	1	1
	v22	0	1	1	1	1	0	1	1	1	1	1	1	1	1
	v23	1	1	1	1	1	1	0	1	1	1	1	1	1	1
	v24	1	1	1	1	1	1	1	0	1	1	1	1	1	1
	v25	1	1	1	1	1	0	1	1	0	1	1	1	1	1
	v26	1	0	1	0	1	1	1	1	1	0	1	1	1	1
	v27	1	0	1	0	1	1	1	1	1	1	0	1	1	1
C3	v31	1	1	1	1	1	1	1	1	0	1	1	0	1	1
	v32	1	1	1	0	1	1	0	1	1	1	1	0	0	1
	v33	1	1	1	1	1	1	1	1	1	1	1	1	0	0

Fig. 10. Interfactors' Dominance Matrix. Source. Self-made.

In Fig. 10, c1, c2, and c3 represent the clusters. From v11 to v33 are the identified factors impacting the drug candidate's price. The value of 0 means that there is no influence between the factors, while the value of 1 implies influence with certain intensity. Fig. 10 shows the interfactors' dominance matrix resulting from the influence score offered by the researcher responsible for the clinical trial.

Step 4. Calculate intracluster priorities

Once influences have been identified, they should be quantified via paired comparison matrices (Saaty & Vargas, 2013). To calculate the intracluster priorities, the importance of each factor is quantified in relation to the others that also influence the considered criteria, using the fundamental scale of absolute numbers in Table 5.

Table 5. Saaty's fundamental scale of absolute numbers.

Intensity of Influence (Weight)	**Definition**	
1	Equal influence	If a factor *i* has a nonzero number assigned to it when compared with other factor *j*, then *j* has the reciprocal value when compared with *i*.
2	Weak influence	
3	Moderate influence	
4	Moderate plus influence	
5	Strong influence	
6	Strong plus influence	
7	Very strong influence	
8	Very, very strong influence	
9	Extreme influence	

Source. Adapted from Saaty (1996).

Starting with factor v11 and ending with factor v33, 40 paired comparisons are made. After that, the resulting matrices are normalized by addition to obtain the eigenvectors. Fig. 11 shows an example of those paired comparisons. The resulting eigenvectors of all the paired comparison matrices form the Original Super Matrix.

	v11	v12	v13	v14	Eigenvector
v11	1	7	1	6	0,42
v12		1	1/5	1/3	0,05
v13			1	8	0,44
v14				1	0,09

Fig. 11. Weighted influence of cluster 1 factors on factor v11. Source. Self-made.

Step 5. Calculate intercluster priorities

Going through the influences network analysis and quantification in step 3 and the factors' prioritization in step 4, the Original Super Matrix must be stochastic, that is, all the columns add up to 1. To rise that result, it is necessary to calculate how each cluster influences other clusters (Senturk et al., 2016; Xu et al., 2022). Fig. 12 shows this comparison according to the opinion of the main researcher responsible for the potential new drug in the Cuban research company.

	C1	C2	C3	Eigenvector
C1	1	1/5	2	0,17
C2		1	7	0,74
C3			1	0,09

Fig. 12. Clusters' paired comparison. Source. Self-made.

The clusters' eigenvector is multiplied by the factor's clusters to obtain the Weighted Super Matrix, in which all the columns add up to 1.

Step 6. Determine the factors' priority

The Weighted Super Matrix (WSM) in step 5 is raised to successive powers (5 times in this case) until its entries converge to a certain value: The Limit Super Matrix. The result of this step is the priority or weighting order of each factor in the network.

4.3 RESULTS

To estimate the price of the drug candidate, the weighting order of each comparable treatment obtained when calculated the WSM is going to be used. Given that this is not a stochastic vector, it is mandatory to normalize it by addition. Table 6 shows these values.

As it can be seen in Table 6, there are no big differences between the Cuban candidate and the comparable treatments. Due to their highly analogous modes of action, the differentiating factor in the weighting of the Cuban candidate lies in its potential applicability for the treatment of an additional ailment (this new application is in phase I of clinical research).

Table 6. Cluster's weighting order normalization.

Comparable Treatments	WSM's priority	WSM's priority normalized
Donezepilo	0,0303	0,3225
Lecanemab	0,0315	0,3360
Cuban Candidate	0,0320	0,3415
Sum	0,0938	1,0000

Source. Self-made.

From the market research developed in step 1 of the ANP methodology, it is possible to know the average price of the comparable treatments. With those prices and the WSM's priorities normalized, a ratio R is calculated as the result of dividing the sum of the prices of both comparable treatments and its WSM's priorities normalized:

$$R = \frac{(Donezepilo\ price + Lecanemab\ price)}{(Donezepilo\ WSM's\ prior.norm. + Lecanemab\ WSM's\ prior.norm.)}$$

The ratio R is multiplied by the Cuban candidate's WSM priority normalized, resulting in a price of $17846,8 per treatment. The estimated price exceeds the average price of the comparable treatments in the market, which suggests a review of the price proposal' adequacy.

In order to determine the Adequacy Index (A_i), this paper proposes to compare the real market price for the comparable treatments with an estimation using their WSM priorities normalized. The best proposal will be the one that has the shortest Manhattan's distance, following Dedania et al. (2015) and Yoon (1987)'s recommendations. Table 7 shows this calculation.

Table 7. Manhattan's distance calculation.

Comparable Treatments	Price	Average Price	Distance	Price with ANP priorities	Distance
Donezepilo	7920	17210	9290	16857,91	8937,91
Lecanemab	26500	17210	9290	17562,09	8937,91
	Manhattan's distance (M1)		18580	**Manhattan's distance (M2)**	17875,81

Source. Self-made.

The distance from the average price reduces in $704,19 per treatment approximately. By calculating the A_i it is possible to understand how many percentage points the average price has been improved. The next expression shows its calculation:

$$A_i = \left(1 - \frac{M_2}{M_1}\right) * 100$$

$$A_i = \left(1 - \frac{17875{,}81}{18580}\right) * 100$$

$$A_i = 38\%$$

According with the A_i value, the price proposal using the results from the ANP methodology improves by 38% the average market price of the comparable treatments. This outcome supports the initial premise of this paper about the relevance of considering the interplay or significance of one factor to another when determining drug candidates' prices.

4.4 CONCLUSIONS

This manuscript delved into the subject of valuation within the life sciences domain, focusing on the challenge of estimating prices for drug candidates. Following a concise elucidation of the health biotech sector and prevalent pricing methodologies, the study highlighted the lack in incorporating appropriately weighted quantitative and qualitative factors in the pricing estimation of drug candidates.

To appropriately capture the impact of price determinants in any health biotech project, the ANP methodology was employed, connected with VC identification to the project under study. A total of fourteen factors influencing price determination of the Cuban drug candidate were identified and categorized into three clusters, distinguishing among VC explanatory factors, intrinsic product specifications, and comparable treatments.

Utilizing the six-step ANP methodology to establish the priority of factors, the order of weighting for each comparable treatment was determined, revealing negligible disparities among the three. Subsequently, the ratio between the sum of prices for both comparable

treatments and their WSM's priorities normalized was computed. This value was then multiplied by the normalized priority of the Cuban candidate in the WSM to derive the treatment's price.

The Adequation Index, computed through Manhattan's distance, affirmed that the proposed model enhances the average market price of both the comparable treatments and the Cuban candidate.

This manuscript highlights the significance of the VC approach for discerning the criteria and alternatives influencing the pricing of any drug candidate. Furthermore, it underscores the full applicability of the ANP methodology to valuation within the life sciences, as it facilitates the consideration of both quantifiable and non-quantifiable factors impacting price determination, along with the interconnections between companies in the network.

Through the estimation of the price using the ratio R and the normalized priorities from the ANP, decision-makers are equipped with a robust parameter for computing the DCF that the project holds. This approach diminishes risk in the valuation process and ensures a more precise assessment of the project when presented to investors, policymakers, and stakeholders at large.

REFERENCES

Agarwal, H., Bajpai, S., Mishra, A., Kohli, I., Varma, A., Fouillaud, M., Dufossé, L., & Joshi, N. C. (2023). Bacterial Pigments and Their Multifaceted Roles in Contemporary Biotechnology and Pharmacological Applications. Microorganisms, 11(3), Article 3. https://doi.org/10.3390/microorganisms11030614

Aznar, J., & Guijarro, F. (2012). Nuevos Métodos de Valoración. Modelos Multicriterio (2.a ed.). Editorial Universitat Politècnica de València. http://hdl.handle.net/10251/19181

Bogdan, B., & Villiger, R. (2010). Valuation in Life Sciences: A Practical Guide (Third edition). Springer. https://doi.org/10.1007/978-3-642-10820-4

Büyüközkan, G., & Çifçi, G. (2012). A novel hybrid MCDM approach based on fuzzy DEMATEL, fuzzy ANP and fuzzy TOPSIS to evaluate green suppliers. Expert Systems with Applications, 39(3), 3000-3011. https://doi.org/10.1016/j.eswa.2011.08.162

CDER. (2022). CDER FY 2022 GDUFA science and research report (FY 2022, p. 134). FDA. https://www.fda.gov/drugs/generic-drugs/science-research

CDER. (2023). FY 2022 GDUFA Science and Research Report. FDA, 128.

Dedania, H. V., Shah, V. R., & Sanghvi, R. C. (2015). Portfolio Management: Stock Ranking by Multiple Attribute Decision Making Methods. Technology and Investment, 6(4), Article 4. https://doi.org/10.4236/ti.2015.64016

Deore, A. B., Dhumane, J. R., Wagh, R., & Sonawane, R. (2019). The Stages of Drug Discovery and Development Process. Asian Journal of Pharmaceutical Research and Development, 7(6), 62-67. https://doi.org/10.22270/ajprd.v7i6.616

Freeborn, L., Andringa, S., Lunansky, G., & Rispens, J. (2023). Network analysis for modeling complex systems in SLA research. Studies in Second Language Acquisition, 45(2), 526-557. https://doi.org/10.1017/S0272263122000407

Gantait, S., Mahanta, M., Bera, S., & Verma, S. K. (2021). Advances in biotechnology of Emblica officinalis Gaertn. syn. Phyllanthus emblica L.: A nutraceuticals-rich fruit tree with multifaceted ethnomedicinal uses. 3 Biotech, 11(2), 62. https://doi.org/10.1007/s13205-020-02615-5

Ifiok, E. (2024). Microbial Biotechnology: Application of Bacteria in Various Industrial Processes and Environment Remediation. https://doi.org/10.5281/zenodo.10511013

Kim, T. H., Shin, S., & Shin, B. S. (2018). Model-based drug development: Application of modeling and simulation in drug development. Journal of Pharmaceutical Investigation, 48(4), 431-441. https://doi.org/10.1007/s40005-017-0371-3

Lai, J. H. K., Hou, H. (Cynthia), Edwards, D. J., & Yuen, P. L. (2021). An analytic network process model for hospital facilities management performance evaluation. Facilities, 40(5/6), 333-352. https://doi.org/10.1108/F-09-2021-0082

Magableh, G. M., & Mistarihi, M. Z. (2022). Applications of MCDM approach (ANP-TOPSIS) to evaluate supply chain solutions in the context of COVID-19. Heliyon, 8(3), e09062. https://doi.org/10.1016/j.heliyon.2022.e09062

Mak, K.-K., & Pichika, M. R. (2019). Artificial intelligence in drug development: Present status and future prospects. Drug Discovery Today, 24(3), 773-780. https://doi.org/10.1016/j.drudis.2018.11.014

Mitincu, C.-G., Niţă, M.-R., Hossu, C.-A., Iojă, I.-C., & Nita, A. (2023). Stakeholders' involvement in the planning of nature-based solutions: A network analysis approach. Environmental Science & Policy, 141, 69-79. https://doi.org/10.1016/j.envsci.2022.12.022

Mohanty, R. P., Agarwal, R., Choudhury, A. K., & Tiwari, M. K. (2005). A fuzzy ANP-based approach to R&D project selection: A case study. International Journal of Production Research, 43(24), 5199-5216. https://doi.org/10.1080/00207540500219031

Nazari-Shirkouhi, S., Tavakoli, M., Govindan, K., & Mousakhani, S. (2023). A hybrid approach using Z-number DEA model and Artificial Neural Network for Resilient supplier Selection. Expert Systems with Applications, 222, 119746. https://doi.org/10.1016/j.eswa.2023.119746

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023). The value chain approach in red biotechnology companies from a bibliometric perspective. International Journal of Production Management and Engineering, 11(2), 187-196. https://doi.org/10.4995/ijpme.2023.19135

Peñalver, A. (2018). Business Plan: New Heart UK [Tesis de Máster]. Cranfield University.

Polentinos, E. (2015). La disposición a pagar por un Año de Vida Ajustado por Calidad: Umbral de aceptabilidad mediante el método de la Valoración Contingente [Tesis de Doctorado, Universidad Rey Juan Calos]. https://eciencia.urjc.es/handle/10115/13184

Saaty, T. L. (1996). Decision Making with Dependence and Feedback: The Analytic Network Process (Vol. 4922). RWS Publications.

Saaty, T. L., & Vargas, L. G. (2013). The Analytic Network Process. En T. L. Saaty & L. G. Vargas (Eds.), Decision Making with the Analytic Network Process: Economic, Political, Social and Technological Applications with Benefits, Opportunities, Costs and Risks (pp. 1-40). Springer US. https://doi.org/10.1007/978-1-4614-7279-7_1

Senturk, S., Binici, Y., & Erginel, N. (2016). The theoretical structure of Fuzzy Analytic Network Process (FANP) with Interval Type-2 Fuzzy Sets. IFAC-PapersOnLine, 49(12), 1318-1322. https://doi.org/10.1016/j.ifacol.2016.07.706

Sharma, V., Sehrawat, N., Sharma, A., Yadav, M., Verma, P., & Sharma, A. K. (2022). Multifaceted antiviral therapeutic potential of dietary flavonoids: Emerging trends and future perspectives. Biotechnology and Applied Biochemistry, 69(5), 2028-2045. https://doi.org/10.1002/bab.2265

Ting, N. (Ed.). (2006). Dose Finding in Drug Development. Springer. https://doi.org/10.1007/0-387-33706-7

Valipour, A., Yahaya, N., Md Noor, N., Kildienė, S., Sarvari, H., & Mardani, A. (2015). A fuzzy analytic network process method for risk prioritization in freeway PPP projects: An Iranian case study. Journal of Civil Engineering and Management, 21(7), 933-947. https://doi.org/10.3846/13923730.2015.1051104

Van Looy, B., Grabowska, M., Vlaisavljevic, V., Lecocq, C., & Debackere, K. (2024). Growth of biotech clusters over several decades through pioneering, variety and entrepreneurial science. Nature Biotechnology, 42(1), Article 1. https://doi.org/10.1038/s41587-023-02062-6

Viganò, M., & Vella, E. (2022). Mergers and acquisitions in life science: What multiples for relative valuation? [Master, Politecnico Milano]. https://www.politesi.polimi.it/handle/10589/198590?mode=complete

Weinstein, M. C., Torrance, G., & McGuire, A. (2009). QALYs: The Basics. Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research, 12(1), 5-9. https://doi.org/10.1111/j.1524-4733.2009.00515.x

Xu, J., Li, L., & Ren, M. (2022). A Hybrid ANP Method for Evaluation of Government Data Sustainability. Sustainability, 14(2), Article 2. https://doi.org/10.3390/su14020884

Yontar, E. (2023). Critical success factor analysis of blockchain technology in agri-food supply chain management: A circular economy perspective. Journal of Environmental Management, 330, 117173. https://doi.org/10.1016/j.jenvman.2022.117173

Yoon, K. (1987). A Reconciliation among Discrete Compromise Situations. Journal of Operational Research Society, 38, 277-286.

Zarbakhshnia, N., Govindan, K., Kannan, D., & Goh, M. (2023). Outsourcing logistics operations in circular economy towards to sustainable development goals. Business Strategy and the Environment, 32(1), 134-162. https://doi.org/10.1002/bse.3122

CAPÍTULO V. ESTIMATING VALUE IN HEALTH BIOTECH PROJECTS: FUZZY MODELLING, FUNDING, AND CHAIN MANAGEMENT IN A CUBAN CASE

Oramas Santos, O., Ortiz Torres, M., Canós-Darós, L., & Babiloni, E. (2024). Estimating Value in Health Biotech Projects: Fuzzy Modelling, Funding, and Chain Management in a Cuban Case. *Journal of Economic Literature*. (Submitted October 26th, 2023; Accepted for review December 8th, 2023; Accepted for publication March 3rd, 2024)

Estimating value in health biotech projects: Fuzzy modelling, funding, and chain management in a Cuban case

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ABSTRACT

This research recognizes the significance of the biotech sector, given its impact on human life, health, and the economy. Focused on the valuation challenges within health biotech projects, this paper proposes a mathematical model to estimate the value of any health biotech project, starting from the identification and definition of the value chain it implies. The model integrates three pivotal components—economic, financial, and sustainability—by estimating the risk-adjusted Net Present Value, the value of funding options, and the long-term project sustainability. Utilizing fuzzy sets theory, Analytic Network Process method, and Integer Goal Programming enhances the model's capability to address qualitative and quantitative factors. The proposal outcome serves as a unified indicator for decision-makers, gauging the impact of uncertainty across the research and development, manufacturing, and marketing stages of a drug candidate. Applied to a Cuban project, it emerges as an invaluable management tool, providing profound insights for improved decision-making and strategic project valuation.

Keywords: Analytic Network Process, Cuba, funding options, fuzzy numbers, health biotech projects, Integer Goal Programming, uncertainty, valuation methods, value chain.

5.1 INTRODUCTION

Creating value through a well-managed product value chain is at the top of research topics in economics and business (Akyüz et al., 2023; Mazzucato & Ryan-Collins, 2022). This analysis was introduced by Porter (1985) as a part of the strategy definition process in any organization. The value chain (VC hereafter) serves as a crucial tool that interconnects business activities throughout a product's supply, production, and commercialization process (Kaplinsky & Morris, 2000). Porter (1991) delineates these activities into two essential categories: primary activities, encompassing production, marketing, and delivery; and support activities, responsible for creating or sourcing inputs required for the primary activities, which includes planning and management.

In VC identification, the primary focus often lies on existing products, where companies comprehensively understand all the requirements to deliver the product to the client. However, in the specialized field of medical biotechnology (biotech hereafter), the particulars of business management are intricately tied to the stages in the drug candidate development process: Discovery and Development, Preclinical Research, Clinical Research, Drug Review and Market Access, and Monitoring and Marketing. According to BioCubaFarma (2019), if the drug candidate is in one of the three first stages, it is under Research and Development (R&D).

The R&D assumes paramount importance in the landscape of medical biotech, recognized by the U.S. Center for Drug Evaluation and Research (CDER, 2023) as not only the most significant but also the broadest and most uncertain stage. During this stage, companies engage in pioneering research, experimental trials, and the challenging process of translating scientific innovations (also called projects or drug candidates) into tangible products. The inherent complexity and unpredictability of R&D activities make the valuation of health biotech projects challenging and intrinsically inaccurate.

According to Bogdan & Villiger (2010), Craighead et al. (2020), Ghamlouch et al. (2019), and Kamel et al. (2023), the most widely used method for projects' valuation in the medical biotech industry is the binomial real options tree. This method, in its primary version and usage in the health biotech valuation field, exhibits certain rigidity, lacking a nuanced

consideration of qualitative, extrinsic, and intangible factors. In first place, the origin, characteristics, policies, and conditions of all organizations engaged in the commercial relationship throughout the drug candidate's development process, determine the product quality and disposition as well as the waste treatment. Additionally, the cultural, political, and economic conditions of the region or country where the drug candidate is developed and sold, affect the publication of research results (Burns, 2022) and the overall visibility and credibility of the company and the researchers involved in the drug development process, impact the access to favorable financial resources (Mazzucato & Ryan-Collins, 2022), as well as the clients' willingness to pay for a product, and the insurance coverage policies, ensuring the safety of volunteers participating in clinical trials, and determining the possibility to buy new, clean, and innovative technologies. Finally, the social trends or dynamics, such as a growing inclination towards natural products or a shift towards vegetarianism, can either broaden or narrow the range of market opportunities for a particular therapy (Oramas Santos et al., 2023a).

Moreover, the use of the real options method in the health biotech field may fall short in considering various qualitative, intrinsic, and intangible factors that contribute to the value of a drug candidate, thereby influencing the profit it generates. These factors encompass but are not limited to the product's use value, the associated sacrifices it may entail (Cornelissen et al., 2021), its classification as a first-in-class within its category, or its potential to replace another product in the market. Furthermore, aspects like the feasibility of selling the product's patent, the intellectual property rights (DiMasi, 2014), the long-term drug candidate sustainability, as well as other strategic considerations related to the company's goals may not be adequately accounted for within the framework of the real options method.

These missing elements when valuing a biotech project have been identified in this research as gaps in the valuation of health biotech projects, which can be succinctly summarized as follows: (1) neglect of inter-company relationships, (2) rigidity in uncertainty management, and (3) limited consideration of qualitative factors and management goals.

In the complex landscape of health biotech, where collaborative efforts and strategic partnerships play a pivotal role, a more flexible and comprehensive approach is needed.

Acknowledging the diversity of factors and organizations and understanding the specific conditions and goals that influence their contributions to the drug candidate' value, is essential for a more accurate and holistic valuation in the health biotech sector. In addition, recognizing and incorporating qualitative dimensions is critical for a more complete and truthful valuation of a drug candidate in the field of health biotech, where factors beyond the purely financial contribute significantly to therapeutic innovation's overall success and market positioning.

In light of the identified gaps, this study seeks to address the following research questions: (1) How can the value of a health biotech project be measured, taking into consideration all interconnected companies? (2) What constitutes an effective and adaptable tool for navigating uncertainty in a health biotech project? (3) Which methodologies can be employed to appropriately consider the influence of qualitative and quantitative factors on the value of a drug candidate?

To address the research questions, the objective of this paper is to develop and apply a mathematical model that estimates the added value by all companies linked along the VC of any health biotech project, taking into consideration qualitative and quantitative factors, as well as the uncertainty management, and applying scoring methods and fuzzy tools to provide a comprehensive and flexible assessment.

This paper is divided into four main sections. Section I introduced the research problem and stated the study's objective. Section II describes the model proposal to improve decision-making for investors, clients, and managers of health biotech projects. With that purpose, the Analytic Network Process (ANP) methodology, the Integer Goal Programming (IGP), the Fuzzy Sets theory (specifically the Fuzzy Triangular Numbers), and the Real Options theory are mixed in a model that allows more flexible valuation outcomes. Section III specifies the basis for the model's application in a Cuban health biotech project. Finally, section IV presents the major conclusions of this study.

5.2 THE ESTIMATION OF VALUE IN HEALTH BIOTECH PROJECTS: THE MODEL PROPOSAL

Even though every drug candidate goes through the five-stage development process mentioned in the introduction section, each product has distinctive characteristics and qualities that make its valuation process also particular. This is why life sciences valuation doesn't have a unique and thoroughly recommended formula (Bogdan & Villiger, 2010). It is based on the scientific expectations of the drug candidate, and its main goal is to show how the project promises to be profitable in attracting livelihood sources (Burns, 2022). With that purpose in mind, this paper proposes a mathematical model to estimate the value of any health biotech project, starting from the identification and definition of the VC it implies. This is flexible model which highlights the value-added by each node, measuring the qualitative and quantitative factors impacting the value of the experimental treatment from the perspective of customers, managers, and other stakeholders linked in the drug candidate's R&D, manufacturing, and marketing processes.

The proposal of model comprises three primary components: economic, financial, and sustainability. In the economic facet, the model computes the cash flow generated by the project, spanning from the Discovery and Development stage to the Monitoring and Marketing stage. The financial component quantifies the value added by the funding options utilized for the experimental treatment. Lastly, the sustainability component assesses the impact of externalities generated by the drug candidate and the value derived from its future applications. From a mathematical perspective, the model integrates Zadeh's fuzzy sets theory (1965) and Koller et al.'s real options method (2010) to explore flexibility in valuation. Additionally, the ANP methodology proposed by Saaty (1996), and the IGP developed by Charnes & Cooper (1962) are employed to prioritize variables and address key issues in the valuation process. This combination of mathematical frameworks enhances the model's ability to handle uncertainties, assess flexibility, and prioritize factors for a comprehensive and holistic analysis. Fig. 13 explains the model proposal.

When estimating the value of a health biotech project, the VC tool allows managers to identify all the actors and activities involved in the process of value creation and capture,

highlighting the factual resources combination such as raw materials, workforce, tools, knowledge, skills, etc. (Acharjee et al., 2023; Hossain et al., 2013; Hu et al., 2019; ILO, 2015; Kaplinsky & Morris, 2000; Porter, 1985). That is why the model's foundation relies on the project's VC, enabling the precise identification of factors contributing to value creation, incorporating widely validated financial valuation techniques. The calculation of the value generated through the drug candidate's VC also allows to decide in which project invest, in the event of several profitable projects and capital restrictions, if they are mutually exclusive. The mathematical expression to estimate the project's added value is presented in the equation (1).

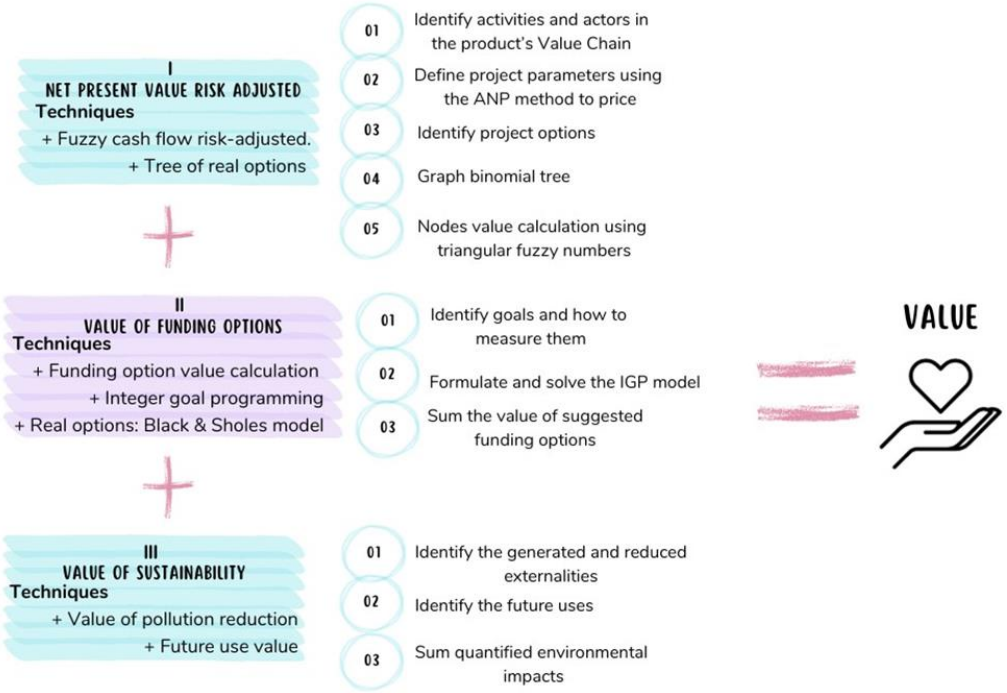


Fig. 13. Framework of the model for value calculation in biotech business. Source. Self-made.

$$Value = rNPV + Vf + Vs \quad (1)$$

In equation (1):

Value: represents the value created through the VC.

rNPV: represents the Net Present Value risk adjusted.

Vf: represents the value of funding options.

Vs: represents the value of sustainability.

The first component of the calculation of the value created through the VC is the Net Present Value risk adjusted, a metric that represents the net value of inputs and outputs considering the time value of money and adjustments for the level of risk associated with the investment. The second component is the value of funding options, which refers to the financial benefit or worth associated with the available funding options for the health biotech project. The third component consist of the value of sustainability, which encompasses social and environmental aspects, as well as the long-term project's results. The upcoming three subsections will explain the appropriate methods for calculating rNPV, Vf, and Vs to offer a suitable understanding of the model proposal and its potential applications, as well as to highlight the usefulness of the selected techniques.

5.2.1 Formulation of the Net Present Value risk adjusted (rNPV)

The basis of the rNPV calculation is the binomial tree, which is also considered a form of management by Bogdan & Villiger (2010). In that sense, this paper proposes a seven-steps methodology to calculate the rNPV.

Step 1. Identification of the project's actors and activities

In the rNPV calculation it is important to estimate all the incomes and outcomes a project produces. To arise precise results in the computation of these values, this paper recommends starting by the identification of the actors and activities linked during the five stages of the drug candidate development process, through the VC tool.

By decomposing all stages from I to V, identifying the critical inputs and outputs, listing the support and complementary supplies, as well as the gains or benefits of belonging to the network, it is possible to understand all the value determinant factors or parameters. This will allow a better and more precise estimate of the cash inflows and outflows that the project promises.

Step 2. Calculation of the market share

To determine the market share, or what is the same, the population to be treated, this paper proposes to follow the procedure summarized in Fig. 14.

When delineating the target population, it is crucial to consider the geographic scope, such as the specific region or country where the treatment will be introduced. Additionally, assessing the uniformity of disease incidence and the prevalence rates, it is essential to ensure an ample pool of subjects for clinical trials and a viable market for product sales. The prevalence rate indicates the percentage of the population that suffers from a disease, while the incidence will determine how many new cases appear each year. Since not all new cases are identified, it is necessary to obtain the diagnosis rate of the disease. Additionally, in each nation, the access levels to health services are different; therefore, a patient cannot be treated if he/she never arrives at a medical facility; hence it is also appropriate to identify the extent of access to health services and, of these patients, how many do it in conditions where they are still treatable. Finally, the adherence rate reflects the number of patients who faithfully adhere to their doctor's orders regarding dosage, frequency, etc.

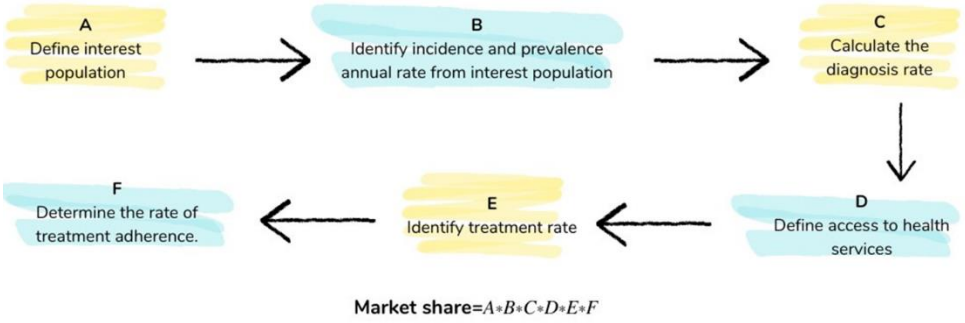


Fig. 14. Procedure for market share calculation. Source. Self-made.

The percentage of diagnosis, the access to the health system, and the adherence rate are inherently uncertain as they may only capture a fraction of the cases they represent. To address this uncertainty, the model proposal recommends employing confidence intervals and fuzzy numbers, allowing for a more nuanced and flexible representation of the vagueness involved in these factors.

A confidence interval can be represented as:

$$A = [a_1; a_2];\ a_1, a_2 \in \mathbb{R}$$

When a magnitude is expressed in the previous confidence interval, it means that it is neither below a1 nor above a_2, but that what happens between the two extremes of the interval is

unknown. These confidence intervals are used to denote fuzzy numbers, which are represented by the pair presumption level; confidence interval, corresponding to each presumption level α a confidence interval. Thus, the fuzzy number A at the presumption level α, can be written as follows:

$$A^{\alpha} = (a_1^{\alpha}; a_2^{\alpha});\ a_1, a_2 \in \mathbb{R};\ \alpha \in [0,1]$$

In this research, triangular fuzzy numbers will be used due to their relative ease of manipulation. The peculiarity of the triangular fuzzy number is that it is determined by three quantities: one below which it will not go down (a_1^{α}), another which it will not be possible to reach above (a_3^{α}), and finally, the one that represents the maximum level of presumption (a_2^{α}):

$$A^{\alpha} = (a_1^{\alpha}; a_2^{\alpha}; a_3^{\alpha});\ a_1, a_2, a_3 \in \mathbb{R};\ \alpha \in [0,1]$$

Step 3. Computation of the sales price

To calculate the price of a treatment, this research considers the significance of price determinants. With that purpose, the use of the ANP methodology allows to determine the priority among the drug candidate price determinants. This methodology synthesizes all the interdependencies network wide, and that is the main reason why it is used in this research. Once defined all actors and activities involved in the project development process in step 1, it is possible to identify accurately the factors determining the candidate's price.

Going through the influences network analysis and quantification as well as the clusters' prioritization, it is possible to obtain the priority or weighting order of each element and comparable treatment in the network (Aznar & Guijarro, 2012; Lai et al., 2021; Magableh & Mistarihi, 2022; Xu et al., 2022), which is used as a coefficient in the equation (2) to determine the treatment sales price.

$$Pr = \left(\frac{C_1 + C_2 + \cdots + C_{n-1}}{w_1 + w_2 + \cdots + w_{n-1}}\right) * w_n \qquad (2)$$

In equation (2):

Pr: price of drug candidate under valuation.

C_1, C_2, C_{n-1}: price of comparable treatments.

w_1, w_2, w_{n-1}: weight of each comparable treatment in the network.

w_n: weight of the drug candidate under valuation.

Step 4. Definition of the binomial tree parameters

In addition to the market share and the drug candidate's price, it is necessary to consider other parameters that allow the cash flow estimation. The binomial tree parameters encompass the decision points, the magnitude of the time interval elapsed between decision points, the sales growth rate in the time interval, the volatility of sales, the project expenses, the success rate of each stage, and the project implementation time. The inherent uncertainty of the sales growth rate, the project expenses, and the success rate of each stage, as well as the cost of capital, is going to be palliate adopting triangular fuzzy numbers.

Step 5. Identification of the future project's options

In this step, scientists in the research need to advance the future of the project. By determining the possibility of going forward to the next stage or abandon the research, the decision-makers should establish the succeeding activities to do as well as their costs. The possibility of move ahead the next stage (Q) is an uncertain parameter that is going to be computed using confidence intervals:

$$Q^{\alpha} = (q_1^{\alpha}; q_2^{\alpha});\ q_1, q_2 \in \mathbb{R};\ \alpha, q_1, q_2 \in [0,1]$$

Step 6. Graph the binomial tree

Once know all the actors, activities, parameters, and future options related to the project, it is time to place all of those in the binomial tree. In this step, it is necessary to estimate the cash flows the project promises, which constitute the value of the terminal branches of the binomial tree. Fig. 15 shows a general picture of the binomial tree.

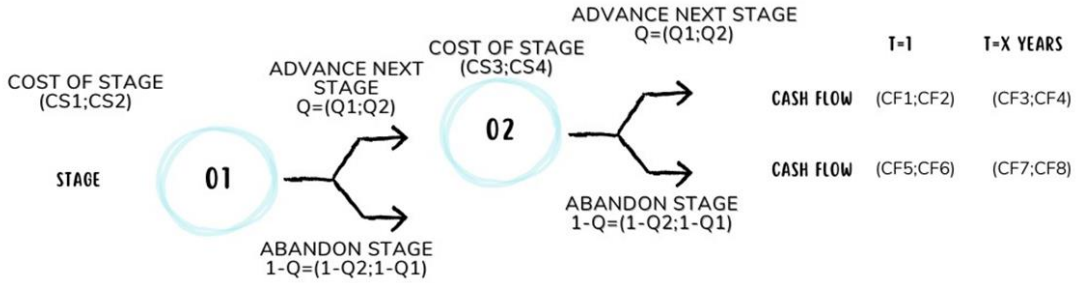


Fig. 15. Generic binomial tree of a biotech project. Source. Self-made.

Step 7. Calculation of the nodes' value

Once the binomial tree has been graphed, it is time to compute each node's value, from the last node to the first one. The initial node's value is the project rNPV, which means the value added by the cash flow the drug candidate promises to the total value created by the project. This rNPV is going to be expressed as a fuzzy triangular number because most of its parameters are uncertain.

5.2.2 Formulation of the Value of funding options (Vf)

The experimental treatment through to the end of the Monitoring and Marketing stage is a long, expensive, and risky process, subsequently one of the main problems facing biotech health companies is the lack of funding. In the opinion of Mazzucato (2013), Molina (2023), and Pisano (2010) there are three basic sources of external funding for this type of business: public capital, venture capital, and property monetization. Aranda et al. (2016) also proposes associations (by merger, acquisition, or absorption) of pharmaceutical and biotech companies, because of their advantages not only for drug development and process production and subsequent commercialization, but also for the expansion of the supply of entities that join the association. In the case of startups, it is advisable to approach business incubators and accelerators as they not only provide capital, but also provide knowledge, experience, and the ability to forge relationships with other companies and investors (Excedr, 2023). In all cases, employment and access to funding depend on the project stage.

Furthermore, when computing the value of the funding options, it is necessary to consider the value added by every applied funding option. In this paper, the model proposal

determines the most recommended funding options for the health biotech project according to the firm's constraints and prioritized goals.

Hence, to select the most appropriate funding option at each stage of the biotech product development process, the IGP is proposed as a multicriteria decision technique that yields an efficient solution for conflicting objectives (Aznar & Guijarro, 2012). This is the case due to the nature of the value-added determinants of the different financing options that can be used throughout the value chain of a health biotech product. Based on Aznar & Guijarro (2012)'s proposal, the algebraic formulation of the model is:

$$\text{Min Z} = \sum_{i=1}^{Q} (u_i * n_i + v_i * p_i) \tag{3}$$

$$f_i(x_j) + n_i - p_i = b_i \tag{4}$$

$$n_i, p_i \geq 0;\ i = 1 \dots Q \tag{5}$$

$$0 \leq x_j \leq 1\ and\ integer; j = 1 \dots m \tag{6}$$

Through the goals programming, the model (3) minimizes the prioritized (u_i, v_i) sum of the negative (n_i) and positive (p_i) deviations concerning each goal (b_i). Model constraints (4) represent the goals and the contribution of each decision variable (x_j). Non-negative deviations condition (5) and non-negative, integer and binary variable conditions (6) are included. The model solution concerns the funding options to be used and the deviations from each goal.

Beside the most common funding options used in health biotech projects, in this paper, its authors also recommend including the value of the flexibility represented by the possible sale of the product patent as a source of funding. With that purpose, the real options theory can be considered to determine the patent sale value, specifically the Black and Scholes model (Black & Scholes, 1973). The Black & Scholes model initially calculates the selling price of a call option (Hussain et al., 2023), but in this case, what is sought is buying a put, allowing the intangible asset to be sold in the future (de Andrés-Sánchez, 2023). The put option's value corresponds to the patent's sale value, representing the impact derived from this funding option (Oramas Santos et al., 2023b). The Vf will be determined by the linear sum

of the value added by each funding option once solved the prioritized IGP model and estimated the value of the patent sale.

5.2.3 Formulation of the Value of sustainability (Vs)

The value of sustainability for the drug candidate refers to whether its production and marketing are sustainable in the long term for the company and society. It can be determined by looking for the following:

- The reduction of pollutant emissions. This reduction is multiplied by the social price of pollutant emissions, and the savings are calculated.
- The reduction in waste generation. This reduction is multiplied by the cost of waste disposal, and the savings are calculated.
- The use of recycled products. The percentage of the product that is reused is multiplied by its cost, and the savings are calculated.
- The potential use. It refers to the future use value of a drug or treatment other than its patented use.

The Vs consists of the sum of contributions from each sustainability dimension. A positive value is attributed when the health biotech project mitigates pollutant effects and demonstrates high potential use. Conversely, a negative value is assigned if the project generates increased or worsened contaminants and lacks long-term usableness. The sustainability dimensions are inherently uncertain as they may only capture a fraction of the real effects they represent. For this reason, this paper suggests using variation intervals, specifically triangular fuzzy numbers as in the rest of the model components, to express the value of the sustainability components.

5.3 AN APPLICATION OF THE MODEL PROPOSAL IN A CUBAN HEALTH BIOTECH PROJECT

The model proposal is applied in a Cuban drug candidate consisting of a novel treatment athwart a degenerative disease developed by a Cuban biotech company. The project began phase III of the clinical trial in January 2023. Its main objective is to reduce the rate of progression of cognitive impairment in people with Alzheimer's and improve their functional activity. The actors mostly involved in the projects are the Cuban biotech company, the clinical trials medical providers, the inputs suppliers, and the patients, as well as the national and international regulatory agencies that indicate general procedures and best practices to be followed to produce and market a health biotech product.

According to the characteristics of the drug candidate and the disease it will work against, the target population is the Cuban people older than 65 years old (Llibre, 2013). Uncertainty was considered on parameters such as the access rate, prevalence, incidence, cost of phase III clinical trials and stages IV and V, cost of capital, and risk to go from stages. The population growth rate was obtained from ONEI (2023)' estimations, and the project valuation period is from 2023 to 2048. The data entry for rNPV estimation is summarized in Table 8.

Table 8. Data entry for the fuzzy cash flow calculation.

Variable	Source	a_1	a_2	a_3
$Population_{2023}$	ONEI (2023)	1.000.806	1.000.806	1.000.806
New cases over the total cases for a year (%)	BrightFocus Foundation (2021)	9,09	9,09	9,09
Symptom rate	Cubadebate (2023)	1	1	1
Diagnostic rate	Cubadebate (2023)	0,93	0,93	0,93
Annual dosage per patient	Enterprise's information	209	209	209
Access rate	Trabajadores (2023)	0,25	0,96	0,98
Prevalence	MINSAP (2022), Trabajadores (2023)	60	70	80
Incidence	Tom et al. (2015), Alzheimer's Association (2023)	2,12	2.84	3,00
Phase III cost (CUP[1] million)	Enterprise's information	2.127.901.356	2.915.224.858	3.191.852.034
Stage IV cost (CUP million)	Enterprise's information	12.000.000	15.000.000	15.600.000
Stage V cost (CUP million)	Enterprise's information	11.760.000	14.400.000	15.000.000
Cost of capital (%)	Rennane et al. (2021)	7	11	13
Risk from stage III to stage IV (%)	Scott et al. (2014), Rennane et al. (2021)	16	47	68
Risk from stage IV to stage V (%)	Scott et al. (2014), Rennane et al. (2021)	77,8	86,7	91,2
Distribution cost (%)	Enterprise's information	31	31	31
Manufacturing cost (%)	Enterprise's information	18	18	18
Tax rate (%)	Enterprise's information	15	15	15

Source. Self-made.

[1]: CUP means Cuban Pesos and represents the Cuban currency.

In the ANP practice to estimate the drug price, fourteen explanatory variables were identified and grouped into three clusters. Once computed the priority factors and the equation (2), the resultant price equals 17846,8 CUP/treatment.

In the valuation of this project the considered options were to move from the phase III of clinical trials to the stages IV and V or abandon the project. This paper didn't consider the increase or decrease of the initial sales peak because it was already reflected when estimating the maximum presumption level in the fuzzy triangular number. At this point, it is possible to plot the binomial tree as a visual tool that reflects the expected cash flows of the project options from 2023 to 2048. Fig. 16 shows the project options, their q-occurrence range, and the estimated cash flow confidence intervals for the first and the last year of operations (T=2 and T=25 respectively).

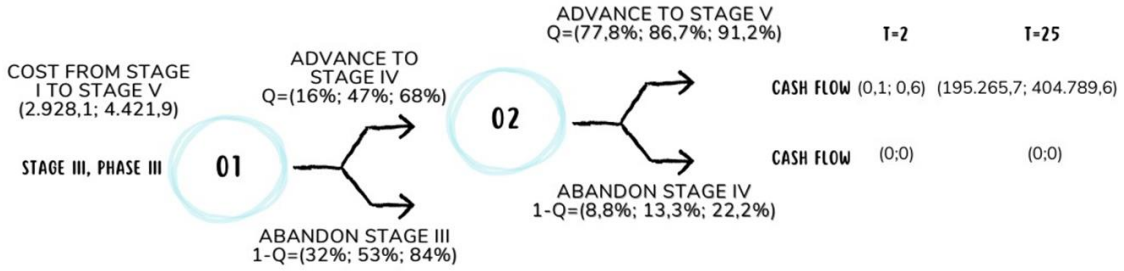


Fig. 16. Project's binomial tree. Self-made.

Note: Cash flows and costs are cumulated, and risk adjusted at time T. They represent CUP billion.

Once plotted the binomial tree, it is time to calculate the value of each node, by adding the cumulative discounted adjusted cash flows and the investment cost from stage I to stage V. The rNPV during the 25 valuation years, is a fuzzy number defined in the confidence interval (-3.639.461.106,58; 12.359.331.191,00) CUP. In the worst conditions, the result from the product marketing is a loss of 3,64 CUP billion in contrast with a gain of 12,36 CUP billion in the best conditions. The result from the highest level of presumption is a gain of 3,94 CUP billion.

To calculate the value added by the funding options, as was mentioned in the 2.2 section, first it is necessary to select the most convenient to apply for. With that purpose, the IGP model was formulated considering five decision variables. Solving the model formulated with the LINGO software version 20.0, the solution recommends the self-funding, venture capital, and public capital as funding options that allow the prioritized objectives. The value added by those three funding options is 4.382,57 CUP billion. Property monetization is also possible in this project. Table 9 summarizes the data entry for this purpose.

Table 9. Data entry for put option value calculation.

Parameter	Value
Strike price	898,80 CUP million
Underlying price	840,00 CUP million
Underlying volatility	0,3
Risk-free rate	0,04
Time to expiration	1 year

Source. Self-made.

In selling the product patent, the value increases by 115,06 CUP million. When adding this value to the added value by the other three funding options, the total Vf is approximately 4.382,6 CUP million. Since the Vf is positive, the selected funding options will increase the value of the biotech health project and its attractiveness when looking for investors.

From the sustainability point of view, in this project it is possible to reduce the use of the chemical pollutant named chlorine dioxide, in a measure of 0,13 lb. every 1000 doses. The cost of this product is 2.466,7 CUP/lb., which means a saving of 0,35 CUP/dose. When producing this project, the wastewater generated can be also diminished. The reduction cost in sewage treatment arises 0,032 CUP/dose, given a sewage treatment cost of 6,13 CUP/l.

In addition to the quantitative results, it is recognizable the future use of the drug candidate in the treatment of stroke and spinocerebellar ataxias, which are so frequent diseases in Cuba. This small country has the highest global incidence of spinocerebellar ataxia disease, reaching 33 per 100.000 inhabitants (Fariñas, 2022). Additionally, the stroke is the Cuban population third cause of death, with an incidence of 786,2 per 100.000 people per year according to Noda (2022). In this research was not possible to estimate the value of the future use for this drug candidate because the dosage is unknown.

By considering the elements explained, the value created for this project will be in the (196.008.816.573,90; 421.531.500.432,05) CUP million confidence interval. As can be seen, the results are higher than the usual adjusted cash flow valuation (rNPV) and more flexible given the calculation of confidence intervals. These are some of the model's attributes that stand out a difference in the decision-making process.

5.4 CONCLUSIONS

This research aimed to develop and apply a model that estimates the added value by all companies linked along the VC of any health biotech project, taking into consideration qualitative and quantitative factors, as well as the uncertainty management, and applying scoring methods and fuzzy tools to provide a comprehensive assessment. To apply it, a Cuban health biotech project was selected.

The model proposal is structured around three primary components: rNPV, Vf, and Vs. The foundational element of the model is the definition of the project's VC, facilitating binomial tree analysis to discern the impact of funding options and the sustainability of the drug candidate.

For rNPV calculation, the initial step involves defining the health biotech project's VC. Subsequently, tree parameters are defined, and the ANP multicriteria technique, fuzzy set theory, and real options method are applied to compute the rNPV.

Vf calculation involves using the IGP for selecting optimal funding options and the Black and Scholes model to estimate the drug patent's value. Using this proposal, decision-makers can reduce the time and effort employed in looking for funding options, which means a more accurate and efficient planning process. It also represents more flexibility due to the possibility to sale product's patent.

Vs is determined by identifying externalities generated and the future uses of the treatment, employing confidence intervals. The total added value is then computed by combining rNPV, Vf, and Vs.

After applying this model, decision-makers benefit from a single indicator that compresses critical project impacts, considering market uncertainty and associated risks. The model proposes a flexible combination of funding options aligned with the company's objectives, enhancing the consideration of value addition. It also provides a well-balanced perspective on the project's position through objective contrasts of price determinants. The inclusion of sustainability components highlights the enduring value and attractiveness of the project compared to other drug candidates. Uncertainty management is a crucial aspect, addressed

through fuzzy logic and the VC tool. The model offers a novel approach to life sciences project valuation by linking VC with binomial trees.

The model is positioned as a management tool for decision-makers, aiding in long-term strategic planning within an uncertain environment. From the customer perspective, there is an increase in consumer surplus due to a fair treatment price and a positive impact on waiting times, enhancing the quality of life for patients and their families. This model, adaptable to various projects and sectors beyond biotechnology, stands out for its potential cost savings, improved investment assessment, and strategic planning, contributing to a better resource management.

REFERENCES

Acharjee, D. C., Alam, G. M. M., Gosh, K., Haque, A. B. M. M., & Hossain, M. I. (2023). Fish value chain and the determinants of value addition decision: Empirical evidence from Bangladesh. Journal of the World Aquaculture Society, 1-14. https://doi.org/10.1111/jwas.12941

Akyüz, Y., Salali, H. E., Atakan, P., Günden, C., Yercan, M., Lamprinakis, L., Kårstad, S., Solovieva, I., Kasperczyk, N., Mattas, K., Lazaridou, D., Yener, G., Alayidi, A., Kunchulia, I., Basilidze, L., & Knez, M. (2023). Case Study Analysis on Agri-Food Value Chain: A Guideline-Based Approach. Sustainability, 15(7), Article 7. https://doi.org/10.3390/su15076209

Alzheimer's Association. (2023). Treatments. Alzheimer's Disease and Dementia. https://alz.org/alzheimer-demencia/tratamientos

Aranda, S., Lopez Torres, V., & Guerra, G. (2016). Propuesta de Modelo de Negocio Base Para las Empresas de Biotecnología en México. Revista Global de Negocios, 4, 29-51.

Aznar, J., & Guijarro, F. (2012). Nuevos Métodos de Valoración. Modelos Multicriterio (2.a ed.). Editorial Universitat Politècnica de València. http://hdl.handle.net/10251/19181

BioCubaFarma. (2019). A changing pharma industry and biotech´s business model. V, 39.

Black, F., & Scholes, M. (1973). The Pricing of Options and Corporate Liabilities. Journal of Political Economy, 81(3), 637-654. https://doi.org/10.1086/260062

Bogdan, B., & Villiger, R. (2010). Valuation in Life Sciences: A Practical Guide (Third edition). Springer. https://doi.org/10.1007/978-3-642-10820-4

Brealey, R. A., Allen, F., & Myers, S. C. (2011). Principles of corporate finance. McGraw-Hill/Irwin.

BrightFocus Foundation. (2021). Alzheimer's Disease: Facts and Figures. https://www.brightfocus.org/espanol/alzheimer/la-enfermedad-de-alzheimer-y-la-demencia/enfermedad-de-alzheimer-datos-y-cifras

Burns, L. R. (2022). The Healthcare Value Chain: Demystifying the Role of GPOs and PBMs. Springer International Publishing. https://doi.org/10.1007/978-3-031-10739-9

CDER. (2023). FY 2022 GDUFA Science and Research Report. FDA, 128.

Charnes, A., & Cooper, W. W. (1962). Management models and industrial applications of linear programming: Vol. I. John Wiley & Sons. https://doi.org/10.1002/nav.3800090109

Cornelissen, M., Małyska, A., Nanda, A. K., Lankhorst, R. K., Parry, M. A. J., Saltenis, V. R., Pribil, M., Nacry, P., Inzé, D., & Baekelandt, A. (2021). Biotechnology for Tomorrow's World: Scenarios to Guide Directions for Future Innovation. Trends in Biotechnology, 39(5), 438-444. https://doi.org/10.1016/j.tibtech.2020.09.006

Craighead, C. W., Ketchen Jr., D. J., & Darby, J. L. (2020). Pandemics and Supply Chain Management Research: Toward a Theoretical Toolbox*. Decision Sciences, 51(4), 838-866. https://doi.org/10.1111/deci.12468

Cubadebate. (2023, febrero 25). Ensayo clínico con NeuralCIM® (NeuroEPO) para alzhéimer leve o moderado comienza en Cuba el próximo lunes (+ Video). Cubadebate. http://www.cubadebate.cu/noticias/2023/02/25/ensayo-clinico-con-neuralcim-neuroepo-para-alzheimer-leve-o-moderado-comienza-en-cuba-el-proximo-lunes/

de Andrés-Sánchez, J. (2023). A systematic review of the interactions of fuzzy set theory and option pricing. Expert Systems with Applications, 223, 119868. https://doi.org/10.1016/j.eswa.2023.119868

DiMasi, J. A. (2014). Pharmaceutical R&D performance by firm size: Approval success rates and economic returns. American Journal of Therapeutics, 21(1), 26-34. https://doi.org/10.1097/MJT.0b013e318269198f

Excedr. (2023, enero 5). Biotech Funding for Startups: What are Your Options? Excedr. https://www.excedr.com/resources/biotech-funding-for-startups/

Fariñas, L. (2022, septiembre 13). Ataxia hereditaria: La enfermedad en que Cuba tiene la mayor prevalencia global y es campo de incesante investigación. Cubadebate. http://www.cubadebate.cu/especiales/2022/09/13/ataxia-hereditaria-la-enfermedad-en-que-cuba-tiene-la-mayor-prevalencia-global-y-es-campo-de-incesante-investigacion-video/

Ghamlouch, H., Fouladirad, M., & Grall, A. (2019). The use of real option in condition-based maintenance scheduling for wind turbines with production and deterioration uncertainties. Reliability Engineering & System Safety, 188, 614-623. https://doi.org/10.1016/j.ress.2017.10.001

Hossain, M., Akteruzzaman, M., Parvin, Mst. T., Bhuiya, M., & Hossain, S. (2013). Marketing Channel of Fish and Value Addition by Different Actors in Haor Area of Netrakona District. Bangladesh Journal of Crop Sceince, 24, 131-140.

Hu, C., Zhang, X., Reardon, T., & Hernandez, R. (2019). Value-chain clusters and aquaculture innovation in Bangladesh. Food Policy, 83(C), 310-326. https://doi.org/10.1016/j.foodpol.2017.07.009

Hussain, S., Arif, H., Noorullah, M., & Pantelous, A. A. (2023). Pricing American Options under Azzalini Ito-McKean Skew Brownian Motions. Applied Mathematics and Computation, 451, 128040. https://doi.org/10.1016/j.amc.2023.128040

ILO. (2015). Value chain development for decent work: How to create employment and improve working conditions in targeted sectors (2nd ed.). International Labour Office. www.ilo.org/publns

Kamel, A., Elwageeh, M., Bonduà, S., & Elkarmoty, M. (2023). Evaluation of mining projects subjected to economic uncertainties using the Monte Carlo simulation and the binomial tree method: Case study in a phosphate mine in Egypt. Resources Policy, 80, 103266. https://doi.org/10.1016/j.resourpol.2022.103266

Kaplinsky, R., & Morris, M. (2000). A Handbook for Value Chain Research, (Vol. 113). Brighton: University of Sussex, Institute of Development Studies.

Koller, T., Goedhart, M., & Wessels, D. (2010). Valuation. Measuring and Managing the Value of Companies (Fifth). John Wiley & Sons.

Lai, J. H. K., Hou, H. (Cynthia), Edwards, D. J., & Yuen, P. L. (2021). An analytic network process model for hospital facilities management performance evaluation. Facilities, 40(5/6), 333-352. https://doi.org/10.1108/F-09-2021-0082

Llibre, J. de J. (2013). Demencias y enfermedad de Alzheimer: Una prioridad nacional. Revista Cubana de Salud Pública, 39(4), 804-806.

Magableh, G. M., & Mistarihi, M. Z. (2022). Applications of MCDM approach (ANP-TOPSIS) to evaluate supply chain solutions in the context of COVID-19. Heliyon, 8(3), e09062. https://doi.org/10.1016/j.heliyon.2022.e09062

Mazzucato, M. (2013). Financing innovation: Creative destruction vs. destructive creation. Industrial and Corporate Change, 22(4), 851-867. https://doi.org/10.1093/icc/dtt025

Mazzucato, M., & Ryan-Collins, J. (2022). Putting value creation back into "public value": From market-fixing to market-shaping. Journal of Economic Policy Reform, 25(4), 345-360. https://doi.org/10.1080/17487870.2022.2053537

MINSAP. (2022, septiembre 23). Alzheimer: Preguntas y respuestas. Sitio oficial de gobierno del Ministerio de Salud Pública en Cuba. https://salud.msp.gob.cu/alzheimer-preguntas-y-respuestas/

Molina, E. (2023). El financiamiento a la biotecnología en el mundo. Alternativas para Cuba. Economía y Desarrollo, 167(1), 9.

Noda, S. (2022, octubre 29). Prevenir el Ictus, llamado necesario ante un problema de salud mundial. Ministerio de Salud Pública en Cuba. https://salud.msp.gob.cu/prevenir-el-ictus-llamado-necesario-ante-un-problema-de-salud-mundial/

ONEI. (2023, abril 11). Estudios y Datos de la Población. Cuba y sus Territorios. Oficina Nacional de Estadística e Información. http://www.onei.gob.cu/node/13818

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023a). The value chain approach in red biotechnology companies from a bibliometric perspective. International Journal of Production Management and Engineering, 11(2), 187-196. https://doi.org/10.4995/ijpme.2023.19135

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023b). Valoración de un producto biotecnológico cubano a partir de su cadena de valor. II Simposium Predoctoral de Organización de Empresas, II, 108-113. ttp://hdl.handle.net/10251/196663

Oramas Santos, O., Canós-Darós, L., Babiloni, E., & Ortiz Torres, M. (2023). De cadena de suministros a cadena de valor: Devenir y pertinencia de los conceptos. Economia y Desarrollo, 167(1). http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S0252-85842023000100012&lng=es&nrm=iso&tlng=es

Pisano, G. (2010). The Evolution of Science-Based Business: Innovating How We Innovate. Industrial and Corporate Change, 19, 465-482. https://doi.org/10.2139/SSRN.1545806

Porter, M. E. (1985). Competitive advantage: Creating and sustaining superior performance. The Free Press.

Porter, M. E. (1991). Towards a dynamic theory of strategy. Strategic Management Journal, 12(S2), 95-117. https://doi.org/10.1002/smj.4250121008

Rennane, S., Baker, L., & Mulcahy, A. (2021). Estimating the Cost of Industry Investment in Drug Research and Development: A Review of Methods and Results. Inquiry: A Journal of Medical Care Organization, Provision and Financing, 58, 1-11. https://doi.org/10.1177/00469580211059731

Saaty, T. L. (1996). Decision Making with Dependence and Feedback: The Analytic Network Process (Vol. 4922). RWS Publications.

Scott, T. J., O'Connor, A. C., Link, A. N., & Beaulieu, T. J. (2014). Economic analysis of opportunities to accelerate Alzheimer's disease research and development. Annals of the New York Academy of Sciences, 1313(1), 17-34. https://doi.org/10.1111/nyas.12417

Tom, S. E., Hubbard, R. A., Crane, P. K., Haneuse, S. J., Bowen, J., McCormick, W. C., McCurry, S., & Larson, E. B. (2015). Characterization of Dementia and Alzheimer's Disease in an Older Population: Updated Incidence and Life Expectancy With and Without Dementia. American Journal of Public Health, 105(2), 408-413. https://doi.org/10.2105/AJPH.2014.301935

Trabajadores. (2023, febrero 25). Alzheimer en Cuba: Comienza ensayo clínico fase III con NeuralCIM® • Trabajadores. Trabajadores. https://www.trabajadores.cu/20230224/alzheimer-en-cuba-comienza-ensayo-clinico-fase-iii-con-neuralcim/

Xu, J., Li, L., & Ren, M. (2022). A Hybrid ANP Method for Evaluation of Government Data Sustainability. Sustainability, 14(2), Article 2. https://doi.org/10.3390/su14020884

Zadeh, L. A. (1965). Fuzzy Sets. Information and Control, 8, 338-353.

CAPÍTULO VI. DISCUSIÓN

En el recorrido que implicó la presente tesis, se plantearon cinco objetivos específicos, los cuales se fueron alcanzando y compartiendo con la comunidad científica a través de la publicación de cinco artículos, cuatro de los cuales conforman la estructura capitular de este documento. El estudio y valoración del enfoque de cadena de valor (CV) centrado específicamente en el sector de la biotecnología sanitaria, es un hilo que trasciende transversalmente a todas las publicaciones, dado que esta categoría constituye la variable principal que sustenta la propuesta metodológica de esta investigación.

El estudio de la CV en la biotecnología de la salud saca a luz la necesidad de profundizar en el análisis de estas variables en países desarrollados y en vías de desarrollo, lo cual se aborda a través de la categoría Sistemas Nacionales de Innovación. Esta última investigación permite identificar los actores que intervienen en la obtención de un candidato a fármaco, así como las actividades llevadas a cabo por estos, lo cual se emplea en la propuesta de aplicación de la metodología Proceso Analítico en Red (ANP por sus siglas en inglés) en el establecimiento de los clústeres para el cálculo del precio de un tratamiento médico. Este proceder, constituye una etapa en la propuesta de modelo planteada. Adicionalmente, el estudio del sector biotecnológico en Cuba sirvió de fundamento para las aplicaciones prácticas de las propuestas.

Iniciando con el estudio de la CV, es posible plantear que esta sintetiza las actividades a ejecutar para llevar un bien o servicio a manos del cliente final, así como la consecuente disposición de desechos, dando como resultado el margen de beneficios que la empresa nodal obtendrá al finalizar cada ciclo. Este es un enfoque que permite analizar el sistema en estudio como un todo, lo cual es recomendable para obtener la visión integral que requieren los procesos de valoración de proyectos biotecnológicos. Los artículos recogidos en los capítulos II y III abordan específicamente los fundamentos teóricos de esta metodología.

La capacidad de la biotecnología sanitaria cubana para proveer de bienestar y desarrollo a la economía nacional, la empresa, y la sociedad en general, es demostrada a través del estudio de la categoría Sistema Nacional de Innovación (SNI) en el Capítulo III. El enfoque de sistema ofrece una visión holística que desvela la función e importancia de la Industria

Biotecnológica Cubana (IBC) como sector abierto y generador de encadenamientos, así como sus complejas particularidades.

Una de estas complejas particularidades es el proceso de valoración de candidatos a fármacos. Los métodos y herramientas comúnmente empleados en este campo, como segunda variable fundamental de esta investigación, se encuentran expuestos en los capítulos I, IV y V. A través de la explicación de las bondades y brechas persistentes en dichos métodos, se construye el sustento de la propuesta de modelo que estima el valor añadido por todas las actividades y negocios interconectados a través de la CV de un proyecto de la biotecnología sanitaria. Dicha propuesta, expuesta en el Capítulo V, se aplica a un tratamiento cubano en fase experimental, cuyos resultados igualmente forman parte del artículo presentado como colofón de la parte central de esta tesis doctoral.

Analizando la investigación realizada desde una perspectiva general, es apreciable que muestra importantes resultados desde los puntos de vista teórico y práctico. Desde la óptica teórica, se destacan algunas brechas en la intersección de los campos de la biotecnología y la CV. Bajo este proyecto de tesis doctoral se realizó el primer estudio bibliométrico que vincula estos dos campos, analizando el concepto moderno de CV en proyectos biotecnológicos, y abriendo paso a la profundización en los impactos de la Industria 5.0 en futuros trabajos, la cual incluye la interacción entre las personas y la inteligencia artificial. Por tanto, esta investigación no sólo resuelve el problema que la inició, sino que guía la ruta de ulteriores estudios.

El estudio bibliométrico realizado revela la necesidad de crear redes de investigadores que analicen el sector de la biotecnología sanitaria desde el punto de vista de los negocios, con visión gerencial y global, dado que esta es una de las características distintivas de este campo. Publicaciones que desvelen las peculiaridades de un mismo proceso en naciones y culturas diferentes, sin dudas favorecerán el aprendizaje colectivo, permitirán identificar pros y contras de cada una de las partes involucradas, y constituirán lecciones para futuros aprendices. Llama la atención en este punto el hecho de que el autor seminal en lo concerniente a las CV, Michael E. Porter y su trabajo *Competitive advantage: creating and sustaining superior performance* (1985), no aparecen dentro de los más citados, siendo la

publicación de Gereffi et al. (2005) el único *paper* relevante citado. Esto refuerza la conclusión planteada que señala que la mayoría de los trabajos publicados en el campo de la biotecnología de la salud no se refieren a los resultados de este sector como un negocio, sino como una ciencia con resultados tecnológicos, innovadores y sociales.

Por otro lado, la propuesta del SNI cubano es fundamental para este país. Incluso si las políticas generales de invención, ciencia y técnica abordan y gestionan las innovaciones que pueden insertarse en la isla, se necesitaba una herramienta con visión holística que vinculase a las empresas de la IBC y del resto de la economía nacional, y que tuviese en cuenta las relaciones internacionales que también afectan el desenvolvimiento de las finanzas internas y de la sociedad cubana. Desde un punto de vista práctico, la propuesta de SNI cubano es desafiante, especialmente porque el entorno institucional no la favorece. Sin embargo, los beneficios de su implementación superan los esfuerzos y cambios que se deben realizar para que funcione. Su aplicación también inicia nuevas investigaciones dirigidas a mejorar esta sugerencia inicial.

Otro resultado relevante es la propuesta del modelo matemático. Este abarca tres dimensiones críticas, por lo general analizadas de forma independiente, y cuantifica algunos factores cualitativos que usualmente no se estudian. La novedad de la contribución de la propuesta, al leal saber y entender de su autora, constituye el cálculo de un indicador integral y único con una visión holística del proyecto o negocio estudiado. Representa una metodología paso a paso que permite visualizar todos los nodos vinculados en la CV de cualquier proyecto de biotecnología sanitaria, así como el valor añadido por cada uno de ellos. Induce a una investigación más profunda para revelar los *value-drivens*, incluso los no percibidos a simple vista, y medirlos. Gestiona la incertidumbre aplicando herramientas difusas. Desde el punto de vista práctico puede resultar complicado de utilizar, pero supone un ahorro de tiempo y esfuerzo a la hora de valorar cualquier proyecto.

Un parámetro crítico en la valoración es la estimación del precio. En esta investigación y como parte de la propuesta de modelo, se sugiere aplicar la metodología multicriterio ANP basada en la CV que implica un proyecto. Con este fin, es crucial revelar los determinantes del precio y las interdependencias entre ellos y entre otros medicamentos comparables. La

metodología ANP se encuentra perfectamente alineada con el enfoque de CV que sustenta esta tesis, dado que analiza y mesura el impacto de los factores que afectan el precio de un candidato a fármaco, tras examinar y puntuar las relaciones entre estos. Con el fin atenuar la incertidumbre que incide en los determinantes del precio de un tratamiento en fase experimental, en futuras investigaciones estos podrían fuzzificarse, al igual que el resto de los parámetros en esta investigación.

En concreto y desde la perspectiva financiera y práctica, es genuina la cuantificación del valor que añade cada opción de financiación. Sin embargo, la mayor contribución proviene del uso de la IGP o Programación por Metas Entera para sugerir las opciones de financiamiento a solicitar, en qué orden y el monto a utilizar. El proceso de determinar a qué fuente de financiación aplicar es complejo porque en él intervienen tanto elementos internos como externos a la empresa y al país en el que esta se encuentre, así como los retornos que la inversión en cuestión pueda prometer y el nivel de riesgo inherente al proyecto a financiar. La IGP dota a la propuesta de modelo de flexibilidad, pues a medida que cambien las prioridades, metas e incentivos de la compañía, cambiará la sugerencia del financiamiento a emplear y por ende el valor agregado total del candidato a fármaco, de ahí que los tomadores de decisiones y las partes interesadas podrán decidir a qué fuentes acudir teniendo en cuenta el valor de las diferentes opciones o escenarios proyectados.

El último de los elementos de la propuesta de modelo que se realiza en esta investigación es la determinación del valor de la sostenibilidad, el cual obliga a pensar más allá del presente, dilucidando los efectos a largo plazo del proyecto o negocio. Este acápite, si bien por generalidad es mencionado, pocas veces llega a ser cuantificado. El cómputo de la sostenibilidad a largo plazo de un tratamiento en fase experimental es en extremo relevante dado que esta es una pregunta de obligatoria respuesta para los científicos que participan en la investigación, para los tomadores de decisiones de la empresa nodal que lidera el proyecto, y para los inversionistas que evalúan si merece la pena arriesgar su capital. Especial atención requiere el identificar el valor de uso futuro del tratamiento, bien sea en la cura de otras enfermedades o como materia prima de otros productos. Por tanto, dedicar esfuerzos en ubicar el proyecto en el largo plazo, y emplear las bondades de la lógica difusa para aminorar los efectos de la incertidumbre que este horizonte temporal implica, es altamente beneficioso

y agrega valor al candidato en estudio, lo cual quedó demostrado con la aplicación del modelo propuesto a un caso de estudio cubano.

Si bien el modelo es una propuesta teórica, en la práctica representa un solo indicador flexible que puede ser empleado para gestionar o evaluar escenarios. Esto se fundamenta en el uso de cifras difusas e intervalos de confianza, en el empleo de la teoría de opciones al momento de la valoración, y en la aplicación de la IGP para sugerir las fuentes de financiación por las cuales optar. Esta flexibilidad acentúa la usabilidad de la propuesta para gestionar la posición estratégica de la empresa, en tanto obliga a visualizar el largo plazo, revela los factores claves del éxito del candidato a fármaco y por ende de la empresa nodal, tiene en cuenta el poder negociador de proveedores y clientes, se construye sobre la base de un sistema abierto impactado por externalidades, y desvela los resultados esperados en condiciones adversas, permitiendo la puesta en práctica de acciones de mitigación de riesgos desde etapas tempranas del proyecto. Esta autora considera estos elementos una superioridad respecto a los métodos de valoración indistintamente empleados en proyectos biotecnológicos de la salud.

Esta tesis cierra el ciclo de investigación científica tras estudiar las variables CV y modelos de valoración teóricamente, profundizar en las particularidades de la industria objeto de estudio, revelar y cubrir vacíos de investigación, analizar críticamente las bondades y elementos a mejorar de las metodologías y métodos empleados en la biotecnología de la salud desde la óptica de la gestión, y proponer y aplicar un modelo de valoración que puede extrapolarse y ajustarse a las especialidades de cualquier sector. Cada uno de los elementos abordados favorecen la visión sistémica e integral de las variables estudiadas y de la solución aportada al problema que da origen a la investigación.

CAPÍTULO VII. CONCLUSIONES

Esta tesis doctoral aborda el tema de valoración de proyectos de biotecnología sanitaria. Para proponer e implementar un modelo matemático que estime el valor agregado de todas las actividades y empresas interconectadas a lo largo de la CV de un proyecto de biotecnología de la salud, esta investigación trasciende por varias etapas.

En primer lugar, se analiza el enfoque del CV en el ámbito de la biotecnología. Desde una perspectiva bibliométrica, esta investigación muestra que el enfoque más significativo de los artículos publicados en biotecnología de la salud no está en el campo de la gestión sino en las aplicaciones biomédicas de terapias y tratamientos. Aunque los trabajos difundidos están aumentando, no existen conexiones entre los científicos que investigan este sector, ni tampoco entre los temas de investigación, o los científicos que investigan un mismo tema. Específicamente, existe un vacío en las publicaciones de tópicos gerenciales sobre los procesos de desarrollo de candidatos a medicamentos, así como en el análisis del desempeño de este sector en los países menos desarrollados.

Considerando estos resultados, en segundo lugar, esta tesis evalúa la capacidad de la biotecnología sanitaria cubana para ser un motor de bien y desarrollo. Al elegir la categoría de SNI y estudiar sus principales componentes en países desarrollados y menos desarrollados, se propone un SNI cubano, sustentado en las cadenas de valor de la IBC. La propuesta revela y considera todos los actores conectados y cómo pueden mejorar la economía y la sociedad cubanas a partir de cinco indicadores clave: regulaciones, políticas de tecnología e innovación, sistemas financieros, actividades empresariales, y sistema de investigación y educación. Una vez más, el enfoque de CV es la piedra angular del desarrollo de la IBC y del SNI cubano, ahora con una variación en la agrupación de actividades primarias y de apoyo debido a la propuesta de cambiar los esfuerzos de financiación a actividad primaria en el diseño de la CV. Esta investigación permitió identificar algunas opciones de financiamiento a postular al momento de valorar un proyecto de biotecnología sanitaria, así como un mejor direccionamiento y composición de los clústeres para la estimación del precio de los candidatos a fármacos.

En tercer lugar, para evaluar la idoneidad de los métodos y herramientas de valoración a aplicar en proyectos de biotecnología sanitaria, se analizan las principales técnicas utilizadas en este campo. A la cabeza se encuentra el método de opciones reales, concretamente el árbol binomial, así como las comparaciones para establecer el precio de mercado de nuevos candidatos a fármacos. Basado en estadísticas para estimar los parámetros de los proyectos, el árbol binomial de opciones reales permite calcular los flujos de efectivo esperados de estos. Estos métodos de valoración se consideran adecuados y validados mediante su aplicación en disímiles casos de estudio, a pesar de presentar el inconveniente de estar basados fundamentalmente en las expectativas de los mercados.

Uno de los parámetros a determinar es el precio del tratamiento, que comúnmente se establece mediante comparaciones con otros similares sin considerar los factores precisos que determinan su valor específico, ya sea que provengan de las condiciones generales del mercado o de la economía nacional y global; del tipo de relaciones comerciales que se establecen entre empresas que interactúan en sus procesos de investigación, producción y comercialización; de las tendencias sociales; o de las políticas y regulaciones que lo afecten; entre otros. Esta investigación cubre esta brecha proponiendo un método de estimación de precios basado en la metodología ANP, que permite considerar todos los actores y actividades en la CV del proyecto y ponderar los factores que impactan el precio del tratamiento según su relevancia. El resultado es un precio más ajustado, preciso y justo.

Algunos otros parámetros del árbol binomial de opciones reales son la cuota de mercado, la tasa de crecimiento y volatilidad de las ventas, los gastos del proyecto, y la tasa de éxito de cada etapa en proceso de desarrollo de un candidato a fármaco. Se trata de parámetros con un desempeño intrínsecamente incierto, así como el costo de capital empleado para ajustar los flujos de caja, por lo que en muchos casos la tendencia que podrían mostrar los modelos predictivos estadísticos y econométricos puede no reflejar el resultado real que generará el proyecto. Al mismo tiempo, este método no considera el efecto de las opciones de financiación utilizadas por el candidato a fármaco, que podrían aumentar o disminuir su valor y atractivo para las partes interesadas.

Dadas estas lagunas, la cuarto etapa consiste en la propuesta de modelo. Esta abarca las dimensiones económica, financiera y de sostenibilidad. Se sustenta en la gestión de la CV de un proyecto de biotecnología sanitaria, capturando el valor agregado por todas las actividades y actores vinculados durante las etapas de Descubrimiento y Desarrollo, Investigación Preclínica, Investigación Clínica, Revisión de Medicamentos y Acceso al Mercado, y Monitoreo y Comercialización del proceso de desarrollo de candidatos a fármacos. La propuesta consiste en un indicador único para computar el valor de cualquier tratamiento.

Desde la perspectiva económica, se plantean siete pasos para estimar los flujos de caja esperados del proyecto, paliando la incertidumbre en los parámetros con herramientas difusas, específicamente números difusos triangulares porque ofrecen un rango de posibilidades en lugar de un solo número. De esta manera, los tomadores de decisiones pueden saber si están cerca del escenario más arriesgado o avanzando hacia uno más rentable. Para ello, el precio del candidato a medicamento se calcula puntuando los factores cualitativos y cuantitativos que lo afectan.

El componente financiero del modelo está dirigido a evaluar si las opciones de financiación están añadiendo valor al proyecto, así como a seleccionar la más conveniente a gestionar. Para ello se utiliza la técnica de decisión multicriterio IGP y el modelo de Black & Scholes. Después de este cálculo, los tomadores de decisiones saben qué opciones de financiamiento son las más recomendadas para el proyecto específico y cuánto valor agregan.

La perspectiva de sostenibilidad muestra dónde se encuentra el candidato a fármaco a largo plazo. Al considerar las implicaciones ambientales y los usos futuros del proyecto, este componente calcula los ahorros y otros ingresos potenciales que genera el tratamiento experimental. En este caso, la incertidumbre también se gestiona mediante números triangulares difusos.

Finalmente, la propuesta del modelo se aplica a un proyecto cubano de biotecnología sanitaria. A través de la recopilación de todos los datos cualitativos y cuantitativos relacionados con el proyecto, fue posible identificar los nodos de la red, estimar un precio de venta más preciso para el candidato a fármaco en estudio, sugerir una combinación de

opciones de financiación, y revelar la rentabilidad del proyecto a largo plazo. En este proceso fue crítico utilizar intervalos de confianza debido a la inexistencia de una base de datos sobre el proyecto y el negocio. Con el cálculo del valor, los tomadores de decisiones en particular, y las partes interesadas en general, tienen una perspectiva más precisa sobre el proyecto debido a la variedad de resultados consiguiente a la herramienta difusa seleccionada para las estimaciones.

Esta propuesta, a pesar de sus bondades, presenta limitaciones. En primer lugar, podría resultar complicado identificar, a priori, todas las actividades y actores de la red debido al surgimiento de nuevos proveedores y competidores y a la velocidad de los cambios tecnológicos, regulatorios y de políticas. La segunda limitación está relacionada con la dificultad para recopilar la información requerida, lo que puede demandar mucho tiempo y esfuerzo. La tercera consiste en la complejidad de la herramienta difusa, debido a la inexistencia de un programa informático que facilite los cálculos. En cuarto lugar, el sesgo en la investigación que implica el uso de algunas informaciones indirectas. Finalmente, el solo analizar la sostenibilidad de los proyectos de biotecnología de la salud desde la perspectiva económica, obviando las dimensiones social y medioambiental.

Los próximos pasos en esta tesis podrían dirigirse a facilitar la aplicación de la herramienta difusa, por ejemplo, desarrollando un *software* que realice todos los cálculos y que considere los fundamentos de la teoría de conjuntos y subconjuntos difusos. Al mismo tiempo, es posible la introducción de otras herramientas y métodos difusos como parte de los cálculos del modelo, como la teoría de los efectos olvidados, que puede revelar conexiones que no se ven a simple vista. En tercer lugar, la oportunidad de ampliar la aplicación del modelo a otros sectores y ajustarlo a las particularidades del negocio demostrará la utilidad de la propuesta. En cuarto lugar, la pertinencia de incluir los pilares social y medioambiental como variables explicativas a la hora de determinar el precio del candidato a medicamento hará de este paso uno más abarcador y, por ende, con mejores resultados en cuanto a valoración. Por último y de cara al futuro, sería interesante estudiar cómo la Industria 5.0 sería capaz de modificar el negocio de la biotecnología sanitaria.

REFERENCIAS

Acharjee, D. C., Alam, G. M. M., Gosh, K., Haque, A. B. M. M., & Hossain, M. I. (2023). Fish value chain and the determinants of value addition decision: Empirical evidence from Bangladesh. *Journal of the World Aquaculture Society*, 1-14. https://doi.org/10.1111/jwas.12941

Agarwal, H., Bajpai, S., Mishra, A., Kohli, I., Varma, A., Fouillaud, M., Dufossé, L., & Joshi, N. C. (2023). Bacterial Pigments and Their Multifaceted Roles in Contemporary Biotechnology and Pharmacological Applications. *Microorganisms*, *11*(3), Article 3. https://doi.org/10.3390/microorganisms11030614

Akhondzadeh, S. (2016). The Economic Aspects of Medical Biotechnology. *Avicenna Journal of Medical Biotechnology*, *8*(1), 1.

Akyüz, Y., Salali, H. E., Atakan, P., Günden, C., Yercan, M., Lamprinakis, L., Kårstad, S., Solovieva, I., Kasperczyk, N., Mattas, K., Lazaridou, D., Yener, G., Alayidi, A., Kunchulia, I., Basilidze, L., & Knez, M. (2023). Case Study Analysis on Agri-Food Value Chain: A Guideline-Based Approach. *Sustainability*, *15*(7), Article 7. https://doi.org/10.3390/su15076209

Alarcon, P., Fèvre, E. M., Murungi, M. K., Muinde, P., Akoko, J., Dominguez-Salas, P., Kiambi, S., Ahmed, S., Häsler, B., & Rushton, J. (2017). Mapping of beef, sheep and goat food systems in Nairobi—A framework for policy making and the identification of structural vulnerabilities and deficiencies. *Agricultural Systems*, *152*, 1-17. https://doi.org/10.1016/j.agsy.2016.12.005

Alzheimer's Association. (2023). *Treatments*. Alzheimer's Disease and Dementia. https://alz.org/alzheimer-demencia/tratamientos

Amador, J., & Di Mauro, F. (Eds.). (2015). *The Age of Global Value Chains: Maps and Policy Issues*. Centre for Economic Policy Research.

Apell, P., & Eriksson, H. (2023). Artificial intelligence (AI) healthcare technology innovations: The current state and challenges from a life science industry perspective. *Technology Analysis & Strategic Management*, *35*(2), 179-193. https://doi.org/10.1080/09537325.2021.1971188

Aranda, S., Lopez Torres, V., & Guerra, G. (2016). Propuesta de Modelo de Negocio Base Para las Empresas de Biotecnología en México. *Revista Global de Negocios*, *4*, 29-51.

Atkinson, R. D. (2014). *Understanding the U.S. National Innovation System* (ID 3079822; p. 27). Information Technology and Innovation Foundation. https://doi.org/10.2139/ssrn.3079822

Aznar, J., & Guijarro, F. (2012). *Nuevos Métodos de Valoración. Modelos Multicriterio* (2.ª ed.). Editorial Universitat Politècnica de València. http://hdl.handle.net/10251/19181

Babbie, E. R. (2007). *The Practice of Social Research* (11th ed.). Thomson/Wadsworth.

Balzat, M., & Hanusch, H. (2004). Recent trends in the research on national innovation systems. *Journal of Evolutionary Economics*, *14*(2), 197-210. https://doi.org/10.1007/s00191-004-0187-y

Bartels, F. L., Voss, H., Lederer, S., & Bachtrog, C. (2012). Determinants of National Innovation Systems: Policy implications for developing countries. *Innovation*, *14*(1), 2-18. https://doi.org/10.5172/impp.2012.14.1.2

Becker, J., & Wittmann, C. (2019). A field of dreams: Lignin valorization into chemicals, materials, fuels, and health-care products. *Microbial Engineering Biotechnologies*, *37*(6), 107360. https://doi.org/10.1016/j.biotechadv.2019.02.016

Benington, J., & Moore, M. (Eds.). (2011). *Public Value: Theory and Practice*. Bloomsbury Publishing.

BioCubaFarma. (2019). *A changing pharma industry and biotech´s business model*. *V*, 39.

Black, F., & Scholes, M. (1973). The Pricing of Options and Corporate Liabilities. *Journal of Political Economy*, *81*(3), 637-654. https://doi.org/10.1086/260062

Bogdan, B., & Villiger, R. (2010). *Valuation in Life Sciences: A Practical Guide* (Third edition). Springer. https://doi.org/10.1007/978-3-642-10820-4

Brealey, R. A., Allen, F., & Myers, S. C. (2011). *Principles of corporate finance*. McGraw-Hill/Irwin.

BrightFocus Foundation. (2021). *Alzheimer's Disease: Facts and Figures*. https://www.brightfocus.org/espanol/alzheimer/la-enfermedad-de-alzheimer-y-la-demencia/enfermedad-de-alzheimer-datos-y-cifras

Burns, L. R. (2022). *The Healthcare Value Chain: Demystifying the Role of GPOs and PBMs*. Springer International Publishing. https://doi.org/10.1007/978-3-031-10739-9

Büyüközkan, G., & Çifçi, G. (2012). A novel hybrid MCDM approach based on fuzzy DEMATEL, fuzzy ANP and fuzzy TOPSIS to evaluate green suppliers. *Expert Systems with Applications*, *39*(3), 3000-3011. https://doi.org/10.1016/j.eswa.2011.08.162

Byrne, P. (1996). Fuzzy analysis: A vague way of dealing with uncertainty in real estate analysis. *Journal of Property Valuation and Investment*, *13*(3), 22-41.

Canós, L., Casasús, T., Liern, V., & Pérez, J. C. (2014). Soft Computing Methods for Personnel Selection Based on the Valuation of Competences. *International Journal of Intelligent Systems*, *29*(12), 1079-1099. https://doi.org/10.1002/int.21684

Canós, L., & Liern, V. (2008). Soft computing-based aggregation methods for human resource management. *European Journal of Operational Research*, *189*(3), 669-681. https://doi.org/10.1016/j.ejor.2006.01.054

Carden, C. W., Chamberlain, T., & Hill, J. W. (2010). The brave new world of valuing life sciences and healthcare enterprises. *Business Horizons*, *53*(2), 183-197. https://doi.org/10.1016/j.bushor.2009.11.004

Carrizo, D., & Moller, C. (2018). Estructuras metodológicas de revisiones sistemáticas de literatura en Ingeniería de Software: Un estudio de mapeo sistemático. *Ingeniare. Revista chilena de ingeniería*, *26*, 45-54. https://doi.org/10.4067/S0718-33052018000500045

Castro, A. R., Portinha, C., & Logarinho, E. (2023). The booming business of hair loss. *Trends in Biotechnology*, *41*(6), 731-735. https://doi.org/10.1016/j.tibtech.2022.12.020

Castro, E., & Fernández, I. (2001). *Innovación y Sistemas de Innovación*. https://www.coursehero.com/file/56306932/Sistemas-de-Innovacionpdf/

CDER. (2022, agosto 8). *Development & Approval Process | Drugs*. FDA; FDA. https://www.fda.gov/drugs/development-approval-process-drugs

CDER. (2023). FY 2022 GDUFA Science and Research Report. *FDA*, 128.

CEPDE. (2014). *Proyecciones de la Población Cubana 2015–2050* (5; p. 550). Centro de Estudios de Población y Desarrollo. http://www.onei.gob.cu/sites/default/files/proyecciones_de_poblacion_2015_2050.pdf

Chandra, A., & Mazumdar, S. (2024). Biotech asset valuation methods: A practitioner's guide. *Journal of Investment Management*, *22*(2), 36-57.

Charnes, A., & Cooper, W. W. (1962). *Management models and industrial applications of linear programming: Vol. I*. John Wiley & Sons. https://doi.org/10.1002/nav.3800090109

Chen, L., Dong, T., Peng, J., & Ralescu, D. (2023). Uncertainty Analysis and Optimization Modeling with Application to Supply Chain Management: A Systematic Review. *Mathematics*, *11*(11), Article 11. https://doi.org/10.3390/math11112530

Cheng, L., Rao, C., & Chen, L. (2017). Multidimensional knapsack problem based on uncertain measure. *Scientia Iranica*, *24*(5), 2527-2539.

Chesbrough, H. (2006). Open Innovation: A New Paradigm for Understanding Industrial. En *Open innovation: Researching a new paradigm* (Chesbrough HW, Vanhaverbeke W, West J). Oxford University Press.

Choudhri, A. F., Siddiqui, A., Khan, N. R., & Cohen, H. L. (2015). Understanding Bibliometric Parameters and Analysis. *RadioGraphics*, *35*(3), 736-746. https://doi.org/10.1148/rg.2015140036

Chowdhury, T. U., & Saima, F. (2023). Relative valuation of stocks: Evidence from the listed cement manufacturing companies of Bangladesh. *AU eJournal of Interdisciplinary Research*, *8*(1), Article 1.

Chrysafis, K. A., & Papadopoulos, B. K. (2021). Decision Making for Project Appraisal in Uncertain Environments: A Fuzzy-Possibilistic Approach of the Expanded NPV Method. *Symmetry*, *13*(1), Article 1. https://doi.org/10.3390/sym13010027

Codina, L. (2019). *Taller de bases de datos académicas Scopus, WoS y Mendeley*. 91.

Consejo de Ministros. (2020). De las Empresas de Alta Tecnología. *Gaceta Oficial*, *156*(O16), 433-437.

Cornelissen, M., Małyska, A., Nanda, A. K., Lankhorst, R. K., Parry, M. A. J., Saltenis, V. R., Pribil, M., Nacry, P., Inzé, D., & Baekelandt, A. (2021). Biotechnology for Tomorrow's World: Scenarios to Guide Directions for Future Innovation. *Trends in Biotechnology*, *39*(5), 438-444. https://doi.org/10.1016/j.tibtech.2020.09.006

Craighead, C. W., Ketchen Jr., D. J., & Darby, J. L. (2020). Pandemics and Supply Chain Management Research: Toward a Theoretical Toolbox*. *Decision Sciences*, *51*(4), 838-866. https://doi.org/10.1111/deci.12468

Cubadebate. (2014, abril 17). *Cuba en números: Lo que el Censo nos dejó*. Cubadebate. http://www.cubadebate.cu/noticias/2014/04/16/cuba-en-numeros-lo-que-el-censo-nos-dejo/

Cubadebate. (2023, febrero 25). *Ensayo clínico con NeuralCIM® (NeuroEPO) para alzhéimer leve o moderado comienza en Cuba el próximo lunes (+ Video)*. Cubadebate. http://www.cubadebate.cu/noticias/2023/02/25/ensayo-clinico-con-neuralcim-neuroepo-para-alzheimer-leve-o-moderado-comienza-en-cuba-el-proximo-lunes/

Damodaran, A. (2012). *Investment valuation: Tools and techniques for determining the value of any asset* (Vol. 666). John Wiley & Sons. https://scholar.google.com/scholar_lookup?title=Investment%20valuation%3A%20Tools%20and%20techniques%20for%20determining%20the%20value%20of%20any%20asset&publication_year=2002&author=A.%20Damodaran

Danishev, D. (2024). Approaches to Assessing the Sustainability of Business Development. *International Journal on Economics, Finance and Sustainable Development*, *6*(1), Article 1.

de Andrés-Sánchez, J. (2023). A systematic review of the interactions of fuzzy set theory and option pricing. *Expert Systems with Applications*, *223*, 119868. https://doi.org/10.1016/j.eswa.2023.119868

De la O, R., & Myers, S. (2021). Subjective Cash Flow and Discount Rate Expectations. *The Journal of Finance*, *73*(3), 1339-1387. https://doi.org/10.1111/jofi.13016

De la Vega, I., Requena, J., & Fernández-Gómez, R. (2015). The colors of biotechnology in Venezuela: A bibliometric analysis. *Technology in Society*, *42*, 123-134. https://doi.org/10.1016/j.techsoc.2015.03.007

Dedania, H. V., Shah, V. R., & Sanghvi, R. C. (2015). Portfolio Management: Stock Ranking by Multiple Attribute Decision Making Methods. *Technology and Investment*, *6*(4), Article 4. https://doi.org/10.4236/ti.2015.64016

Deore, A. B., Dhumane, J. R., Wagh, R., & Sonawane, R. (2019). The Stages of Drug Discovery and Development Process. *Asian Journal of Pharmaceutical Research and Development*, *7*(6), 62-67. https://doi.org/10.22270/ajprd.v7i6.616

Déry, J., Ruiz, A., Routhier, F., Bélanger, V., Côté, A., Ait-Kadi, D., Gagnon, M.-P., Deslauriers, S., Lopes Pecora, A. T., Redondo, E., Allaire, A.-S., & Lamontagne, M.-E. (2020). A systematic review of patient prioritization tools in non-emergency healthcare services. *Systematic Reviews*, *9*(1), 227. https://doi.org/10.1186/s13643-020-01482-8

Dhiaf, M. M., Atayah, O. F., Nasrallah, N., & Frederico, G. F. (2021). Thirteen years of Operations Management Research (OMR) journal: A bibliometric analysis and future research directions. *Operations Management Research*, *14*, 235-255. https://doi.org/10.1007/s12063-021-00199-8

DiMasi, J. A. (2014). Pharmaceutical R&D performance by firm size: Approval success rates and economic returns. *American Journal of Therapeutics*, *21*(1), 26-34. https://doi.org/10.1097/MJT.0b013e318269198f

Excedr. (2023, enero 5). *Biotech Funding for Startups: What are Your Options?* Excedr. https://www.excedr.com/resources/biotech-funding-for-startups/

Fabrini, K. L. (2011). *Real options theory: An approach to investment analysis in the expansion of the power sector*. Universidade Federal de Minas Gerais.

Fagerberg, J., & Srholec, M. (2008). National innovation systems, capabilities and economic development. *Research Policy*, *37*(9), 1417-1435. https://doi.org/10.1016/j.respol.2008.06.003

Fariñas, L. (2022, septiembre 13). *Ataxia hereditaria: La enfermedad en que Cuba tiene la mayor prevalencia global y es campo de incesante investigación*. Cubadebate. http://www.cubadebate.cu/especiales/2022/09/13/ataxia-hereditaria-la-enfermedad-en-que-cuba-tiene-la-mayor-prevalencia-global-y-es-campo-de-incesante-investigacion-video/

Fernández, P. (2007). Valuing companies by cash flow discounting: Ten methods and nine theories. *Managerial Finance*, *33*(11), 853-876. https://doi.org/10.1108/03074350710823827

Freeborn, L., Andringa, S., Lunansky, G., & Rispens, J. (2023). Network analysis for modeling complex systems in SLA research. *Studies in Second Language Acquisition*, *45*(2), 526-557. https://doi.org/10.1017/S0272263122000407

French, N., & Gabrielli, L. (2005). Discounted cash flow: Accounting for uncertainty. *Journal of Property Investment & Finance*, *23*(1), 75-89. https://doi.org/10.1108/14635780510575102

Gantait, S., Mahanta, M., Bera, S., & Verma, S. K. (2021). Advances in biotechnology of Emblica officinalis Gaertn. syn. Phyllanthus emblica L.: A nutraceuticals-rich fruit tree with multifaceted ethnomedicinal uses. *3 Biotech*, *11*(2), 62. https://doi.org/10.1007/s13205-020-02615-5

García, F., Domínguez, A. L., & Galván, A. (2018). *Sistema de innovación y cadena de valor de la soya en el noroeste de México*. Editorial Fomento.

Gereffi, G. (1994). *The Organization of Buyer-Driven Global Commodity Chains: How U. S. Retailers Shape Overseas Production Networks* (Korzeniewicz & Gereffi, Eds.). Praeger.

Gereffi, G., Humphrey, J., & Sturgeon, T. (2005). The Governance of Global Value Chains. *Review of International Political Economy*, *12*, 78-104. https://doi.org/10.1080/09692290500049805

Ghamlouch, H., Fouladirad, M., & Grall, A. (2019). The use of real option in condition-based maintenance scheduling for wind turbines with production and deterioration uncertainties. *Reliability Engineering & System Safety*, *188*, 614-623. https://doi.org/10.1016/j.ress.2017.10.001

Gil-Lafuente, A. M., Boria, J., Torres, A., Merigó, J. M., & Kacprzyk, J. (Eds.). (2022). *Computational and Decision Methods in Economics and Business: Proceedings of the International Workshop "Innovation, Complexity and Uncertainty in Economics and Business"* (Vol. 388). Springer International Publishing. https://doi.org/10.1007/978-3-030-93787-4

Gilson Dranka, G., Cunha, J., Donizetti de Lima, J., & Ferreira, P. (2020). Economic evaluation methodologies for renewable energy projects. *AIMS Energy*, *8*(2), 339-364. https://doi.org/DOI: 10.3934/energy.2020.2.339

Gómez-Cedeño, M., Castán, J. M. [a], & Guitart-Tarrés, L. (2014). La importancia de los recursos humanos en la cadena de suministro. *Dirección y Organización*, *54*, 13-25.

Hassan, M. ghozali, Akanmu, D., Mohamad, A., Melan, M., Prapinit, P., Netsangsee, R., & Boonyarit, P. (2022). Development of Framework for Achieving Sustainability through Benchmarking. *CENTRAL ASIA AND THE CAUCASUS English Edition*, *22*(5), 524-540. https://doi.org/10.37178/ca-c.21.5.046

Hazır, Ö., & Ulusoy, G. (2020). A classification and review of approaches and methods for modeling uncertainty in projects. *International Journal of Production Economics*, *223*, 107522. https://doi.org/10.1016/j.ijpe.2019.107522

Head, M. G., Fitchett, J. R., Cooke, M. K., Wurie, F. B., Hayward, A. C., & Atun, R. (2013). UK investments in global infectious disease research 1997–2010: A case study. *The Lancet Infectious Diseases*, *13*(1), 55-64. https://doi.org/10.1016/S1473-3099(12)70261-X

Hendrawan, R., Susilowati, N., & Kristanti, F. (2020). Share Valuation of Indonesian Regional Development Bank using Free Cash Flow to Equity and Relative Valuation Methods. *Proceedings of the 2nd International Conference on Inclusive Business in the Changing World (ICIB 2019)*, 94-105. https://doi.org/10.5220/0008427900940105

Herrera-González, R., & Quesada, A. (2013). Determinantes de la cadena de valor y la gestión de la innovación en el sector metalmecánico en Costa Rica. *Revista Dirección y Organización*, *51*, 18-32.

Hirsch, J. (2005). An index to quantify an individual's scientific research output. *Proc Natl Acad Sci U S A*, *102*(46), 16569-16572. https://doi.org/10.1073/pnas.0507655102

Hitchner, J. R. (2017). *Financial Valuation,+ Website: Applications and Models*. John Wiley & Sons. https://books.google.com/books?hl=es&lr=&id=daRcDgAAQBAJ&oi=fnd&pg=PR21&ots=8gLeWg868D&sig=-6trzjAsY3UP95UKj6eLIyAhdPs

Holgado de Frutos, E., Trapero, J. R., & Ramos, F. (2020). A literature review on operational decisions applied to collaborative supply chains. *PLoS ONE*, *15*(3), e0230152. https://doi.org/10.1371/journal.pone.0230152

Hossain, M., Akteruzzaman, M., Parvin, Mst. T., Bhuiya, M., & Hossain, S. (2013). Marketing Channel of Fish and Value Addition by Different Actors in Haor Area of Netrakona District. *Bangladesh Journal of Crop Sceince*, *24*, 131-140.

Hu, C., Zhang, X., Reardon, T., & Hernandez, R. (2019). Value-chain clusters and aquaculture innovation in Bangladesh. *Food Policy*, *83*(C), 310-326. https://doi.org/10.1016/j.foodpol.2017.07.009

Huang, C.-Y., Hsieh, H.-L., & Chen, H. (2020). Evaluating the Investment Projects of Spinal Medical Device Firms Using the Real Option and DANP-mV Based MCDM Methods. *International Journal of Environmental Research and Public Health*, *17*(9), Article 9. https://doi.org/10.3390/ijerph17093335

Hussain, S., Arif, H., Noorullah, M., & Pantelous, A. A. (2023). Pricing American Options under Azzalini Ito-McKean Skew Brownian Motions. *Applied Mathematics and Computation*, *451*, 128040. https://doi.org/10.1016/j.amc.2023.128040

Huttner, S. (1999). Knowledge and the Biotechnology Economy: A Case of Mistaken Identity. *Measuring Knowledge in Learning Economies and Societies*, 11. https://www.oecd.org/education/innovation-education/1855200.pdf

Ideascale. (2017). *5 Industries with the Most Innovative Companies*. InnovationManagement. https://innovationmanagement.se/2017/03/30/5-industries-with-the-most-innovative-companies/

Ifiok, E. (2024). *Microbial Biotechnology: Application of Bacteria in Various Industrial Processes and Environment Remediation*. https://doi.org/10.5281/zenodo.10511013

ILO. (2015). *Value chain development for decent work: How to create employment and improve working conditions in targeted sectors* (2nd ed.). International Labour Office. www.ilo.org/publns

Ishizaka, A., & Labib, A. (2009). Analytic hierarchy process and expert choice: Benefits and limitations. *OR Insight*, *22*(4), 201-220. https://doi.org/10.1057/ori.2009.10

Kahraman, C., Oztaysi, B., Onar, S. Ç., & Cebi, S. (2023). Fuzzy Investment Assessment Techniques: A State-of-the-Art Literature Review. En A. Abraham, A. Bajaj, N. Gandhi, A. M. Madureira, & C. Kahraman (Eds.), *Innovations in Bio-Inspired Computing and Applications* (pp. 649-657). Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-27499-2_60

Kaiser, R., & Prange, H. (2004). The reconfiguration of National Innovation Systems—The example of German biotechnology. *Research Policy*, *33*(3), 395-408. https://doi.org/10.1016/j.respol.2003.09.001

Kalpana Sastry, R., Rashmi, H. B., & Rao, N. H. (2011). Nanotechnology for enhancing food security in India. *Food Policy*, *36*(3), 391-400. https://doi.org/10.1016/j.foodpol.2010.10.012

Kamel, A., Elwageeh, M., Bonduà, S., & Elkarmoty, M. (2023). Evaluation of mining projects subjected to economic uncertainties using the Monte Carlo simulation and the binomial tree method: Case study in a phosphate mine in Egypt. *Resources Policy*, *80*, 103266. https://doi.org/10.1016/j.resourpol.2022.103266

Kaplinsky, R., & Morris, M. (2000). *A Handbook for Value Chain Research,* (Vol. 113). Brighton: University of Sussex, Institute of Development Studies.

Kaufmann, A. A. J. G. A. (1990). *Las Matematicas Del Azar y De La Incertidumbre*.

Kayal, A. (2008). National innovation systems a proposed framework for developing countries. *International Journal of Entrepreneurship and Innovation Management*, *8*(1), 74-86. https://doi.org/10.1504/IJEIM.2008.018615

Khan, S. A. R., Godil, D. I., Jabbour, C. J. C., Shujaat, S., Razzaq, A., & Yu, Z. (2021). Green data analytics, blockchain technology for sustainable development, and sustainable supply chain practices: Evidence from small and medium enterprises. *Annals of Operations Research*. https://doi.org/10.1007/s10479-021-04275-x

Kim, T. H., Shin, S., & Shin, B. S. (2018). Model-based drug development: Application of modeling and simulation in drug development. *Journal of Pharmaceutical Investigation*, *48*(4), 431-441. https://doi.org/10.1007/s40005-017-0371-3

Koller, T., Goedhart, M., & Wessels, D. (2010). *Valuation. Measuring and Managing the Value of Companies* (Fifth). John Wiley & Sons.

Kurpayanidi, K. (2021). National innovation system as a key factor in the sustainable development of the economy of Uzbekistan. *E3S Web of Conferences*, *258*(05026), 1-13. https://doi.org/10.1051/e3sconf/202125805026

Lai, J. H. K., Hou, H. (Cynthia), Edwards, D. J., & Yuen, P. L. (2021). An analytic network process model for hospital facilities management performance evaluation. *Facilities*, *40*(5/6), 333-352. https://doi.org/10.1108/F-09-2021-0082

León, T., Liern, V., & Vercher, E. (2002). Viability of infeasible portfolio selection problems: A fuzzy approach. *European Journal of Operational Research*, *139*(1), 178-189. https://doi.org/10.1016/S0377-2217(01)00175-8

Link, A. N., & Siegel, D. S. (2007). *Innovation, Entrepreneurship, and Technological Change*. OUP Oxford. Google-Books-ID: iw9REAAAQBAJ

Little, A. D. (1991). *Logistics in Service Industries*. Council of Logistics Management.

Liu, B. (2010). Uncertainty Theory. En B. Liu (Ed.), *Uncertainty Theory: A Branch of Mathematics for Modeling Human Uncertainty* (pp. 1-79). Springer. https://doi.org/10.1007/978-3-642-13959-8_1

Llibre, J. de J. (2013). Demencias y enfermedad de Alzheimer: Una prioridad nacional. *Revista Cubana de Salud Pública*, *39*(4), 804-806.

Lokko, Y., Heijde, M., Schebesta, K., Scholtès, P., Van Montagu, M., & Giacca, M. (2018). Biotechnology and the bioeconomy—Towards inclusive and sustainable industrial development. *Bioeconomy*, *40*, 5-10. https://doi.org/10.1016/j.nbt.2017.06.005

Lundvall, B.-Å. (1992). *National Systems of Innovation: Towards a Theory of Innovation and Interactive Learning*. Pinter Publishers.

Magableh, G. M., & Mistarihi, M. Z. (2022). Applications of MCDM approach (ANP-TOPSIS) to evaluate supply chain solutions in the context of COVID-19. *Heliyon*, *8*(3), e09062. https://doi.org/10.1016/j.heliyon.2022.e09062

Mahata, P., & Mahata, G. C. (2020). Production and payment policies for an imperfect manufacturing system with discount cash flows analysis in fuzzy random environments. *Mathematical and Computer Modelling of Dynamical Systems*, *26*(4), 374-408. https://doi.org/10.1080/13873954.2020.1771380

Mak, K.-K., & Pichika, M. R. (2019). Artificial intelligence in drug development: Present status and future prospects. *Drug Discovery Today*, *24*(3), 773-780. https://doi.org/10.1016/j.drudis.2018.11.014

Mallo, P. E., Artola, M. A., García, M. V., Martínez, D., Galante, M. J., Pascual, M. E., & Morettini, M. (2001). La distribución triangular y los números borrosos triangulares. *Nülan. Deposited Documents*, Article 897. https://ideas.repec.org//p/nmp/nuland/897.html

Marcus, H. J., Ramirez, P. T., Khan, D. Z., Layard Horsfall, H., Hanrahan, J. G., Williams, S. C., Beard, D. J., Bhat, R., Catchpole, K., Cook, A., Hutchison, K., Martin, J., Melvin, T., Stoyanov, D., Rovers, M., Raison, N., Dasgupta, P., Noonan, D., Stocken, D., … McCulloch, P. (2024). The IDEAL framework for surgical robotics: Development, comparative evaluation and long-term monitoring. *Nature Medicine*, *30*(1), 61-75. https://doi.org/10.1038/s41591-023-02732-7

Martin, D. K., Vicente, O., Beccari, T., Kellermayer, M., Koller, M., Lal, R., Marks, R. S., Marova, I., Mechler, A., Tapaloaga, D., Žnidaršič-Plazl, P., & Dundar, M. (2021). A brief overview of global biotechnology. *Biotechnology & Biotechnological Equipment*, *35*(sup1), S5-S14. https://doi.org/10.1080/13102818.2021.1878933

Martínez-Ceseña, E. A., & Mutale, J. (2011). Application of an advanced real options approach for renewable energy generation projects planning. *Renewable Sustainable Energy*, *15*, 2087-2094.

Mazzucato, M. (2013). Financing innovation: Creative destruction vs. destructive creation. *Industrial and Corporate Change*, *22*(4), 851-867. https://doi.org/10.1093/icc/dtt025

Mazzucato, M., & Ryan-Collins, J. (2022). Putting value creation back into "public value": From market-fixing to market-shaping. *Journal of Economic Policy Reform*, *25*(4), 345-360. https://doi.org/10.1080/17487870.2022.2053537

McCarthy, B., Liu, H.-B., & Chen, T. (2016). Innovations in the agro-food system. *British Food Journal*, *118*(6), 1334-1349. https://doi.org/10.1108/BFJ-10-2015-0375

Merigó, J. M., Gil-Lafuente, A. M., & Yager, R. R. (2015). An overview of fuzzy research with bibliometric indicators. *Applied Soft Computing*, *27*, 420-433.

Meseguer-Sánchez, V., Gálvez-Sánchez, F. J., López-Martínez, G., & Molina-Moreno, V. (2021). Corporate social responsibility and sustainability. A bibliometric analysis of their interrelations. *Sustainability (Switzerland)*, *13*(4), 1-18. https://doi.org/10.3390/ su13041636

MINSAP. (2022, septiembre 23). *Alzheimer: Preguntas y respuestas*. Sitio oficial de gobierno del Ministerio de Salud Pública en Cuba. https://salud.msp.gob.cu/alzheimer-preguntas-y-respuestas/

Mitincu, C.-G., Niţă, M.-R., Hossu, C.-A., Iojă, I.-C., & Nita, A. (2023). Stakeholders' involvement in the planning of nature-based solutions: A network analysis approach. *Environmental Science & Policy*, *141*, 69-79. https://doi.org/10.1016/j.envsci.2022.12.022

Mohanty, R. P., Agarwal, R., Choudhury, A. K., & Tiwari, M. K. (2005). A fuzzy ANP-based approach to R&D project selection: A case study. *International Journal of Production Research*, *43*(24), 5199-5216. https://doi.org/10.1080/00207540500219031

Molina, E. (2023). El financiamiento a la biotecnología en el mundo. Alternativas para Cuba. *Economía y Desarrollo*, *167*(1), 9.

Molina, Y. (2021, septiembre 21). Envejecimiento y Alzheimer, retos de la sociedad cubana • Trabajadores. *Trabajadores*. https://www.trabajadores.cu/20210921/envejecimiento-y-alzheimer-retos-de-la-sociedad-cubana/

Mollenhauer, K., & Hormazábal, J. (2012). Sistema de innovation basado en La red de valor. *Revista Chilena de Diseño*, *2*, 15-35.

Movahedipour, M., Yang, M., Zeng, J., Wu, X., & Salam, S. (2016). Optimization in supply chain management, the current state and future directions: A systematic review and bibliometric analysis. *Journal of Industrial Engineering and Management*, *9*(4), 933-963. http://dx.doi.org/10.3926/jiem.2035

Nassif, A. (2007). National Innovation System And Macroeconomic Policies: Brazil And India In Comparative Perspective. En *UNCTAD Discussion Papers* (184; UNCTAD Discussion Papers). United Nations Conference on Trade and Development. https://ideas.repec.org/p/unc/dispap/184.html

Nazari-Shirkouhi, S., Tavakoli, M., Govindan, K., & Mousakhani, S. (2023). A hybrid approach using Z-number DEA model and Artificial Neural Network for Resilient supplier Selection. *Expert Systems with Applications*, *222*, 119746. https://doi.org/10.1016/j.eswa.2023.119746

Niv, Y., & Tal, Y. (2023). Risk Management and Patient Safety Processes in a Healthcare Organization. En Y. Niv & Y. Tal (Eds.), *Patient Safety and Risk Management in Medicine: From Theory to Practice* (pp. 129-174). Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-49865-7_11

Noda, S. (2022, octubre 29). *Prevenir el Ictus, llamado necesario ante un problema de salud mundial*. Ministerio de Salud Pública en Cuba. https://salud.msp.gob.cu/prevenir-el-ictus-llamado-necesario-ante-un-problema-de-salud-mundial/

Ochuba, N. A., Okafor, E. S., Akinrinola, O., Usman, F. O., & Amoo, O. O. (2024). STRATEGIC PARTNERSHIPS IN THE SATELLITE AND TELECOMMUNICATIONS SECTORS: A CONCEPTUAL REVIEW OF DATA ANALYTICS-ENABLED IDENTIFICATION AND CAPITALIZATION OF SYNERGIES. *Engineering Science & Technology Journal*, *5*(3), Article 3. https://doi.org/10.51594/estj.v5i3.867

OECD. (2010). The changing consumer and market landscape. Consumer policy toolkit. En *Consumer Policy Toolkit* (p. 15). https://read.oecd-ilibrary.org/governance/consumer-policy-toolkit/the-economics-of-consumer-policy_9789264079663-4-en#page1

ONEI. (2023, abril 11). *Estudios y Datos de la Población. Cuba y sus Territorios.* Oficina Nacional de Estadística e Información. http://www.onei.gob.cu/node/13818

Oramas Santos, O., Anido, L. S., & Torres, M. O. (2022). *Investment Evaluation Proposal with Fuzzy Tools: Case Molecular Immunology Center*. https://doi.org/10.1007/978-3-030-93787-4_5

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2022). The value chain of the Cuban biotechnological industry in the core of the national innovation system. *I International Conference of Entrepreneurship, Education and Digital Transformation. Book of Proceedings*, *1*, 185.

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023a). The value chain approach in red biotechnology companies from a bibliometric perspective. *International Journal of Production Management and Engineering*, *11*(2), 187-196. https://doi.org/10.4995/ijpme.2023.19135

Oramas Santos, O., Canós-Darós, L., & Babiloni, E. (2023b). Valoración de un producto biotecnológico cubano a partir de su cadena de valor. *II Simposium Predoctoral de Organización de Empresas*, *II*, 108-113. http://hdl.handle.net/10251/196663

Ortega Cerda, J. J., Sánchez Herrera, D., Rodríguez Miranda, Ó. A., Ortega Legaspi, J. M., Ortega Cerda, J. J., Sánchez Herrera, D., Rodríguez Miranda, Ó. A., & Ortega Legaspi, J. M. (2018). Adherencia terapéutica: Un problema de atención médica. *Acta médica Grupo Ángeles*, *16*(3), 226-232.

Padilla, R. (Ed.). (2014). *Fortalecimiento de las Cadenas de Valor como Instrumento de la Política Industrial: Metodología y Experiencia de la CEPAL en Centroamérica*. Publicaciones de las Naciones Unidas. https://doi.org/10.18356/65e17760-es

Padilla, R., & Oddone, N. (2016). Manual para el fortalecimiento de cadenas de valor. *Repositorio CEPAL*, 114.

Parent-Johnson, W. S., & Duncan, A. W. (2024). Inclusive Dissemination: Inclusive Research Dissemination With Individuals With Intellectual and Developmental Disabilities. *Inclusion*, *12*(1), 75-82. https://doi.org/10.1352/2326-6988-12.1.75

PCC. (2019). *Lineamientos de la política económica y social del Partido y la Revolución.* Gaceta Oficial. https://www.tsp.gob.cu/documentos/lineamientos-de-la-politica-economica-y-social-del-partido-y-la-revolucion

Peces Prieto, M. C., & Trillo Holgado, M. A. (2019). The influence of relational capital and networking on the internationalization of the university spin-off. *Intangible Capital*, *15*(1), 22-37. https://doi.org/10.3926/ic.1186

Peñalver, A. (2018). *Business Plan: New Heart UK* [Tesis de Máster]. Cranfield University.

Philp, J. (2018). The bioeconomy, the challenge of the century for policy makers. *Bioeconomy*, *40*, 11-19. https://doi.org/10.1016/j.nbt.2017.04.004

Pietrobelli, C., & Rabellotti, R. (2011). Global value chains meet innovation systems: Are there learning opportunities for developing countries? *World Development*, *39*(7), 1261-1269.

Pisano, G. (2010). The Evolution of Science-Based Business: Innovating How We Innovate. *Industrial and Corporate Change*, *19*, 465-482. https://doi.org/10.2139/SSRN.1545806

Polentinos, E. (2015). *La disposición a pagar por un Año de Vida Ajustado por Calidad: Umbral de aceptabilidad mediante el método de la Valoración Contingente* [Tesis de Doctorado, Universidad Rey Juan Calos]. https://eciencia.urjc.es/handle/10115/13184

Porter, M. E. (1985). *Competitive advantage: Creating and sustaining superior performance*. The Free Press.

Porter, M. E. (1991). Towards a dynamic theory of strategy. *Strategic Management Journal*, *12*(S2), 95-117. https://doi.org/10.1002/smj.4250121008

Rajan, K. B., Weuve, J., Barnes, L. L., McAninch, E. A., Wilson, R. S., & Evans, D. A. (2021). Population Estimate of People with Clinical AD and Mild Cognitive Impairment in the United States (2020–2060). *Alzheimer's & Dementia : The Journal of the Alzheimer's Association*, *17*(12), 1966-1975. https://doi.org/10.1002/alz.12362

Rennane, S., Baker, L., & Mulcahy, A. (2021). Estimating the Cost of Industry Investment in Drug Research and Development: A Review of Methods and Results. *Inquiry: A Journal of Medical Care Organization, Provision and Financing*, *58*, 1-11. https://doi.org/10.1177/00469580211059731

Ricciotti, F. (2020). From value chain to value network: A systematic literature review. *Management Review Quarterly*, *70*(2), 191-212. https://doi.org/10.1007/s11301-019-00164-7

Rodríguez Batista, A., & Núñez Jover, J. R. (2021). El sistema de ciencia, tecnología e innovación y la actualización del modelo de desarrollo económico de Cuba. *Revista Universidad y Sociedad*, *13*, 7-19.

Saaty, T. L. (1996). *Decision Making with Dependence and Feedback: The Analytic Network Process* (Vol. 4922). RWS Publications.

Saaty, T. L. (2005). Making and validating complex decisions with the AHP/ANP. *Journal of Systems Science and Systems Engineering*, *14*, 1-36.

Saaty, T. L. (2010). *Principia Mathematica Decernendi: Mathematical Principles of Decision-Making*.

Saaty, T. L., & Vargas, L. G. (2013). The Analytic Network Process. En T. L. Saaty & L. G. Vargas (Eds.), *Decision Making with the Analytic Network Process: Economic, Political, Social and Technological Applications with Benefits, Opportunities, Costs and Risks* (pp. 1-40). Springer US. https://doi.org/10.1007/978-1-4614-7279-7_1

Saaty, T. L., Vargas, L. G., & Whitaker, R. (2009). Addressing with Brevity Criticisms of the Analytic Hierarchy Process. *International Journal of the Analytic Hierarchy Process*, *1*(2). https://doi.org/10.13033/ijahp.v1i2.53

Salter, B., Zhou, Y., Datta, S., & Salter, C. (2016). Bioinformatics and the Politics of Innovation in the Life Sciences: Science and the State in the United Kingdom, China, and India. *Science, Technology, & Human Values*, *41*(5), 793-826. https://doi.org/10.1177/0162243916631022

Samara, E., Georgiadis, P., & Bakouros, I. (2012). The impact of innovation policies on the performance of national innovation systems: A system dynamics analysis. *Technovation*, *32*(11), 624-638. https://doi.org/10.1016/j.technovation.2012.06.002

Santa Cruz, J. S. (2023). *The Application of Strategic Real Options for the Evaluation of a Mining Project* [University of Arizona]. https://repository.arizona.edu/handle/10150/668405

Santana, N. B., Rebelatto, D. A. do N., & Périco, A. E. (2015). Eficiência na conversão de recursos produtivos em desenvolvimento sustentável: O caso do Brasil entre os BRICS. *Produção Online*, *15*(2), 601-621.

Savchuk, V. (2023). *Real Options Technique as a Tool of Strategic Risk Management* (arXiv:2303.09176). arXiv. https://doi.org/10.48550/arXiv.2303.09176

Schumpeter, J. A. (1961). *The Theory of Economic Development: An Inquiry Into Profits, Capital, Credit, Interest, and the Business Cycle* (Harvard economic studies, Vol. 46). Oxford University Press.

Scott, T. J., O'Connor, A. C., Link, A. N., & Beaulieu, T. J. (2014). Economic analysis of opportunities to accelerate Alzheimer's disease research and development. *Annals of the New York Academy of Sciences*, *1313*(1), 17-34. https://doi.org/10.1111/nyas.12417

Secretary of State and Commerce. (2021). *Informe económico y comercial Cuba* (p. 44). Oficina Económica y Comercial de España. https://www.icex.es/icex/es/navegacion-principal/todos-nuestros-servicios/informacion-de-mercados/paises/navegacion-principal/el-pais/informacion-economica-y-comercial/estructura-de-la-oferta/index.html?idPais=CU

Senturk, S., Binici, Y., & Erginel, N. (2016). The theoretical structure of Fuzzy Analytic Network Process (FANP) with Interval Type-2 Fuzzy Sets. *IFAC-PapersOnLine*, *49*(12), 1318-1322. https://doi.org/10.1016/j.ifacol.2016.07.706

Seoni, S., Jahmunah, V., Salvi, M., Barua, P. D., Molinari, F., & Acharya, U. R. (2023). Application of uncertainty quantification to artificial intelligence in healthcare: A review of last decade (2013–2023). *Computers in Biology and Medicine*, *165*, 107441. https://doi.org/10.1016/j.compbiomed.2023.107441

Sergi, D., & Sari, I. U. (2021). Fuzzy Capital Budgeting Using Fermatean Fuzzy Sets. En C. Kahraman, S. Cevik Onar, B. Oztaysi, I. U. Sari, S. Cebi, & A. C. Tolga (Eds.), *Intelligent and Fuzzy Techniques: Smart and Innovative Solutions* (pp. 448-456). Springer International Publishing. https://doi.org/10.1007/978-3-030-51156-2_52

Sharma, V., Sehrawat, N., Sharma, A., Yadav, M., Verma, P., & Sharma, A. K. (2022). Multifaceted antiviral therapeutic potential of dietary flavonoids: Emerging trends and future perspectives. *Biotechnology and Applied Biochemistry*, *69*(5), 2028-2045. https://doi.org/10.1002/bab.2265

Shulin, G. (1999). *Implications of National Innovation Systems for Developing Countries: Managing Change and Complexity in Economic Development*. United Nations University, Institute for New Technologies. https://www.researchgate.net/publication/4777136_Implications_Of_National_Innovation_Systems_For_Developing_Countries_Managing_Change_And_Complexity_In_Economic_Development?enrichId=rgreq-32dbe9409ac5f60c8418c31c8967319f-XXX&enrichSource=Y292ZXJQYWdlOzQ3NzcxMzY7QVM6MTgyMDk3MTYzNTk1Nzc2QDE0MjA0MjY3NTUwMTc%3D&el=1_x_2&_esc=publicationCoverPdf

Stewart, E. C., Davis, J. S., Walters, T. S., Chen, Z., Miller, S. T., Duke, J. M., Alexander, L. R., Akohoue, S. A., Russell, R., Rowan, N., Campbell, L., Baxter, I., Tolbert, S., & Erves, J. C. (2023). Development of strategies for community engaged research dissemination by basic scientists: A case study. *Translational Research*, *252*, 91-98. https://doi.org/10.1016/j.trsl.2022.09.001

Su, Y.-S., & Wu, F.-S. (2015). Regional systems of biotechnology innovation—The case of Taiwan. *Technological Forecasting and Social Change*, *100*, 96-106. https://doi.org/10.1016/j.techfore.2015.10.002

Terzi, A., Singh, A., & Sherwood, M. (2022). Industrial Policy for the 21st Century: Lessons from the Past. *European Economy Discussion Papers*, *157*. http://data.europa.eu/doi/10.2765/xxxxx

Tian, N., Gan, J., & Lu, F. (2023). A real options model for evaluating a tree and mushroom vertical agroforestry system in Shandong, China. *Agroforestry Systems*, *97*(2), 163-174. https://doi.org/10.1007/s10457-022-00795-y

Tibell, L. A. E., & Rundgren, C.-J. (2010). Educational Challenges of Molecular Life Science: Characteristics and Implications for Education and Research. *CBE—Life Sciences Education*, *9*(1), 25-33. https://doi.org/10.1187/cbe.08-09-0055

Ting, N. (Ed.). (2006). *Dose Finding in Drug Development*. Springer. https://doi.org/10.1007/0-387-33706-7

Tom, S. E., Hubbard, R. A., Crane, P. K., Haneuse, S. J., Bowen, J., McCormick, W. C., McCurry, S., & Larson, E. B. (2015). Characterization of Dementia and Alzheimer's Disease in an Older Population: Updated Incidence and Life Expectancy With and Without Dementia. *American Journal of Public Health*, *105*(2), 408-413. https://doi.org/10.2105/AJPH.2014.301935

Trabajadores. (2023, febrero 25). Alzheimer en Cuba: Comienza ensayo clínico fase III con NeuralCIM® • Trabajadores. *Trabajadores*. https://www.trabajadores.cu/20230224/alzheimer-en-cuba-comienza-ensayo-clinico-fase-iii-con-neuralcim/

Uecke, O. (2012). *How to Commercialise Research in Biotechnology?* Springer Gabler. https://doi.org/10.1007/978-3-8349-4134-3

Valipour, A., Yahaya, N., Md Noor, N., Kildienė, S., Sarvari, H., & Mardani, A. (2015). A fuzzy analytic network process method for risk prioritization in freeway PPP projects: An Iranian case study. *Journal of Civil Engineering and Management*, *21*(7), 933-947. https://doi.org/10.3846/13923730.2015.1051104

Van Horenbeek, A., & Pintelon, L. (2014). Development of a maintenance performance measurement framework—Using the analytic network process (ANP) for maintenance performance indicator selection. *Omega*, *42*(1), 33-46. https://doi.org/10.1016/j.omega.2013.02.006

Van Looy, B., Grabowska, M., Vlaisavljevic, V., Lecocq, C., & Debackere, K. (2024). Growth of biotech clusters over several decades through pioneering, variety and entrepreneurial science. *Nature Biotechnology*, *42*(1), Article 1. https://doi.org/10.1038/s41587-023-02062-6

Viganò, M., & Vella, E. (2022). *Mergers and acquisitions in life science: What multiples for relative valuation?* [Master, Politecnico Milano]. https://www.politesi.polimi.it/handle/10589/198590?mode=complete

von Solms, S. (2011). VALIDITY OF THE AHP/ANP: COMPARING APPLES AND ORANGES. *International Journal of the Analytic Hierarchy Process*, *3*(1). https://doi.org/10.13033/ijahp.v3i1.60

Wang, J. J., Shen, J., & Pretorius, F. (2023). Valuing options to renew at future market value: The case of commercial property leases. *Financial Innovation*, *9*(1), 70. https://doi.org/10.1186/s40854-023-00479-1

Wang, M., Wu, Y., Chen, B., & Evans, M. (2020). Blockchain and Supply Chain Management: A New Paradigm for Supply Chain Integration and Collaboration. *Operations and Supply Chain Management: An International Journal*, *14*(1), 111-122. https://doi.org/10.31387/oscm0440290

Wang, R. (2024). Safeguarding Enterprise Prosperity: An In-depth Analysis of Financial Management Strategies. *Journal of the Knowledge Economy*. https://doi.org/10.1007/s13132-024-01752-z

Wang, S.-Y., & Lee, C.-F. (2021). A Fuzzy Real Option Valuation Approach To Capital Budgeting Under Uncertainty Environment. En C.-F. Lee & A. C. Lee (Eds.), *Encyclopedia of Finance* (pp. 1-24). Springer International Publishing. https://doi.org/10.1007/978-3-030-73443-5_112-1

Watkins, A., Papaioannou, T., Mugwagwa, J., & Kale, D. (2014). National innovation systems, developing countries, and the role of intermediaries: A critical review of the literature. *15th International Conference of the (ISS)*, 25.

Weinstein, M. C., Torrance, G., & McGuire, A. (2009). QALYs: The Basics. *Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research*, *12*(1), 5-9. https://doi.org/10.1111/j.1524-4733.2009.00515.x

WHO. (2022). *Towards a global guidance framework for the responsible use of life sciences: Summary report of consultations on the principles, gaps and challenges of biorisk management* (WHO/SCI/RFH/2022.01; p. 34). World Health Organization. https://apps.who.int/iris/bitstream/handle/10665/354600/WHO-SCI-RFH-2022.01-eng.pdf

Wiedmer, R., & Griffis, S. E. (2021). Structural characteristics of complex supply chain networks. *Journal of Business Logistics*, *42*(2), 264-290. https://doi.org/10.1111/jbl.12283

Womack, J. P., & Jones, D. T. (1996). *Lean Thinking: Banish Waste and Create Wealth in Your Corporation*. Simon & Schuster.

Xu, J., Li, L., & Ren, M. (2022). A Hybrid ANP Method for Evaluation of Government Data Sustainability. *Sustainability*, *14*(2), Article 2. https://doi.org/10.3390/su14020884

Yin, S., Zhang, N., Li, B., & Dong, H. (2021). Enhancing the effectiveness of multi-agent cooperation for green manufacturing: Dynamic co-evolution mechanism of a green technology innovation system based on the innovation value chain. *Environmental Impact Assessment Review*, *86*, 106475. https://doi.org/10.1016/j.eiar.2020.106475

Yontar, E. (2023). Critical success factor analysis of blockchain technology in agri-food supply chain management: A circular economy perspective. *Journal of Environmental Management*, *330*, 117173. https://doi.org/10.1016/j.jenvman.2022.117173

Yoon, K. (1987). A Reconciliation among Discrete Compromise Situations. *Journal of Operational Research Society*, *38*, 277-286.

Yu, Z., Liang, Z., & Xue, L. (2022). A data-driven global innovation system approach and the rise of China's artificial intelligence industry. *Regional Studies*, *56*(4), 619-629. https://doi.org/10.1080/00343404.2021.1954610

Zadeh, L. A. (1965). Fuzzy Sets. *Information and Control*, *8*, 338-353.

Zarbakhshnia, N., Govindan, K., Kannan, D., & Goh, M. (2023). Outsourcing logistics operations in circular economy towards to sustainable development goals. *Business Strategy and the Environment*, *32*(1), 134-162. https://doi.org/10.1002/bse.3122

Zhang, C., & Chen, Y. (2020). A review of research relevant to the emerging industry trends: Industry 4.0, iot, blockchain, and business analytics. *Journal of Industrial Integration and Management*, *5*(1), 165-180. https://doi.org/10.1142/S2424862219500192

Zhang, C., Zhong, H., & Hu, A. (2022). A Method for Financial System Analysis of Listed Companies Based on Random Forest and Time Series. *Mobile Information Systems*, *2022*, e6159459. https://doi.org/10.1155/2022/6159459

Zhirui, F. (2023). Research and Application of Company Valuation Methods. *BCP Business & Management*, *45*, 109-114.

ANEXOS

Appendix 1. Characteristics and information sources of the studied NISs.

Country	Indicators					Remarks
	Regulations	**Technology and Innovation Policies**	**Financial System**	**Business Activities**	**Research and Education System**	
Germany (Kaiser & Prange, 2004)	Biotechnology-related regulations rest with the states. They become organized across territorial levels and have developed typical multi-level characteristics.	BioRegio program stimulating the creation of biotech clusters, BioChange program stimulating highly risky R&D projects conducted by small and medium-sized biotech companies.	Bank-centered financial system. Private venture capital hardly available for biotech start-up companies. Public engagement has taken place both at the federal and the regional level.	More and more firms engage in drug development programs conducted in cooperation with traditional pharmaceutical companies and other biotech firms. Cooperation at the local and the international level has increased significantly.	Government financing the research and education systems and creating reforms to reforming the German university system.	Biotech focused on. Authors conclude that national institutional framework is still important even in federalized or decentralized countries, but also in a coordinated manner with other levels.
US (Atkinson, 2014)	The United States has embraced an approach to competition and competition policy based on maximizing consumer welfare. It appears that the U.S. regulatory burden on innovation has grown over the last decade, both in extent and orientation.	Allows and promotes to continuously use updated technologies. Policies to protect the intellectual property.	Fully compose by venture and risk capital including angel capitals. Firms have access to a wide array of financing sources, the vast majority provided by the private sector. Government financing for firms is quite limited.	To manage talent, time horizon, risk appetite, the adoption of information and communications technologies.	The U.S. system for supporting scientific research is based on two fundamental aspects: support for mission-oriented research largely to federal labs, and support for basic, curiosity-directed research through university funding. The NIS recognizes the relevance of the educational system since the elementary school.	Cultural factors such as trust, group orientation, and risk taking have impacts on innovation and growth. The NIS is supported by a Systems of Knowledge Flows, which consist of the innovation clusters, the industry collaboration system, the acquisition of foreign technology and the exportation of U.S. technology. The author remarks that the U.S. has reasonably good business and regulatory environments, but a weak innovation policy environment.

Greece (Samara et al., 2012)	Policies promoting R&D.	Classify as a moderate innovator. Has been essential the Government intervention to develop and promote innovations in the country.	Affects the innovation process, but it is external to it. Public engagement has taken place.	Market conditions and business activities affect the innovation process but are external to it.	Knowledge and human resources affect the innovation process but are external to it.	Not focused in a specific sector. Technology policies, regulations, market and financial conditions, as well as human resources are external actors impacting the innovation process, which is mainly focused on products and processes. Formulating innovation performance as the output of many independent variables, their model allows policymakers to reveal structures for generating change and also develop and test strategies for the government.
Taiwan (Kayal, 2008)	Essential to allow Taiwan's competitive advantage through alleviation of taxation, loan subsidy, technological assistance, government procurement, etc.	Based on the supply, demand, and environment sides.	Not included	The main activities are those related with the innovations on processes.	Promotes and diffuses process technologies and how to go through the reverse VC.	Consists on start developing process capabilities, after that the extension into product design capabilities, and finally new product creation activities.

Singapore (Kayal, 2008)	New regulations to promote the growth of new technology start-ups: stock exchange listing regulations, stock option rules and tax incentives for business angel investment	In favor of the multinational corporations. The government has accelerated the establishment and funding of university R&D to encourage multinational companies to start product R&D operations. Also encouraging venture capitalists and angel investors.	Policies to attract foreign investors.	Aimed at encouraging the innovations in products. Multinational companies induce substantial technological capability development among many local firms. Promoting the growth of new technology start-ups	Universities as the first step in R&D. The innovations should be developed and tested at the universities and then transferred to business activities.	Characterized as one emphasizing government facilitation of technological learning. Author concludes that for a developing country to gain economic strength it must start by understanding its competitive advantage, weaknesses, and strengths; in addition to the statement that a NIS in a developing country should be designed to first build up the local firms' capacity to absorb, adapt and apply new technologies from abroad.
Brazil (Nassif, 2007)	The innovation law. Regulations to create regulatory agencies for preventing anti-competitive practices in industries that are either strongly concentrated or natural monopolies.	Industrial and technological policies. Redirected to the improvement and expansion of the infrastructure system. Promote efficiency in exporting companies.	Financial-economic depression inducing the search of external investors.	Productive industries' disarticulation.	Represents networks of transmission from the knowledge generated in basic research to the applied technologies of firms.	Not focused in a specific sector. The author affirms that there has been a lack of coordination between the aims and results of the macroeconomic policies adopted and those pursued by the policies involving Brazilian industry, trade, technology and the NIS itself.

India (Nassif, 2007)	Promote exportations.	Liberalized strategies and active industrial and technological policies.	Indian government created schemes to support the absorption of imported technologies by industry, and develop, implement and commercialize indigenous innovations. There are a lot of fiscal incentives for R&D. Innovations have been financed by using foreign investment.	Strongly concentrated on creating active ingredients, new molecules and drug delivery systems, as well as the development of the software industry.	Not directed to the innovator sectors.	The NIS has been focused on the pharmaceutical and the information technology industries. These sectors, despite showing the highest economic growth rates, need to generate financial and technological spillovers to the economy as a whole.
Chile (Mollenhauer & Hormazábal, 2012)	To articulate and guide all actors in the NIS: companies, markets, educational system. Focused on encouraging actors and transferring resources to innovation.	In the core of Government policies to develop the productive sector.	Not included	The core of the NIS. Developed through incorporating innovations and updated technology.	Needs to redirect its methods to be aligned with the business activities and innovation policies from the Government.	Impact of the NIS in achieving greater economic and social dynamism. Their NIS promotes product-based innovation. A NIS based on value chains is a highly effective tool, especially for micro-enterprises.
Costa Rica (Herrera-González & Quesada, 2013)	Not included	Not included	Analyzed only from the firm perspective.	Not focused on the technological development and strategic policies. Remak the significance of the innovations in marketing activities.	Lower relationship between the universities and the productive sector.	Metalworking focused on. The authors conclude that major changes are necessary to promote innovation as a distinctive and competitive factor. The innovation processes and the VC management could be stronger and have a sectoral or national impact.

Source. Self-made from Oramas Santos et al. (2022).

Appendix 2. Results from the application of the ANP methodology*.

*Note. This methodology was applied in Spanish language; therefore, the content of this appendix is in Spanish language.

Tabla 1. Agrupación de las variables en clúster por los expertos.

Clúster 1: Variables explicativas CV	
v11	Veracidad y visibilidad de los resultados
v12	Generación y tratamiento de residuales
v13	Cumplimiento de las normas de las agencias reguladoras nacional e internacional
v14	Entorno país: acceso a financiamiento, a tecnología
Clúster 2: Variables explicativas Producto	
v21	Acción sobre la enfermedad: cura/ralentiza/predice la enfermedad
v22	Forma de aplicación: auto aplicable/en centros de atención médica
v23	Primero en su clase
v24	Aplicable para más de una dolencia
v25	Necesita medicamentos complementarios
v26	Produce beneficios en la memoria, el pensamiento y la vida cotidiana
v27	Efectos adversos: leves, severos
Clúster 3: Comparables	
v31	Donezepilo
v32	Lecanemab
v33	NeuroEOP

Tabla 2. Comparación pareada. Efectos de las variables del clúster 2 sobre v11. Cálculo del vector propio tras normalizar por la suma.

	v21	v22	v23	v24	v25	v26	v27	Vector Propio
v21		0	9	4	3	6	2	0,4762055
v22	0		0	0	0	0	0	0
v23	0,11111111	0		5	6	2	5	0,19228817
v24	0,25	0	0,2		3	0,2	2	0,06785763
v25	0,33333333	0	0,166666667	0,333333333		0,25	2	0,05349155
v26	0,16666667	0	0,5	5	4		6	0,15622711
v27	0,5	0	0,2	0,5	0,5	0,16666667		0,05393003
Suma	2,36111111	1	11,06666667	15,83333333	17,5	9,61666667	18	

Tabla 3. Comparación pareada. Efectos de las variables del clúster 3 sobre v11. Cálculo del vector propio tras normalizar por la suma.

	v31	v32	v33	Vector Propio
v31		0	0	0,333333333
v32	0		0	0,333333333
v33	0	0		0,333333333
Suma	1	1	1	

Tabla 4. Comparación pareada. Efectos de las variables del clúster 1 sobre v12. Cálculo del vector propio tras normalizar por la suma.

	v11	v13	v14	Vector Propio
v11		0	3	0,749995708
v13	0		0	5,72201E-06
v14	0,33333333	0		0,249998569
Suma	1,33333333	1	4	

Tabla 5. Comparación pareada. Efectos de las variables del clúster 2 sobre v12. Cálculo del vector propio tras normalizar por la suma.

	v21	v22	v23	v24	v25	v26	v27	Vector Propio
v21		2	3	4	5	6	2	0,2923368
v22	0,5		2	2	7	3	2	0,2086003
v23	0,33333333	0,5		3	4	5	6	0,18405424
v24	0,25	0,5	0,333333333		5	4	3	0,12938776
v25	0,2	0,14285714	0,25	0,2		6	7	0,09430206
v26	0,16666667	0,33333333	0,2	0,25	0,16666667		4	0,04747199
v27	0,5	0,5	0,166666667	0,333333333	0,14285714	0,25		0,04384684
Suma	2,95	4,97619048	6,95	10,78333333	22,3095238	25,25	25	

Tabla 6. Comparación pareada. Efectos de las variables del clúster 3 sobre v12. Cálculo del vector propio tras normalizar por la suma.

	v31	v32	v33	Vector Propio
v31		4	2	0,564752195
v32	0,25		5	0,30418043
v33	0,5	0,2		0,131067374
Suma	1,75	5,2	8	

Tabla 7. Comparación pareada. Efectos de las variables del clúster 1 sobre v13. Cálculo del vector propio tras normalizar por la suma.

	v11	v12	v14	Vector Propio
v11		2	3	0,53961455
v12	0,5		2	0,296961331
v14	0,33333333	0,5		0,163424119
Suma	1,83333333	3,5	6	

Tabla 8. Comparación pareada. Efectos de las variables del clúster 2 sobre v13. Cálculo del vector propio tras normalizar por la suma.

	v21	v22	v23	v24	v25	v26	v27	Vector Propio
v21		2	3	4	5	6	2	0,2923368
v22	0,5		2	2	7	3	2	0,2086003
v23	0,33333333	0,5		3	4	5	6	0,18405424
v24	0,25	0,5	0,333333333		5	4	3	0,12938776
v25	0,2	0,14285714	0,25	0,2		6	7	0,09430206
v26	0,16666667	0,33333333	0,2	0,25	0,16666667		4	0,04747199
v27	0,5	0,5	0,166666667	0,333333333	0,14285714	0,25		0,04384684
Suma	2,95	4,97619048	6,95	10,78333333	22,3095238	25,25	25	

Tabla 9. Comparación pareada. Efectos de las variables del clúster 3 sobre v13. Cálculo del vector propio tras normalizar por la suma.

	v31	v32	v33	Vector Propio
v31		4	2	0,564752195
v32	0,25		5	0,30418043
v33	0,5	0,2		0,131067374
Suma	1,75	5,2	8	

Tabla 10. Comparación pareada. Efectos de las variables del clúster 1 sobre v14. Cálculo del vector propio tras normalizar por la suma.

	v11	v12	v13	Vector Propio
v11		2	3	0,53961455
v12	0,5		2	0,296961331
v13	0,33333333	0,5		0,163424119
Suma	1,83333333	3,5	6	

Tabla 11. Comparación pareada. Efectos de las variables del clúster 2 sobre v14. Cálculo del vector propio tras normalizar por la suma.

	v21	v22	v23	v24	v25	v26	v27	Vector Propio
v21		2	3	4	5	6	2	0,2923368
v22	0,5		2	2	7	3	2	0,2086003
v23	0,33333333	0,5		3	4	5	6	0,18405424
v24	0,25	0,5	0,333333333		5	4	3	0,12938776
v25	0,2	0,14285714	0,25	0,2		6	7	0,09430206
v26	0,16666667	0,33333333	0,2	0,25	0,16666667		4	0,04747199
v27	0,5	0,5	0,166666667	0,333333333	0,14285714	0,25		0,04384684
Suma	2,95	4,97619048	6,95	10,78333333	22,3095238	25,25	25	

Tabla 12. Súper matriz ponderada.

		C1				C2							C3		
		v11	v12	v13	v14	v21	v22	v23	v24	v25	v26	v27	v31	v32	v33
C1	v11	0	0	0,08989614	0,10412296	0,03981884	0,0361199	0,08707717	0,07030479	0,03244217	0,03791814	0,03848081	0,10139257	0,10139257	0,06004128
	v12	0,123211388	0	0,04947176	0,03973035	0,02339368	0,03823678	0,04740643	0,05711852	0,07531594	0,04918226	0,06375085	0,03473396	0,03473396	0,04542564
	v13	0,015628555	0,138827713	0	0,02273995	0,05659339	0,0714409	0,02260656	0,02347919	0,04592393	0,06334829	0,05157692	0,01267472	0,01267472	0,04943213
	v14	0,027753313	0,027765543	0,02722536	0	0,04678735	0,02079568	0,00950309	0,01569076	0,01291122	0,01614457	0,01278468	0,01779201	0,01779201	0,0116942
C2	v21	0,262017508	0	0	0	0	0,07701884	0,04179838	0,18233314	0,13583722	0,11145554	0,08733917	0,18233314	0,27349971	0,07814277
	v22	0	0,077939939	0,12539513	0,23105653	0,1517657	0	0,01136573	0,05184068	0,16604122	0,15605977	0,15858164	0,03080285	0,06160569	0,02464228
	v23	0,151765703	0,225744176	0,02273146	0,28595673	0,10368137	0,14297836	0	0,02431189	0,12691089	0,10904953	0,09260143	0,03035314	0,07588285	0,05058857
	v24	0,103681367	0,333743119	0,26152831	0,15001316	0,02315418	0,15751382	0,06663089	0	0,10523187	0,08135763	0,10398308	0,03010043	0,0254696	0,02361726
	v25	0,100272248	0,102166859	0,20055044	0,07256768	0,09870309	0	0,20656695	0,07146478	0	0,13674986	0,11556399	0,25541715	0,11136188	0,10523187
	v26	0,098703089	0	0,06345799	0	0,26201751	0,07474471	0,20055044	0,20055044	0,20055044	0	0,18152478	0,07293566	0,02649996	0,02455501
	v27	0,023154178	0	0,06593076	0	0,10027225	0,28733836	0,2126817	0,20909316	0,00502246	0,14492177	0	0,13765172	0,16527441	0,43281634
C3	v31	0,008800813	0,022373109	0,05863413	0,05169018	0,0205323	0,02258553	0,08208607	0,04864075	0	0,01954471	0,01734582	0	0,09381265	0,02057338
	v32	0,015628555	0,012805408	0,01118655	0	0,04864075	0,02432038	0	0,0136882	0,07035949	0,04191782	0,0503202	0	0	0,07323927
	v33	0,069383282	0,058634133	0,02399196	0,04212247	0,0246396	0,04690675	0,01172658	0,0314837	0,02345316	0,03235012	0,02614663	0,09381265	0	0

Tabla 12. Súper matriz límite.

0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456	0,04979456
0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839	0,05073839
0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542	0,04657542
0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488	0,01948488
0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218	0,09774218
0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204	0,09549204
0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108	0,09512108
0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917	0,09737917
0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523	0,10341523
0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386	0,12632386
0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053	0,12412053
0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793	0,03025793
0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186	0,03152186
0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287	0,03203287

Appendix 3. Results from the application of the model proposal in the Cuban case.

Tabla 1. Cálculo de la curva de ventas 2023-2037.

	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Población Cubana Total	11089511	11079275,56	11069015,12	11058719,1	11048373,5	11037960,2	11027455,5	11016827,9	11006036,9	10995028,7	10983733,5	10972059,4	10959886,6	10947057,8	10933367,6
Población 65-74	1000806	999882,2719	998956,2878	998027,09	997093,424	996153,649	995205,613	994246,501	993272,627	992279,164	991259,79	990206,232	989107,658	987949,889	986714,373
Población 75-84	574754	574223,5112	573691,7267	573158,097	572621,901	572082,196	571537,747	570986,938	570427,651	569857,114	569271,697	568666,648	568035,746	567370,85	566661,304
Población 85y+	193096	192917,7755	192739,1156	192559,836	192379,694	192198,373	192015,459	191830,407	191642,507	191450,828	191254,15	191050,876	190838,916	190615,536	190377,155
Población Objetivo (Población con Alzheimer) 65-74	137315,1089	137188,3693	137061,3201	136933,83	136805,727	136676,785	136546,71	136415,116	136281,496	136145,188	136005,326	135860,773	135710,043	135551,192	135381,674
Población Objetivo (Población con Alzheimer) 75-84	111938,2148	111834,8976	111731,3281	111627,399	111522,97	111417,858	111311,822	111204,548	111095,622	110984,505	110870,49	110752,651	110629,778	110500,284	110362,094
Población Objetivo (Población con Alzheimer) 85y+	35126,40493	35093,98382	35061,48352	35028,8704	34996,1005	34963,1162	34929,8419	34896,1789	34861,9977	34827,1291	34791,351	34754,3731	34715,8152	34675,1797	34631,8154
Porciento de casos nuevos sobre el total de casos de un año	0,090909091	0,090909091	0,090909091	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909
Población Objetivo con Incidencia y Muerte 65-74	137315,1089	149814,042	163450,6745	178328,564	194560,695	212270,334	231591,971	252672,336	275671,513	300764,162	328140,837	358009,439	390596,793	426150,369	464940,164
Población Objetivo con Incidencia y Muerte 75-84	111938,2148	122204,7605	133412,9145	145649,038	159007,411	173590,964	189512,064	206893,387	225868,859	246584,688	269200,494	293890,536	320845,053	350271,737	382397,323
Población Objetivo con Incidencia y Muerte 85y+	35126,40493	38143,94514	41420,70768	44978,9611	48842,8869	53038,744	57595,047	62542,7599	67915,5071	73749,8011	80085,2912	86965,0327	94435,7796	102548,302	111357,733
Población con Alzheimer total	284379,7287	310162,7476	338284,2966	368956,563	402410,993	438900,042	478699,083	522108,483	569455,879	621098,651	677426,623	738865,008	805877,626	878970,408	958695,22
Tasa de Sintomatología	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Número de Pacientes sintomáticos	284379,7287	310162,7476	338284,2966	368956,563	402410,993	438900,042	478699,083	522108,483	569455,879	621098,651	677426,623	738865,008	805877,626	878970,408	958695,22
Tasa de Diagnóstico	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93
Número de Pacientes con Potencial Diagnóstico	264473,1477	288451,3552	314604,3959	343129,603	374242,223	408177,039	445190,147	485560,889	529593,968	577621,746	630006,759	687144,457	749466,192	817442,479	891586,554
Porciento de pacientes con capacidad de acceder al tratamiento	0,363	0,363	0,1	0,25	0,35	0,45	0,55	0,65	0,75	0,85	0,96	0,96	0,96	0,96	0,96
Pacientes Potenciales a tratar	96003,7526	104707,842	31460,43959	85782,4008	130984,778	183679,668	244854,581	315614,578	397195,476	490978,484	604806,489	659658,679	719487,544	784744,78	855923,092
Curva de Ventas (%)	0	0	0,672	0,631	0,59	0,549	0,508	0,558	0,658	0,848	1	1	1	1	1
Número de pacientes siendo tratados con la droga (Cuba&China)	0	0	21141,4154	54128,6949	77281,0191	100840,138	124386,127	176112,934	261354,623	416349,754	415924232	1652932940	3272673793	4818975625	6260052711
Cantidad de dosis por paciente por año	209	209	209	209	209	209	209	209	209	209	209	209	209	209	209

Fuente: Elaboración propia a partir de BrightFocus Foundation (2021); Cubadebate (2014, 2023); Llibre (2013); y Trabajadores (2023).

Tabla 2. Cálculo de la curva de ventas 2038-2048.

	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048
	15	16	17	18	19	20	21	22	23	24	25
Población Cubana Total	10918546,92	10902244,02	10883999,02	10863211,1	10839095,7	10810629,6	10776480,1	10734913,7	10683681,5	10619874,4	10539743,5
Población 65-74	985376,8368	983905,5328	982258,9587	980382,888	978206,523	975637,52	972555,589	968804,306	964180,709	958422,24	951190,594
Población 75-84	565893,1685	565048,2117	564102,5989	563025,188	561775,321	560299,965	558530,04	556375,711	553720,42	550413,383	546260,313
Población 85y+	190119,0897	189835,2156	189517,5248	189155,555	188735,646	188239,981	187645,352	186921,578	186029,498	184918,457	183523,179
Población Objetivo (Población con Alzheimer) 65-74	135198,158	134996,2884	134770,371	134512,966	134214,358	133861,88	133439,025	132924,332	132289,953	131499,865	130507,651
Población Objetivo (Población con Alzheimer) 75-84	110212,4927	110047,9302	109863,7641	109653,929	109410,507	109123,169	108778,461	108358,887	107841,747	107197,673	106388,828
Población Objetivo (Población con Alzheimer) 85y+	34584,87037	34533,23038	34475,43873	34409,5922	34333,2059	34243,0387	34134,8688	34003,2058	33840,9262	33638,8148	33384,9977
Porciento de casos nuevos sobre el total de casos de un año	0,090909091	0,090909091	0,090909091	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909	0,09090909
Población Objetivo con Incidencia y Muerte 65-74	507260,7504	553433,5146	603809,0959	658770,05	718733,756	784155,581	855532,345	933406,088	1018368,19	1111063,86	1212197,03
Población Objetivo con Incidencia y Muerte 75-84	417469,3453	455758,0397	497558,4269	543192,586	593012,136	647400,945	706778,088	771601,075	842369,38	919628,283	1003973,08
Población Objetivo con Incidencia y Muerte 85y+	120923,9393	131311,9323	142592,3077	154841,726	168143,432	182587,825	198273,065	215305,749	233801,628	253886,399	275696,557
Población con Alzheimer total	1045654,035	1140503,487	1243959,831	1356804,36	1479889,32	1614144,35	1760583,5	1920312,91	2094539,2	2284578,54	2491866,67
Tasa de Sintomatología	1	1	1	1	1	1	1	1	1	1	1
Número de Pacientes sintomáticos	1045654,035	1140503,487	1243959,831	1356804,36	1479889,32	1614144,35	1760583,5	1920312,91	2094539,2	2284578,54	2491866,67
Tasa de Diagnóstico	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93	0,93
Número de Pacientes con Potencial Diagnóstico	972458,2526	1060668,243	1156882,642	1261828,06	1376297,07	1501154,25	1637342,65	1785891,01	1947921,45	2124658,04	2317436
Porciento de pacientes con capacidad de acceder al tratamiento	0,96	0,96	0,96	0,96	0,96	0,96	0,96	0,96	0,96	0,96	0,96
Pacientes Potenciales a tratar	933559,9225	1018241,513	1110607,337	1211354,93	1321245,19	1441108,08	1571848,95	1714455,37	1870004,59	2039671,72	2224738,56
Curva de Ventas (%)	1	1	1	1	1	1	1	1	1	1	1
Número de pacientes siendo tratados con la droga (Cuba&China)	7565940909	8731434490	9729456271	1,0542E+10	1,1153E+10	1,1591E+10	1,1976E+10	1714455,37	1870004,59	2039671,72	2224738,56
Cantidad de dosis por paciente por año	209	209	209	209	209	209	209	209	209	209	209

Fuente: Elaboración propia a partir de BrightFocus Foundation (2021); Cubadebate (2014, 2023); Llibre (2013); y Trabajadores (2023).

Tabla 3. Datos para el cálculo de los casos a tratar.

	Izq	MaxPres	Der	65-74	75-84	85y+
Adherencia al Tratamiento	0,901	0,9166	0,9227			
Prevalencia de población con demencias (%)	6,4	10,2	10,8			
Incidencia en la población con demencias (%)	2,12		3			
Prevalencia de población con Alzheimer (%)	60	70	80			
Prevalencia Alzheimer (%)				13,7204522	19,4758479	18,1911614
Incidencia en la población con Alzheimer (%)				0,4	3,2	7,6
Muertes por Alzheimer anualmente (%)				0,0249	0,2102	1,1913
Precio/dosis (millones CUP)	0,006200957	0,010246965	0,013205742			

Fuente: Elaboración propia a partir de Alzheimer's Association (2023); Cubadebate (2014, 2023); MINSAP (2022); Ortega Cerda et al. (2018); Rajan et al. (2021); Tom et al. (2015); y Trabajadores (2023).

Tabla 4. Población cubana en 2012 (base de cálculo más reciente de la prevalencia de la enfermedad).

Población 2012	11167325
Población con más de 60 años en 2012 (%)	18,3
Población con más de 60 años en 2012	2043620,48
Personas con demencia en Cuba en 2012	150000
Prevalencia demencia	0,07339915
Pacientes de 60 y más con Alzheimer en 2012	130000
Prevalencia de Alzheimer	0,86666667

Fuente. Elaboración propia a partir de Cubadebate (2014); Llibre (2013); y Molina (2021).

Tabla 5. Estructura etaria 2023-2037.

Estructura etaria	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037
0-4	521762	521280,4219	520797,6677	520313,238	519826,479	519336,535	518842,284	518342,259	517834,538	517316,604	516785,162	516235,898	515663,165	515059,572	514415,446
5-9	600543	599988,7083	599433,0629	598875,489	598315,234	597751,313	597182,435	596606,911	596022,529	595426,392	594814,708	594182,51	593523,3	592828,571	592087,188
10-14	612752	612186,4396	611619,498	611050,589	610478,944	609903,558	609323,115	608735,891	608139,628	607531,372	606907,252	606262,202	605589,59	604880,737	604124,282
15-19	587101	586559,1151	586015,9067	585470,813	584923,098	584371,8	583815,655	583253,013	582681,711	582098,918	581500,924	580882,878	580238,423	579559,243	578834,455
20-24	692014	691375,2821	690735,0041	690092,504	689446,915	688797,1	688141,575	687478,391	686804,999	686118,062	685413,21	684684,72	683925,103	683124,556	682270,251
25-29	687254	686619,6755	685983,8017	685345,721	684704,572	684059,228	683408,211	682749,589	682080,829	681398,617	680698,613	679975,134	679220,742	678425,702	677577,273
30-34	798713	797975,8006	797236,8007	796495,236	795750,106	795000,099	794243,5	793478,062	792700,843	791907,99	791094,459	790253,646	789376,907	788452,927	787466,899
35-39	727647	726975,3934	726302,1464	725626,563	724947,731	724264,457	723575,177	722877,844	722169,779	721447,47	720706,323	719940,322	719141,592	718299,823	717401,528
40-44	604339	603781,2047	603222,0471	602660,949	602097,153	601529,667	600957,193	600378,032	599789,956	599190,05	598574,499	597938,306	597274,929	596575,808	595829,739
45-49	814833	814080,9221	813327,0073	812570,476	811810,307	811045,163	810273,295	809492,408	808699,503	807890,648	807060,698	806202,915	805308,482	804365,853	803359,925
50-54	979310	978406,1124	977500,0172	976590,777	975677,165	974757,575	973829,902	972891,391	971938,434	970966,309	969968,83	968937,901	967862,923	966730,022	965521,043
55-59	985156	984246,7166	983335,2125	982420,545	981501,479	980576,399	979643,188	978699,075	977740,43	976762,501	975759,068	974721,985	973640,589	972500,925	971284,73
60-64	709431	708776,2064	708119,8137	707461,143	706799,305	706133,136	705461,111	704781,236	704090,896	703386,67	702664,077	701917,252	701138,517	700317,822	699442,014
65-69	542346	541845,4232	541343,6239	540840,083	540334,121	539824,848	539311,099	538791,347	538263,596	537725,229	537172,821	536601,888	536006,561	535379,155	534709,618
70-74	458460	458036,8487	457612,6639	457187,007	456759,303	456328,801	455894,514	455455,154	455009,031	454553,935	454086,969	453604,344	453101,097	452570,734	452004,756
75-79	345852	345532,7841	345212,7885	344891,682	344569,032	344244,271	343916,655	343585,211	343248,666	342905,352	342553,083	342189,002	341809,363	341409,269	340982,308
80-84	228902	228690,7271	228478,9382	228266,414	228052,868	227837,925	227621,093	227401,727	227178,985	226951,762	226718,613	226477,646	226226,383	225961,581	225678,996
85y+	193096	192917,7755	192739,1156	192559,836	192379,694	192198,373	192015,459	191830,407	191642,507	191450,828	191254,15	191050,876	190838,916	190615,536	190377,155
Total	11089511	11079275,56	11069015,12	11058719,1	11048373,5	11037960,2	11027455,5	11016827,9	11006036,9	10995028,7	10983733,5	10972059,4	10959886,6	10947057,8	10933367,6

Fuente. Elaboración propia a partir de ONEI (2023).

*Nota. Se considera un promedio de disminución de la población cubana en el período 2026-2030 de 0.000912984, de acuerdo con CEPDE (2014).

Tabla 6. Estructura etaria 2038-2048.

Estructura etaria	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048
0-4	513718,1323	512951,08	512092,6521	511114,578	509979,948	508640,619	507033,88	505078,179	502667,705	499665,575	495895,415
5-9	591284,5863	590401,7166	589413,6744	588287,921	586981,972	585440,418	583591,077	581340,084	578565,651	575110,229	570770,812
10-14	603305,3634	602404,545	601396,416	600247,776	598915,278	597342,383	595455,445	593158,69	590327,853	586802,182	582374,545
15-19	578049,8181	577186,7097	576220,783	575120,227	573843,51	572336,46	570528,513	568327,905	565615,572	562237,492	557995,205
20-24	681345,4019	680328,059	679189,5243	677892,303	676387,44	674611,086	672480,065	669886,215	666689,197	662707,466	657707,096
25-29	676658,7856	675648,4404	674517,7371	673229,438	671734,927	669970,791	667854,428	665278,42	662103,393	658149,05	653183,075
30-34	786399,4515	785225,2483	783911,1673	782413,932	780677,041	778626,797	776167,202	773173,416	769483,463	764887,803	759116,445
35-39	716429,0573	715359,3296	714162,1698	712798,152	711215,802	709347,98	707107,229	704379,817	701018,179	696831,422	691573,574
40-44	595022,0644	594133,6141	593139,3266	592006,457	590692,254	589140,955	587279,925	585014,704	582222,734	578745,469	574378,623
45-49	802270,9337	801073,0321	799732,4298	798204,977	796433,031	794341,408	791832,172	788777,964	785013,538	780325,127	774437,289
50-54	964212,2349	962772,5327	961161,3248	959325,55	957195,93	954682,106	951666,371	947995,661	943471,372	937836,588	930760,268
55-59	969968,1087	968519,8121	966898,9862	965052,252	962909,92	960381,089	957347,352	953654,729	949103,433	943435,012	936316,45
60-64	698493,8886	697450,9406	696283,7506	694953,88	693411,142	691590,08	689405,424	686746,29	683468,808	679386,863	674260,64
65-69	533984,7942	533187,481	532295,1873	531278,527	530099,135	528706,968	527036,842	525003,987	522498,417	519377,85	515458,954
70-74	451392,0426	450718,0518	449963,7714	449104,361	448107,388	446930,551	445518,747	443800,319	441682,292	439044,391	435731,64
75-79	340520,0906	340011,6469	339442,6346	338794,314	338042,22	337154,441	336089,408	334793,064	333195,271	331205,297	328706,232
80-84	225373,078	225036,5648	224659,9642	224230,874	223733,101	223145,524	222440,632	221582,648	220525,149	219208,086	217554,081
85y+	190119,0897	189835,2156	189517,5248	189155,555	188735,646	188239,981	187645,352	186921,578	186029,498	184918,457	183523,179
Total	10918546,92	10902244,02	10883999,02	10863211,1	10839095,7	10810629,6	10776480,1	10734913,7	10683681,5	10619874,4	10539743,5

Fuente. Elaboración propia a partir de ONEI (2023).

*Nota. Se considera un promedio de disminución de la población cubana en el período 2026-2030 de 0.000912984, de acuerdo con CEPDE (2014).

Tabla 7. Costos por etapa por paciente y totales.

	Costo/Paciente UM: millones CUP			Costo Total UM: millones CUP			
Inversión	**Cant de pacientes**	**Izq**	**MaxPres**	**Der**	**Izq**	**MaxPres**	**Der**
Etapa I: Descubrimiento y Desarrollo					1169711,237	1388903,238	1436971,671
Etapa II: Investigación Preclínica					1278960	1278960	1278960
Etapa III: Investigación Clínica					2499607786	3286931287	3563558464
Fase I	71		1258485,6		89352477,6	89352477,6	89352477,6
Fase II	248		1138524		282353952	282353952	282353952
Fase III	1869	1138524	1559777,88	1707786	2127901356	2915224858	3191852034
Fase IV							
Etapa IV: Revisión y acceso al mercado					12000000	15000000	15600000
Etapa V: Comercialización y Monitoreo					11760000	14400000	15000000

Fuente. Elaboración propia a partir de información proporcionada por la firma que lidera el proyecto.

*Nota. Los datos de la etapa II no son inciertos, de ahí que los valores de los tres niveles de presunción sean idénticos.

Tabla 8. Otros costos, impuestos y probabilidades.

	Izq	MaxPres	Der
Costo del capital	7%	11%	13%
Probabilidad de pasar de Fase III a Etapa IV	16%	47%	68%
Probabilidad de pasar de Etapa IV a Etapa V	77,80%	86,70%	91,20%
Probabilidad acumulada Fase III Etapa V	12,45%	40,75%	62,02%
Costos operativos Etapa V			
Distribución		31%	
Producción		18%	
Impuesto sobre Utilidades		15%	

Fuente. Elaboración propia a partir de Cubadebate (2023); Rennane et al. (2021); y Scott et al. (2014).

Tabla 9. Cálculo del margen en operaciones ajustado descontado en millones de CUP, 2023-2026.

	2023			2024			2025			2026		
	0			1			2			3		
Ventas anuales (dosis)	0	0	0	0	0	0	3981118,793	4050048,264	4077001,454	10192920,41	10369401,61	10438410,28
Ventas anuales (millones CUP)	**0**	**0**	**0**	**0**	**0**	**0**	**24686,7462**	**41500,7018**	**53839,82782**	**63205,86056**	**106254,8928**	**137846,9492**
Costo Operativo Total (millones CUP)	**0**	**0**	**0**	**0**	**0**	**0**	**5821,134754**	**9785,865483**	**12695,4314**	**14903,94192**	**25054,90372**	**32504,31063**
Costo de Producción	0	0	0	0	0	0	4443,614316	7470,126323	9691,169007	11377,0549	19125,8807	24812,45086
Costo de Distribución	0	0	0	0	0	0	1377,520438	2315,73916	3004,262392	3526,887019	5929,023018	7691,859766
BAIT (millones CUP)	**0**	**0**	**0**	**0**	**0**	**0**	**11991,3148**	**31714,83631**	**48018,69306**	**30701,54994**	**81199,98908**	**122943,0073**
Impuesto sobre Utilidades	0	0	0	0	0	0	1798,69722	4757,225447	7202,80396	4605,232491	12179,99836	18441,45109
Margen en Operaciones (millones CUP)	**0**	**0**	**0**	**0**	**0**	**0**	**4788,510841**	**26957,61087**	**46219,99584**	**12260,09884**	**69019,99071**	**118337,7748**
Margen en Operaciones ajustado al riesgo (millones CUP)	0	0	0	0	0	0	596,0738295	10984,95685	28663,79262	1526,137104	28124,95602	73388,35442
Factor de Descuento	1	1	1	0,934579439	0,900900901	0,884955752	0,873438728	0,811622433	0,783146683	0,816297877	0,731191381	0,693050162
Margen Operaciones ajustado descontado (millones CUP)	**0**	**0**	**0**	**0**	**0**	**0**	**520,6339676**	**8915,637409**	**22447,95413**	**1245,782478**	**20564,72544**	**50861,81094**
Margen ajustado descontado acumulado (millones CUP)	0	0	0	0	0	0	520,6339676	8915,637409	22447,95413	1766,416445	29480,36285	73309,76507
ahorro por menos generación de residuos	0	0	0	0	0	0	1405954,661	1430297,495	1439816,167	3599687,604	3662012,939	3686383,743
aumento en Margen en Operaciones	0	0	0	0	0	0	1195061,462	1215752,87	1223843,742	3059734,464	3112710,998	3133426,182
aumento en Margen en Operaciones ajustado al riesgo	0	0	0	0	0	0	148761,2508	495407,1372	758978,9348	380875,746	1268398,605	1943225,581
aumento en Margen Operaciones ajustado descontado (millones CUP)	**0**	**0**	**0**	**0**	**0**	**0**	**129933,8377**	**402083,5461**	**594391,8355**	**310908,0629**	**927442,1278**	**1346752,804**
aumento en Margen ajustado descontado acumulado (millones CUP)	0	0	0	0	0	0	129933,8377	402083,5461	594391,8355	440841,9006	1329525,674	1941144,64

Fuente. Elaboración propia.

Tabla 10. Cálculo del margen en operaciones ajustado descontado en millones de CUP, 2027-2032.

	2027			2028			2029			2030			2031			2032		
	4			5			6			7			8			9		
Ventas anuales (dosis)	14552711,43	14804678,46	14903204,03	18989105,46	19317884,64	19446445,73	23423027,19	23828575,72	23987155,59	33163650,58	33737849,19	33962375,57	49215427,72	50067548,33	50400749,34	78402405,88	79759872,62	80290676,92
Ventas anuales (millones CUP)	**90240,7369**	**151703,0184**	**196807,8619**	**117750,6252**	**197949,683**	**256804,7379**	**145245,183**	**244170,5754**	**316768,1791**	**205646,3691**	**345710,5514**	**448498,3568**	**305182,748**	**513040,4029**	**665579,2736**	**486169,9427**	**817296,6033**	**1060297,935**
Costo Operativo Total (millones CUP)	**21278,76576**	**35771,57173**	**46407,29384**	**27765,59743**	**46676,53525**	**60554,5572**	**34248,81414**	**57575,42169**	**74693,93663**	**48491,41384**	**81518,54802**	**105755,9125**	**71962,09197**	**120974,927**	**156943,5927**	**114638,8725**	**192718,539**	**250018,253**
Costo de Producción	16243,33264	27306,5433	35425,41514	21195,11254	35630,94294	46224,85283	26144,13293	43950,70358	57018,27224	37016,34644	62227,89925	80729,70422	54932,89464	92347,27253	119804,2693	87510,58969	147113,3886	190853,6282
Costo de Distribución	5035,433119	8465,028424	10981,87869	6570,484888	11045,59231	14329,70438	8104,681209	13624,71811	17675,66439	11475,0674	19290,64877	25026,20831	17029,19734	28627,65448	37139,32347	27128,2828	45605,15046	59164,62475
BAIT (millones CUP)	**43833,44306**	**115931,4466**	**175529,0961**	**57196,06803**	**151273,1477**	**229039,1405**	**70551,24632**	**186595,1537**	**282519,365**	**99890,4566**	**264192,0034**	**400006,9429**	**148239,1553**	**392065,4759**	**593617,1817**	**236151,6897**	**624578,0642**	**945659,062**
Impuesto sobre Utilidades	6575,01646	17389,71699	26329,36442	8579,410205	22690,97216	34355,87108	10582,68695	27989,27306	42377,90474	14983,56849	39628,8005	60001,04144	22235,87329	58809,82139	89042,57725	35422,75346	93686,70963	141848,8593
Margen en Operaciones (millones CUP)	17504,07864	98541,72963	168954,0797	22840,19696	128582,1756	220459,7303	28173,34158	158605,8807	271936,678	39889,41515	224563,2029	385023,3745	59196,57801	333255,6545	571381,3084	94302,83045	530891,3546	910236,3086
Margen en Operaciones ajustado al riesgo (millones CUP)	2178,90771	40154,76941	104778,5621	2843,147717	52395,95073	136720,3063	3507,01756	64630,31032	168644,2502	4965,434398	91507,25953	238776,0959	7368,79003	135798,3467	354347,8322	11738,81633	216332,9181	564492,1491
Factor de Descuento	0,762895212	0,658730974	0,613318728	0,712986179	0,593451328	0,542759936	0,666342224	0,534640836	0,480318527	0,622749742	0,481658411	0,425060644	0,582009105	0,433926496	0,376159862	0,543933743	0,390924771	0,332884833
Margen Operaciones ajustado descontado (millones CUP)	**1662,278259**	**26451,19037**	**64262,65437**	**2027,125029**	**31094,44654**	**74206,30472**	**2336,87388**	**34554,00315**	**81002,95793**	**3092,22299**	**44075,24121**	**101494,321**	**4288,702887**	**58926,50077**	**133291,4316**	**6385,138302**	**84569,89655**	**187910,875**
Margen ajustado descontado acumulado (millones CUP)	3428,694704	55931,55322	137572,4194	5455,819733	87025,99976	211778,7242	7792,693613	121580,0029	292781,6821	10884,9166	165655,2441	394276,0031	15173,61949	224581,7449	527567,4347	21558,75779	309151,6414	715478,3097
ahorro por menos generación de residuos	5139372,506	5228356,093	5263150,956	6706110,198	6822220,43	6867622,508	8271974,782	8415196,543	8471199,924	11711931,13	11914712,62	11994005,39	17380707,19	17681638,41	17799310,23	27688253,92	28167650,99	28355107,54
aumento en Margen en Operaciones	4368466,63	4444102,679	4473678,313	5700193,668	5798887,365	5837479,132	7031178,565	7152917,062	7200519,936	9955141,459	10127505,73	10194904,58	14773601,11	15029392,65	15129413,7	23535015,83	23942503,34	24101841,41
aumento en Margen en Operaciones ajustado al riesgo	543786,7262	1810927,401	2774396,343	709560,1078	2362988,613	3620171,058	875241,1078	2914742,174	4465474,443	1239216,009	4126857,309	6322472,023	1839017,866	6124327,211	9382657,2	2929638,771	9756330,686	14946997,97
aumento en Margen Operaciones ajustado descontado (millones CUP)	**414852,2898**	**1192913,971**	**1701589,235**	**505906,5504**	**1402318,73**	**1964883,812**	**583210,1061**	**1558340,193**	**2144850,109**	**771721,4496**	**1987735,534**	**2687434,028**	**1070325,142**	**2657507,849**	**3529379,035**	**1593529,381**	**3813991,344**	**4975628,928**
aumento en Margen ajustado descontado acumulado (millones CUP)	855694,1903	2522439,645	3642733,875	1361600,741	3924758,375	5607617,686	1944810,847	5483098,568	7752467,795	2716532,297	7470834,101	10439901,82	3786857,438	10128341,95	13969280,86	5380386,819	13942333,29	18944909,79

Fuente. Elaboración propia.

Tabla 11. Cálculo del margen en operaciones ajustado descontado en millones de CUP, 2033-2036, 2048.

	2033			2034			2035			2036			2048		
	10			11			12			13			25		
Ventas anuales (dosis)	78322276277	79678355645	80208617448	3,11262E+11	3,16651E+11	3,18759E+11	6,16274E+11	6,26944E+11	6,31116E+11	9,07456E+11	9,23168E+11	9,29312E+11	418938293,3	426191830,9	429028150
Ventas anuales (millones CUP)	**485673062,5**	**816461301,6**	**1059214278**	**1930123182**	**3244715442**	**4209444977**	**3821488097**	**6424274655**	**8334361259**	**5627098561**	**9459672712**	**12272253913**	**2597818,316**	**4367172,668**	**5665634,9**
Costo Operativo Total (millones CUP)	**114521708,1**	**192521574,9**	**249762726,8**	**455123046,4**	**765103901,3**	**992587125,6**	**901106893,2**	**1514843964**	**1965242385**	**1326869841**	**2230590825**	**2893797473**	**612565,5589**	**1029779,315**	**1335956,709**
Costo de Producción	87421151,24	146963034,3	190658570,1	347422172,8	584048779,6	757700095,9	687867857,4	1156369438	1500185027	1012877741	1702741088	2209005704	467607,2969	786091,0802	1019814,282
Costo de Distribución	27100556,89	45558540,63	59104156,73	107700873,6	181055121,7	234887029,7	213239035,8	358474525,8	465057358,3	313992099,7	527849737,3	684791768,3	144958,262	243688,2349	316142,4274
BAIT (millones CUP)	**235910335,7**	**623939726,7**	**944692570,1**	**937536056,6**	**2479611541**	**3754321931**	**1856245712**	**4909430691**	**7433254366**	**2733301089**	**7229081886**	**10945384072**	**1261861,607**	**3337393,353**	**5053069,341**
Impuesto sobre Utilidades	35386550,35	93590959,01	141703885,5	140630408,5	371941731,1	563148289,6	278436856,8	736414603,7	1114988155	409995163,3	1084362283	1641807611	189279,241	500609,0029	757960,4012
Margen en Operaciones (millones CUP)	**94206450,13**	**530348767,7**	**909306019,8**	**374387766,9**	**2107669810**	**3613691522**	**741257557,1**	**4173016088**	**7154817509**	**1091493478**	**6144719603**	**10535388909**	**503901,2055**	**2836784,35**	**4863790,1**
Margen en Operaciones ajustado al riesgo (millones CUP)	11726818,91	216111819,4	563915221,2	46603789,23	858854370,8	2241066935	92271740,71	1700462326	4437131626	135869108,1	2503911791	6533626786	62725,62206	1155961,255	3016328,069
Factor de Descuento	0,508349292	0,352184479	0,294588348	0,475092796	0,317283314	0,260697653	0,444011959	0,285840824	0,230705888	0,414964448	0,257514256	0,204164502	0,184249178	0,073608087	0,047101953
Margen Operaciones ajustado descontado (millones CUP)	**5961320,093**	**76111228,46**	**166122853,5**	**2214124,55**	**272500161,2**	**584240890,5**	**40969756,37**	**486061551,7**	**1023672391**	**56380849,43**	**644792980,7**	**1333934662**	**11557,14427**	**85088,09647**	**142074,9423**
Margen ajustado descontado acumulado (millones CUP)	5982878,851	76420380,1	166838331,8	28124003,4	348920541,3	751079222,3	69093759,77	834982093	1774751613	125474609,2	1479775074	3108686276	782413288,7	7845516624	15287387648
ahorro por menos generación de residuos	27659955694	28138862807	28326127767	1,09924E+11	1,11827E+11	1,12571E+11	2,17641E+11	2,21409E+11	2,22882E+11	3,20473E+11	3,26022E+11	3,28192E+11	147950432,2	150512060,2	151513722,3
aumento en Margen en Operaciones	23510962340	23918033386	24077208602	93435392972	95053142284	95685723746	1,84995E+11	1,88198E+11	1,8945E+11	2,72402E+11	2,77119E+11	2,78963E+11	125757867,4	127935251,1	128786664
aumento en Margen en Operaciones ajustado al riesgo	2926644592	9746359424	14931721687	11630837717	38733204949	59340458438	23028119813	76688619169	1,17489E+11	33908649348	1,12923E+11	1,73002E+11	15654339,34	52132335,48	79868337,54
aumento en Margen Operaciones ajustado descontado (millones CUP)	**1487757707**	**3432516514**	**4398711226**	**5525727215**	**12289399636**	**15469918255**	**10224760596**	**21920738065**	**27105477327**	**14070883955**	**29079317195**	**35320807760**	**2884299,147**	**3837361,48**	**3761954,665**
aumento en Margen ajustado descontado acumulado (millones CUP)	1493138094	3446458847	4417656136	7018865309	15735858483	19887574391	17243625905	37656596549	46993051718	31314509860	66735913744	82313859478	1,95266E+11	3,53823E+11	4,0479E+11

Fuente. Elaboración propia.

Tabla 12. Cálculo del rVAN.

			p=(77,8%; 86,7%; 91,2%)	Etapa V
	p=(16%; 47%; 68%)	Etapa IV		
Etapa III, Fase III			1-p=(8,8%; 13,3%; 22,2%)	Abandonar
	1-p=(32%; 53%; 84%	Abandonar		
	UM: (millones CUP)			
Partida	**Izq**	**MaxPres**	**Der**	
Margen ajustado descontado acumulado	782.413.288,69	7.845.516.624,39	15.287.387.647,83	
Etapa I: Descubrimiento y Desarrollo	1.169.711,24	1.388.903,24	1.436.971,67	
Etapa II: Investigación Preclínica	1.278.960,00	1.278.960,00	1.278.960,00	
Etapa III: Investigación Clínica	2.499.607.785,60	3.286.931.287,32	3.563.558.463,60	
Fase I	89.352.477,60	89.352.477,60	89.352.477,60	
Fase II	282.353.952,00	282.353.952,00	282.353.952,00	
Fase III	2.127.901.356,00	2.915.224.857,72	3.191.852.034,00	
Etapa IV: Revisión y acceso al mercado	12.000.000,00	15.000.000,00	15.600.000,00	
Etapa V: Comercialización y Monitoreo	414.000.000,00	600.000.000,00	840.000.000,00	
Costo Total Etapa I-Etapa V	2.928.056.456,84	3.904.599.150,56	4.421.874.395,27	
rVAN	-3.639.461.106,58	3.940.917.473,83	12.359.331.191,00	

Fuente. Elaboración propia.

Tabla 13. Calculo del valor de la patente.

precio strike	x	898,80	s/x	0,93		x*e^(-r*t)	865,72
precio subyacente	s	840,00	ln(s/x)	-0,07		C	89,34
volatilidad pr subyacen	v	0,30	v^(2)/2	0,05		P	115,06
tiempo a la expiración	t	1,00	t^(1/2)	1,00			
tasa libre de riesgo (a 1	r	0,04	v*t^(1/2)	0,30			
valor de la put	P		e^(-r*t)	0,96			
valor de la call	C		d1	0,05			
distribución normal			d2	-0,25			
			Nd1	0,52			
			Nd2	0,40			

Fuente. Elaboración propia.

Tabla 14. Amortización de los créditos.

	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Crédito Gob	1.054.241.770,65	1.054.241.770,65	1.054.241.770,65	1.054.241.770,65	1.054.241.770,65	1.054.241.770,65	948.817.593,59	843.393.416,52	737.969.239,46	632.545.062,39	527.120.885,33	421.696.708,26	316.272.531,20	210.848.354,13	105.424.177,07	0,00
Interés		21.084.835,41	21.084.835,41	21.084.835,41	21.084.835,41	21.084.835,41	21.084.835,41	18.976.351,87	16.867.868,33	14.759.384,79	12.650.901,25	10.542.417,71	8.433.934,17	6.325.450,62	4.216.967,08	2.108.483,54
Amortización		0,00	0,00	0,00	0,00	0,00	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07	105.424.177,07
Ahorro fiscal		3.162.725,31	3.162.725,31	3.162.725,31	3.162.725,31	3.162.725,31	3.162.725,31	2.846.452,78	2.530.180,25	2.213.907,72	1.897.635,19	1.581.362,66	1.265.090,12	948.817,59	632.545,06	316.272,53
VA ahorro fiscal	29.479.699,50															
VA coste intereses	167.051.630,52	17.922.110,10	17.922.110,10	17.922.110,10	17.922.110,10	17.922.110,10	17.922.110,10	16.129.899,09	14.337.688,08	12.545.477,07	10.753.266,06	8.961.055,05	7.168.844,04	5.376.633,03	3.584.422,02	1.792.211,01
Crédito Banco	176.511.242,89															
Interés		16.768.568,07		-16.768.568,07	-16.061.738,43	-15.287.759,97	-14.440.253,55	-13.512.234,03	-12.496.052,65	-11.383.334,04	-10.164.907,16	-8.830.729,73	-7.369.805,44	-5.770.093,34	-4.018.408,60	-2.100.313,80
Amortización		0,00	0,00	-7.440.312,06	-8.147.141,70	-8.921.120,16	-9.768.626,58	-10.696.646,10	-11.712.827,48	-12.825.546,09	-14.043.972,97	-15.378.150,40	-16.839.074,69	-18.438.786,79	-20.190.471,53	-22.108.566,33
Ahorro fiscal		2.515.285,21	0,00	-2.515.285,21	-2.409.260,76	-2.293.164,00	-2.166.038,03	-2.026.835,10	-1.874.407,90	-1.707.500,11	-1.524.736,07	-1.324.609,46	-1.105.470,82	-865.514,00	-602.761,29	-315.047,07
Pago				-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13	-24.208.880,13
VA ahorro fiscal	8.734.245,19															
VA coste intereses	49.494.056,10 €	14.253.282,86	0,00	-14.253.282,86	-13.652.477,66	-12.994.595,97	-12.274.215,52	-11.485.398,92	-10.621.644,75	-9.675.833,93	-8.640.171,08	-7.506.120,27	-6.264.334,62	-4.904.579,34	-3.415.647,31	-1.785.266,73

Fuente. Elaboración propia.

Tabla 15. Cálculo del efecto del financiamiento con capital de riesgo.

			2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033
			0	1	2	3	4	5	6	7	8	9	10
emisión de acciones	E	2.647.668.643,29											
costo de la emisión	Ce	0,05											
dividendos pagados	Div	2.159.451,26	0,00	0,00	2.674,69	8.844,11	16.779,47	26.107,80	36.474,00	49.696,57	67.374,52	92.745,49	22.926.114,03
rentabilidad exigida	Ke	0,27											
efecto financiamiento	Ecr	134.542.883,42											

Fuente. Elaboración propia.

Tabla 16. Cálculo del efecto del financiamiento con capital propio.

			2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038
			0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
emisión de acciones	E	353.022.485,77																
costo de la emisión	Ce																	
dividendos pagados	Div	4.840.653.307,78	0,00	0,00	4.457,82	14.740,18	27.965,78	43.513,00	60.790,00	82.827,62	112.290,87	154.575,82	38.210.190,05	174.460.270,65	417.491.046,48	739.887.536,85	1.117.190.822,49	1.528.011.754,34
rentabilidad exigida	Ke	0,11																
efecto financiamiento	Ecr	4.487.630.822,01																

Fuente. Elaboración propia.

Tabla 17. Base de cálculo del componente sostenibilidad.

Acción	Impacto en la sostenibilidad	Valor CUP/dosis	Reducción	Precio/Coste	Reducción lb/dos	Coste CUP/Lb	Ahorro CUP/dosis
Compra de nueva tecnología	Reducción en el uso de contaminantes químicos (dióxido de cloro)	0,320666667	0,13 lb/1000 dosis	3700 CUP/ 1,5lb	0,00013	2466,666667	0,353155667
	Reducción en la emisión de residuos (reducción de aguas residuales)	0,032489	5,3 l/1000 dosis	6,13 CUP/l	0,0053	6,13	Vs
Combinación con otra medicación	Uso futuro (ictus y ataxias espinocerebelosas)	incremento de las ventas futuras					
	ictus: tercera causa de muerte en Cuba. Tiene incidencia de 786,2/100000 personas al año						
	ataxias espinocerebelosas: Cuba tiene la mayor incidencia global de esta enfermedad. Tiene una incidencia de 33/100000 habitantes						
	promedio población cubana 2028-2048	10878658,74					
	cuántos 100 miles hay	108,7865874					
	estimación casos ictus	85528,01505					
	estimación casos ataxia espinocerebelosa	3589,957386					
	total	89117,97244					

Fuente. Elaboración propia a partir de Fariñas (2022); Noda (2022); y ONEI (2023).

Tabla 18. Cálculo del valor de la sostenibilidad.

aumento en el margen acumulado actualizado y ajustado al riesgo UM: (millones CUP)		
Izq	**MaxPres**	**Der**
195.265.709.927,33	353.822.503.178,08	404.789.601.487,90

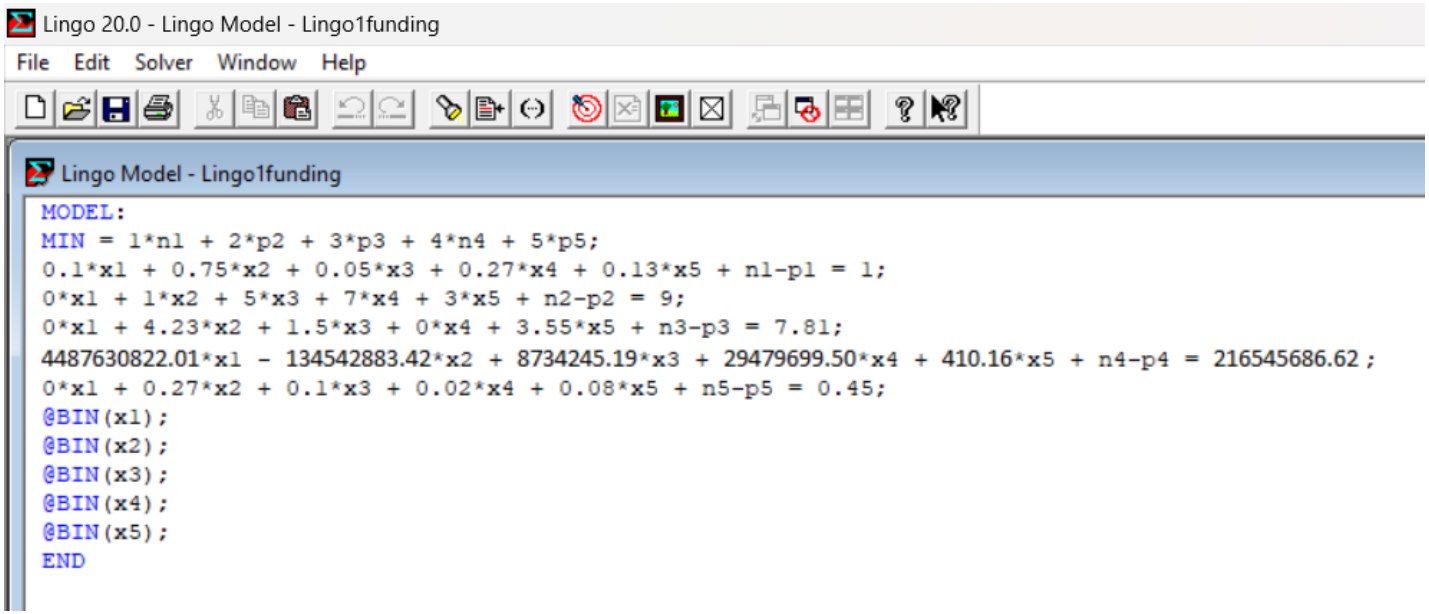
Fuente. Elaboración propia.

Tabla 19. Cómputo del valor total.

	Valor (millones CUP)		
	Izq	**MaxPres**	**Der**
rVAN	-3.639.461.106,58	3.940.917.473,83	12.359.331.191,00
Vs	195.265.709.927,33	353.822.503.178,08	404.789.601.487,90
Vefd	4.382.567.753,15	4.382.567.753,15	4.382.567.753,15
Valor creado	196.008.816.573,90	362.145.988.405,07	421.531.500.432,05

Fuente. Elaboración propia.

Figura 1. Modelo IGP en el software Lingo, versión 20.0.



Fuente. Elaboración propia.

Figura 2. Reporte (solución) proporcionado por el software Lingo, versión 20.0. al modelo de la Figura 1.