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The Chinese pharmaceutical market: an analysis of opportunities and challenges for Italian family firms

Supervisor
Ch. Prof. Alessandra Perri

Assistant supervisor
Ch. Prof. Franco Gatti

Graduand
Carmela Savarese
Matriculation Number 857414

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A mia madre.
Tutto ciò che sono lo devo a te.

中国医药市场：对意大利家族企业的市场机会与风险分析

医药行业是国民经济的重要组成部分。 医药行业在对保护与增进人民健康， 提高生活质量，为计划生育， 救灾防疫以及促进经济发展和社会进步方面均具有十分重要的作用。 随着中国人民生活水平的提高和对医疗保健需求的不断增加， 中国医药行业越来越受到公众及政府的关注， 在国民经济中占据了越来越重要的位置。

自 1978 年至今的近 30 年是中国医药市场发展最辉煌的 30 年，平均销售收入递增幅度超过 17%，远远高于全球医药市场平均增速 8%~10%的水平。国内市场旺盛的需求成为中国医药产业发展的动力源泉。中国医药产品的销售市场目前仍以内需为主，所以内需市场的发展主宰着国内的医药生产。业内人士指出，全球医药中心正在转变，中国内地将成为外资药企扩张业务的首选市场。

中国加入 WTO（世界贸易组织）后， 中国制药业在各个方面有了很大的发展和变化：医药卫生体制改革， 新的药品价格调整以及知识产权保护体系也日益完善。中国已经成为了全球仅次于美国的第二大医药市场。当发达国家的医药行业面临危机，如研发成本不断提高，药品的生命周期加速缩短以及药品申请和药品批准数目不断减少，它们更看好中国经济强健的增长势头，把中国作为研发外包基地，为的是减少产品面市的时间和成本。近年来，中国出台的一系列政策，为医药行业又好又快地发展提供了契机。中共中央、国务院颁布的 2006-2020 年《科技规划纲要的决定》，提出了“实施《规划纲要》，努力建设创新型国家”和“坚持自主创新，全面提升国家竞争力”等五大目标，这是医药行业未来 15 年的创新指南。当然，目前一些影响医药产业健康发展的体制性因素比如“以药养医”的体制尚未改变，一些政策性因素也影响了产业的发展，相信随着国家有关政策的不断完善，随着新的医改方案的出台，这些问题终将得到解决。

由于医药制造业的特征是高投入，高风险，高回报，研发周期长， 并且世界上各地的健康问题差不多， 所以制药公司的国际化比率比较高。

本文的两大主题是：中国医药市场与家族公司的国际化进程。目的是了解家族企业的国际化行为，并为扩大中国医药市场提出一些投资建议。为此，分析了四家意大利制药公司的国际化模式，并与现有的家族企业理论进行了比较。

本文分为五个章节和一个结论部分。第一章是对本文的关键词的理论分析。在第一章中我将介绍一些企业国际化的理论， 重点是家族企业的国际化。目的是确定为什么企业需要国际化，国际化成败的原因，以及确定家族企业是否拥有一些有可能影响国际化过程的特征。

在政治，技术，社会和竞争的推动因素下，全球化即“人民，产品，信息和金钱可以自由跨越的过程”，导致市场趋同，为产品的标准化和位置提供了空间世界各地经济便利的生产中心。本章讨论了三大国际化理论， 即乌普萨拉国际化模式 (Uppsala model), 国际生产折衷论（The Eclectic Paradigm of International Production） 及天生国际化企业(Born Global Firms)理论。然后分析了不同进入国际市场的方式。 最后，我将讨论关于家族企业国际化的理论。一般来说，家族企业的特征是：长期承诺，高度的信任和快速决策的可能性。 同时， 由于家族企业要避免冒风险，它们不常国际化。

第二章重点介绍中国医药市场。中国正处在一个巨大的流行病学的转变中：世界卫生组织 (World Health Organization) 的统计表明，由于膳食结构不合理， 人群体力活动减少， 生活节奏加快以及吸烟率上升了，因此中国社会呈现出慢性疾病得病率的上升。2012 年全国 18 岁及以上成人高血压患病率为 25.2%。糖尿病患病率为 9.7%，与 2002 年相比，患病率呈上升趋势。40 岁以上人群慢性阻塞性肺病患病率为 9.9%。2012 年全国居民慢性病死亡率为 533/10 万，占总死亡人数的 86.6%。心脑血管病、癌症和慢性呼吸系统疾病为主要死因，占总死亡的 79.4%。环境污染和职业暴露也越来越影响居民的健康。而且，统计数字预示，与 22%的全球趋势相比，到 2050 年为止， 超过 60 岁的人数将达到总人数的 30％。同时， 从世界卫生 组织“疾病研究的全球负担” 统计数据表明，到 2020 年在中国，因心血管疾病死亡的人数每年可能达到 400 万人。

2003 年在全球 SARS（非典型肺炎） 疫情的发病下，中国的卫生部门效率低下使全球瞩目。再者，“看病贵”和“看病难”的问题，以及医疗保障覆盖的不公平性，已经成为当前中国最大的社会问题。

因此，中国政府加快了医疗体制改革的过程，为了使自己的卫生系统适应新的社会需求并解决医药卫生体制的诸多缺陷，2009 年中国政府实施了令人期待已久的医疗改革。根据《中共中央　国务院关于深化医药卫生体制改革的意见》，2009 年至 2011 年政府在五个方面进行了改革：第一个是加快推进基本医疗保障制度建设，第二个是初步建立国家基本药物制度，第三个是建全基层医疗卫生服务体系，第四个是促进基本公共卫生服务逐步均等化，第五个是推进公立医院改革试点。同时， 中国政府也开始吸引外资。此外， 从 2009 年起，政府设立的基层医疗卫生机构全部配备和使用基本药物，而其他各类医疗机构也都必须按规定使用基本药物。 基本药物全部纳入基本医疗保障药品报销目录， 报销比例明显高于非基本药物。并且， 为了保证药品的质量与安全性，维护人民身体健康和用药的合法权益， 政府加强了用药的监管。

第三章讨论中国医药市场的各类投资类型，从出口和代工生产企业（Contract Manufacturing Organization）到外商投资企业（Foreign Invested Enterprises）等更多的结构性投资。最后，将介绍执行研发活动的合同研究组织（Contract Research Organization）。中国过去三十年的经济社会发展显著，中国对外国公司构成的挑战往往被视为促进增长，获得竞争优势或确保关键市场的长期生存能力。考虑到这个市场提供的非凡增长机会，大型制药公司正在投入大笔资金来实现两个主要目标：使中国成为药物发现，开发和制造的合适场所，并在这样一个蓬勃发展的市场中获得尽可能多的份额。然而，外商投资受到高度监管，投资中国成为一个棘手的问题，特别是在涉及国家重点行业，如医疗卫生和医药行业。 因此，想要在中国投资的企业最好先参考“外商投资产业指导目录”。 这个目录把外国企业投资的范围介绍得很清楚，让外商很容易了解其投资项目是否被列为鼓励，允许或禁止。

第四章讨论投资中国医药行业的机会与风险。 我将对中国市场进行所谓”国家吸引力分析”(country attractiveness analysis)， 试图用宏观经济学评估中国的整体“吸引力”。首先，将介绍药品市场的大环境分析（PESTLE analysis），然后讨论可能影响中国经商业务容易性的问题，以便对潜在的外国投资者运营的整个环境进行观察。其次，将对市场（在需求方面）和资源（在自然，人力和基础设施/支持行业方面）的机会进行评估，

特别关注与制药公司相关的问题。最后，制药行业主要组成部分的竞争水平将通过波特五力分析 （Porter Five Forces Analysis)进行评估 。

第五章将介绍在制药行业运作的意大利家族企业的四起案例。目的是，通过它们国际化过程的分析来确定家族企业的哪些特征有利于国际化，以及哪些特征具有不利性因素。

最后，本文分析的所有公司都以高水平的创新和在国外市场的存在为特征。他们背离了将家族企业描绘为风险厌恶 （risk averse）的传统文学，因此不如非家族企业倾向于国际化。在我看来，这些公司取得的成果可能与外部 CEO 和熟练管理人员的存在有关，而且在所有情况下，国际化进程都是在新一代现场进入的时候开始或加强的。这些企业经营的行业也起着重要的作用，因为它推动了创新药物的开发，世界各地的健康问题在全球范围内基本相同，因此药物可能销往全球各地。中国在 2015 年成为世界第二个制药市场，由于人口众多，缺乏安全，高效和优质的国内治疗，中国为外国企业提供了巨大的发展机遇，特别是现在老龄化问题的出现，正在经历流行病学转型以及人口快速的城市化，还有生活方式的变化和环境问题。面对发达国家的专利到期，药物研发管道干旱，增长放缓和收入下降，制药公司认为所谓的“医药品新兴国家”（'Pharmerging' countries) 是增长的新引擎。

虽然前景看好，但中国医药市场充满灾难性的风险。家族企业通常资金有限，并缺乏在这样复杂的环境下运营所必需的市场知识 。然而，这些公司仍然有可能进入市场。成功的关键是把“家庭”的特征，即长期承诺，耐心资本，低信息不对称和快速决策，与管理的专门知识结合起来。

制定一个精确的战略计划，与当地人员合作并任命一个专业化的管理团队，使得像 Menarini，Chiesi，Alfasigma 和 Dompé 这样的公司有所不同，仍然可以为家族企业带来不同的影响。

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Chapter 1: The internationalization process

1. The Internationalization Process

Under political, technological, social and competitive push factors, globalization, namely "the process by which people, products, information, and money can move freely across borders", has led to markets convergence, providing room for the standardization of products and the location of production centres at economical and convenient places around the world.[1]

As a consequence, business companies have undertaken unprecedented levels of international operations. By the end of the 1980s, Welch and Luostarinen observed that the term internationalization had not been conceptualized yet, since much of the early research took the multinational, or foreign investment, as a starting point. In reviewing the evolution of this concept, they broadened the rough description of an "outward movement in an individual firm's or larger grouping's international operations" to give the following definition: *"the process of increasing involvement in international operations"*.[2]

This broader definition has two main implications. Firstly, internationalization is perceived dynamically as a process; secondly, this process, usually seen as an outward movement, is strictly related to the company's *inward growth*. Therefore, they conclude that internationalization can be expected to be associated with, and perhaps dependent upon, developments along six dimensions: *operational method* (*how*, the method used to enter foreign markets), *sales objects* (*what*, the offer), *target markets* (*where*), which a focus on actual foreign market activity - the outward - together with *organisational capacity*, *personnel* and *organisational structure*, which in turn reflect the internal company situation - the inward - and form the *"foundation for additional steps forward in the overall process"*.[3]

Investigations into these dimensions can give an overview of the state of internationalization of a given company and allow comparisons to others.

From the discussion so far it is evident that there is a wide range of potential patterns of internationalization, nevertheless, it is generally agreed that *"[I]nternational expansion is based on the capability of the firm to exploit its local advantages in foreign market. On the contrary, the lack of strategic resources and the uncertainty and complexity of the process*

[1] Lasserre, Philippe (2012). Global Strategic Management, Third Edition. Palgrave Macmillan, p. 4
[2] Welch L. S., Luostarinen R. (1988). Internationalization: Evolution of a Concept. Journal of General Management, Vol. 14 No. 2, p. 36
[3] Ibidem, p. 41

make international expansion a difficult goal to achieve."[4]

Internationalization theories have been developed on the basis of consistent patterns observable from research.

Theories of Internationalization

1.1 The Uppsala Model and the business network model

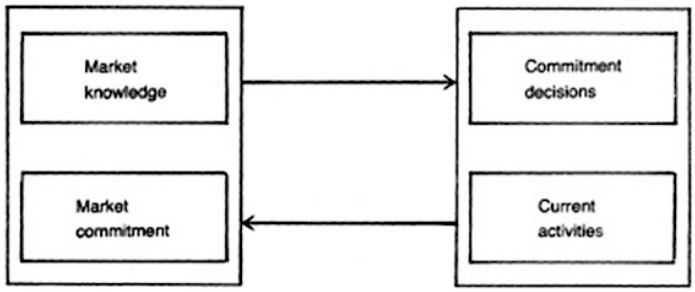
One of the first attempts to define a model to explain the characteristic of the internationalization process on the basis of empirical research was the Uppsala model, developed in 1977 by Johanson and Vahlne of the University of Uppsala by looking at the internationalization process of Swedish firms. The empirical findings supported the theory of internationalization as a learning and gradual process that enables the firm to acquire a deeper knowledge about foreign markets and operations which, in turn, provides the necessary information to keep expanding abroad (increase commitment) with a lower degree of the uncertainty factor. *"[I]nternationalization is the product of a series of incremental decisions"*[5]: the establishment chain of firms abroad usually starts with irregular exports, followed by exports via an independent representative (agent), the establishment of a sales subsidiary and finally that of a foreign manufacturing subsidiary. The time order of such establishment and the target country are related to the *psychic distance* between the home and the import/host country in terms of differences in language, education, business practices, culture and industrial development. *Psychic distance* is "the sum of factors preventing the flow of information from and to the market".[6] Therefore, closer cultural or geographical proximity makes it easier for firms to enter foreign markets, while the *liability of foreignness* captures a series of potential disadvantages that a company could face when going abroad (ie. discrimination against foreign firms, differences in both formal and informal institutions that affect business and so on).

The Uppsala, or stage model, defines a process that involves two main factors: *market commitment* and *market knowledge*. Commitment decisions, which involve both the amount of resources committed and the degree of commitment, are based on market knowledge, which in turn relates mainly to demand and supply, competition, channel of distribution and

[4] Fernàndez Z., Nieto M. J. (2005). Internationalization Strategy of Small and Medium-Sized Family Business: Some Influential Factors. Family Business Review, Vol. XVIII, No. 1. , p.79.
[5] Johanson J., Vahlne J. E. (1977). The internationalization process of the firm – A model of knowledge. Journal of International Business Studies , p. 23.
[6] Ibidem

transferability of money. Particular attention is attached to *experiential knowledge*, which constitutes the critical kind of knowledge of this model. It can only be acquired through personal experience of the foreign market and, being associated with the particular conditions of a market; it cannot be transferred to other individuals or other markets. In this respect, experiential knowledge is a resource for the firm that gives awareness of the opportunities and/or risks; the more the experiential knowledge gained in a foreign market, the stronger the commitment to that market. These two variables are, in turn, linked to two change mechanisms: firms' internationalization process changes according to the current activities in foreign markets, which allows firms to learn from the acquired experience, but also through the commitment decisions they make to strengthen their position in a foreign market.

Fig. 1.1 Uppsala Model



Source: Johanson J., Vahlne J. E. (1977 p. 26)

Johanson and Vahlne have recently revisited the Uppsala model. Following the dramatic changes in the economic and regulatory environments, company behavior and research frontier and, considering the evidence on the importance of networks in the internationalization of firms provided by, among others, Coviello and Munro (1995, 1997), they have further developed their original model into a Business Network Model.[7]

Starting from the assumption that *"relationship development is a bilateral process that involves two parties who learn interactively and make mutual commitment to the relationship (Anderson & Weitz, 1992; Blankenburg Holm, Eriksson, & Johanson, 1999)"*[8], the business network model states that *"markets are networks of relationships in which firms are linked to each other in various […] patterns. […] successful internationalization requires a reciprocal commitment between the firm and its counterparts."*[9] Although psychic distance still plays a

[7] Johanson J., Vahlne J.E. (2009). The Uppsala internationalization process model revisited: From liability of foreignness to liability of liability of outsidership. Journal of International Business Studies, Vol. 40, pp. 1411 – 1431.
[8] Ibidem, p. 1414.
[9] Ibidem

role, since the larger it is, the more difficult it is to build new relationships, a new kind of liability is introduced, namely the *liability of outsidership*, an impediment to successful internationalization due to the outsidership from the relevant network(s).

The second aspect of this model is that relationships among firms have both a learning and building trust and commitment potential. The concept of *experiential knowledge* is complemented with that of *relationship-specific knowledge* to address the kind of knowledge developed through interaction between two partners; in this new concept, interaction may also result in new knowledge. A major innovation concerns the introduction of the new dimension of trust and commitment building, excluded in the original model. Trust is fundamental for relationship development, is a prerequisite for committment, and eases opportunity development, which, in the new model is reconfigured as *"an interactive process characterized by gradually and sequentially increasing recognition (learning) and exploitation (commitment) of an opportunity."*[10]

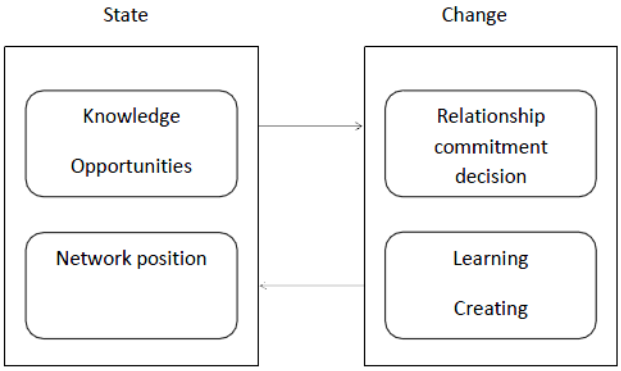
As in the 1977 model, the business network model is based on variables of state and change, which affect each other, but with some variations: *market knowledge* is replaced with *knowledge opportunities*, because opportunity is considered the critical aspect of knowledge that drives the process of internationalization; *market commitment* is replaced by *network position*, that is to say, the position that a firm enjoys in a relationship network which influences the way internationalization is promoted ; *current activities* is changed to *learning, creating, trust-building*, which is the outcome of current activities ; *commitment decisions* is adapted into *relationship commitment decisions* to clarify that commitment is to networks of relationships. This model depicts internationalization as *"a dynamic, cumulative process of learning, as well as trust and commitment."*[11]

This has some important implications, since the development of relationships, based on the development of knowledge, commitment and trust building is the very foundation of internationalization. As a consequence, a firm is likely to go abroad according to its relationship with its partners, especially if the partner has a valuable position in a foreign network. A firm will usually go where it sees opportunities. However, in absence of a relationship network, a firm is likely to go where it might be easy to find a partner (here, the psychic distance plays an important role). An initial step might be to start exports via an agent or distributor, reaffirming the validity of the original model according to which as knowledge

[10] Johanson J., Vahlne J.E. (2009). The Uppsala internationalization process model revisited: From liability of foreignness to liability of liability of outsidership. Journal of International Business Studies, Vol. 40, p. 1420.
[11] Ibidem, p. 1423.

increases, market commitment gradually increases too.

Fig. 1.2 The Business Network Internationalization Process Model (the 2009 version)



Source: Johanson J., Vahlne J. E. (2009 p. 1424)

1.2 The Eclectic Paradigm – OLI model

Dunning's Eclectic framework is another major attempt to investigate how global corporations select specific international entry modes and in particular, it explains the extent and pattern of FDI and international production undertaken by MNEs. The concept was first introduced in 1976 with the intention to offer *"a holistic framework by which it was possible to identify and evaluate the significance of the factors influencing both the initial act of foreign production by enterprises and the growth of such production."*[12] These influential factors can be divided into three sets of forces - Ownership, Location, and Internalization – hence, the presence/ absence of such OLI advantages is to determine the entry mode in a foreign market.

- **O**wnership-specific advantages relate to those assets that only the firm possesses or can acquire on more favorable terms than its competitor(s). Examples are trademark, patents, production technique, entrepreneurial skills, return to scale production. In Dunning's words, O – advantages involve:

> *"The (net) competitive advantages which firms of one nationality possess over those of another nationality in supplying any particular market or set of markets […] arise[n] either from the firm's privileged ownership of, or access to, a set of income-generating assets, or from their ability to coordinate these assets with other assets across national boundaries in a way that benefits them relative to their competitors, or potential competitors."*[13]

- **L**ocation-specific advantages can be summarized as *"the extent to which firms choose to locate these value-adding activities outside their national boundaries."*[14] In other words, the existence of raw materials, low wages, special tax treatment and/or government policies are examples of conditions that make a foreign location appealing for overseas production.

- **I**nternalization advantages are the advantages derived from own production rather than production through a partnership arrangement (ie. licensing or JV), which exist when *"firms perceive it to be in their best interests to internalise the markets for the generation and/or use of these assets; and by so doing add value to them."*[15]

As observed by Dunning in his paper *Toward an Eclectic Theory of International Production:*

[12] Dunning, J. H. (1988). The Eclectic Paradigm of International Production: A Restatement and some possible extensions. Journal of International Business Studies, Vol. 19, No. 1, p. 1.
[13] Dunning J.H. (2001). The Eclectic (OLI) Paradigm of International Production: Past, Present and Future. International Journal of the Economics of Business, Vol. 8, No. 2, p. 176.
[14] Ibidem
[15] Ibidem

some empirical Tests (1980), the more the ownership-specific advantages, the greater the inducement to internalize them and the greater the attractions of a foreign rather than domestic production base, the greater the likelihood that the firm, given the incentive to do so, will engage in international production. Ownership advantages determine which firms will supply a particular foreign market, whereas Location advantages explain the mode of entry, so, whether the firm will supply that market by exports (trade) or by setting up local production (non-trade). To understand the reasons why a firm decides to *internalize* its capital, technology, management skills itself to produce goods instead of *externalizing* their use, among others through licensing, Dunning suggests to consider the Transaction costs. A transaction cost is a cost incurred in making an economic exchange or, in other words, the cost of participating in a market, and encompasses three kinds of costs:

- *Search and information costs* are the costs incurred in determining the availability of the required good on the market and which has the lowest price.
- *Bargaining and decision costs* are the costs required to negotiate an acceptable agreement with the other party of the transaction.
- *Policing and enforcement costs* are the costs related to the legal system to take action for making sure the other party sticks to the terms of the contract.

Since transaction costs have been defined any costs that arise due to the existence of institutions,[16] *"[t]he basic incentive of a firm to internalize its ownership endowments is to avoid the disadvantages, or capitalize on the imperfections, of one or the other of the two main external mechanisms of resource allocation – the market or price system and the public authority fiat."*[17]

Lance Eliot and Keith D. Brouthers and Steve Werner conclude that the main difference between transaction cost theory and the OLI paradigm is that, although they both examine the economic rationale for entry mode selection, the former determines entry choice on a least-cost basis ignoring the impact of locational differences, whereas the latter enriches and extends the transaction cost approach by including locational and ownership-specific advantages as well as transaction cost variables.[18]

The OLI model is also a further development of the Internalization Theory (Buckley &

[16] Cheung, S. N. S. (1987). Economic Organization and transaction costs. The New Palgrave: A Dictionary of Economics, Vol. 2, pp. 55 – 58.
[17] Dunning, J. H. (1980). Toward an Eclectic Theory of International production: some empirical Tests. Journal of International Business Studies, Vol. 11, No. 1, p. 11.
[18] Brouthers L. E., Brouthers K. D., Werner S. (1999). Is Dunning's Eclectic Framework Descriptive or Normative? Journal of International Business Studies, Vol. 30, pp. 831 – 844.

Casson, 1976), which focuses on imperfections in intermediate product markets and distinguishes between knowledge flows – that link R&D to production- and flows of components and raw materials from an upstream production facility to a downstream one. Internalization usually occurs when the transaction costs on the free market are higher than internal transaction costs, otherwise, the firm may choose to license or outsource production to an independent firm; or it may produce at home and export to the foreign country instead.

Dunning's conclusions can be resumed as follows:

-If a firm has only ownership advantages, then, it should choose licensing arrangements means of technology transfer.

-If a firm has ownership advantages and internalization advantages, it should select domestic production and exports.

-If a firm has ownership, location and internalization advantages at the same time, it is likely to choose a foreign direct investment.

Fig. 1.3 Eclectic approach

Source: Dunning (1981)		Categories of advantages		
		Ownership advantages	Internalization advantages	Locational advantages
Form of market entry	Licensing	**Yes**	No	No
	Export	**Yes**	**Yes**	No
	FDI	**Yes**	**Yes**	**Yes**

Source: Dunning (1981)

It is important to note that the significance of each of these advantages and the configuration between them is likely to be context specific and to vary across industries or types of value-added activities, regions, countries and among firms. Moreover, Dunning's underlines that no single theory can explain all kinds of foreign-owned value-added activities because the motivation for and expectation from such production vary greatly. Since we can distinguish among *market - seeking*, *resource- seeking* and *strategic asset - seeking* FDI, the variables necessary to explain these different kinds of investments are likely to be different.[19]

Dunning's OLI paradigm has also been revised to include strategic alliances and even broad

[19] Dunning J.H. (2001). The Eclectic (OLI) Paradigm of International Production: Past, Present and Future. International Journal of the Economics of Business, Vol. 8, No. 2, p. 176.

network relationships.

In his paper *The Eclectic (OLI) Paradigm of International Production: Past, Present and Future* (2001) he introduces the dynamic concept of *Investment Development Path* (IDP) to explain the changing international position of countries as they passed through different stages of development:

> "The basic hypothesis of the IDP is that as a country develops, the configuration of the OLI advantages facing foreign-owned firms that might invest in that country, and that of its own firms that might invest overseas, undergo change, and that it is possible to identify both the conditions making for the change and their effect on the trajectory of the country's development."[20]

The strategic response, together with technological and/or organizational innovations, changes in senior management, increases in labor productivity, new marketing techniques, mergers and acquisitions and so on, is considered one of the main *endogenous* variables which might affect the OLI configuration of firms. Coupled with *exogenous* changes – changes in population, raw material prices, exchange rates, national government policies and so on – changes in endogenous variables, the way in which these two sets of variables interact, is itself an important factor determining the movement towards a new OLI configuration. [21]

Considering the increasing importance of strategic asset-acquiring FDI and non – equity alliances as forms of international economic involvement, the model has been extended, which *"suggests that in future, the eclectic paradigm might better address itself to explaining the changing characteristics of international production than to its level and composition at a particular moment of time."*[22]

More recently, Dunning and Lundan have adopted an institutional approach by incorporating an institutional dimension into the three components of the OLI paradigm, to understand the different forms of contemporary MNEs. Their conclusion is that *"the prevailing ownership-based theories of the firm are increasingly being challenged by new forms of organising, as exemplified by the Asian network multinational enterprise (MNE)"* and that *"in a dynamic, complex and volatile global economy, the role of both firm and location specific institutions in reducing the transaction costs of cross-border value added and exchange activities is becoming more important."*[23]

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[20] Ibidem, p. 180.
[21] Ibidem, pp. 179/182.
[22] Ibidem, p. 186.
[23] Dunning J. H., Lundan S. M. (2008). Institutions and the OLI paradigm of the multinational enterprise. Asia

1.3 The "Born Global" concept

The "born global" phenomenon was first addressed in Australia in the early 1990s by a study conducted by McKinsey & Co (1993), the results of which showed that many Australian firms went global since their very beginning, proving wrong traditional internationalization theories, such as the Uppsala Model, that saw internationalization as an incremental, learning oriented process which may be due to lack of knowledge about foreign markets, high-risk aversion, or high perceived uncertainty.

As reported in a paper draft in occasion of the 23rd Australian and New Zealand Academy of Management Conference, based on 126 studies published from the 1970s to 2009, Born Global firms have been defined as firms that are "less than 20 years old, have internationalised within 3 years of inception and have generated at least 25 percent of their sales from export" (Knight, Madsen and Servais 2004), yet conflicting definitions provide for internationalisation within 2 to 8 years (Chetty & Campbell-Hunt 2004), having an export-to-domestic sales ratio of 50 (Gabrielsson & Gabrielsson 2003) or 76 (Cavusgil 1994) percent, with still other definitions including a requisite for "high technological orientation" (Luostarinen & Gabrielsson 2006), innovation (Jones & Coviello 2005) and a "superior performance" in relation to traditional exporters (Knight & Cavusgil 2004).[24]

Oviatt and McDougall (1994) made a first attempt to develop a theory of what they defined *International New Ventures*, *"a business organization that, from inception, seeks to derive significant competitive advantage from the use of resources and the sale of outputs in multiple countries"*[25], for which stage theories of the MNE and the common emphasis on organizational scale as an important competitive advantage in the international arena are inappropriate explanations, for these firms are instantly international. Their conclusion is that the internalization of some transactions, the extensive use of alternative transaction governance structures, and some advantages over indigenous firms in foreign locations are the necessary conditions for the existence of an international new venture. However, these are not sufficient conditions for sustainable competitive advantage, the development of which requires that its resources be unique and that the international new venture limits the use of its knowledge by outsiders in many countries for it to have commercial value.

Pacific J Management, Vol. 25, pp. 573/588.

[24] 23° Annual Australian and New Zealand Academy of Management Conference (2009)" 'Defining the Born Global Firm'. A Review of the Literature"
http://www.cemi.com.au/sites/all/publications/BaderMazzarolANZAS2009.pdf

[25] Oviatt B. M., McDougall P. P. (1994). Toward a Theory of International New Ventures. Journal of International Business Studies, Vol. 25, No. 1, p. 49.

A major feature that distinguishes new ventures from established organizations is the minimal use of internalization (due to their poverty of resources and power) and the greater use of alternative transaction governance structures; hybrid structures, such as licensing and franchising, are often useful alternatives to both internal control and market control over the exchange of resources, since hybrid partners mutually benefit from sharing complementary assets. Alternatively, new ventures can build on network structure, which has been proved to be a valid resource-conserving alternative when there is a lack of internalization opportunity. This idea is supported by Larson's (1992) empirical study on four entrepreneurial organizations in seven intimate network alliance that show that even after two of the seven relationships failed, proprietary knowledge was protected and trust was maintained.

"Networks depend on the social (i.e., informal) control of behavior through trust and moral obligation, not formal contract. Cooperation dominates opportunism because business and personal reputations are at stake that may greatly affect economic rent in and beyond a spot transaction."[26]

Finally, Oviatt and McDougall's (1994) framework describes sustainable international new ventures as controlling assets, especially unique knowledge, that create value in more than one country. Their internationality occurs at inception largely because competitive forces preclude a successful domestic focus, suggesting that larger sample sizes of international new ventures are likely to be found in industries where international competition for unique knowledge is a dominant characteristic. The framework also identifies ways of protecting rents derived from such knowledge (i.e., direct patent protection, uncertain imitability, license fees, and network alliances) and distinguishes among three main types of international new ventures on the basis of the number of value chain activities that are coordinated and of the number of countries entered:

1) *New International Market Makers* may be either Export/Import Start-ups or Multinational Traders. Export/Import Start-ups serve a few nations with which the entrepreneur is familiar, while Multinational Traders serve an array of countries and are constantly scanning for trading opportunities where their networks are established or where they can quickly be set up.

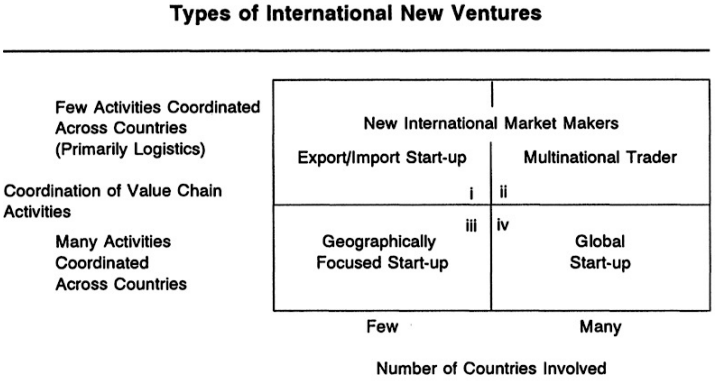
2) *Geographically Focused Start-ups* serve a particular region of the world. Unlike Multinational Trader, they are geographically restricted to the location of the specialized

[26] Ibidem, p. 55.

need, and more than just the activities of inbound and outbound logistics are coordinated, such as technological development, human resources, and production.

3) *"Global Start-ups"* are *"the most radical manifestation of the international new venture because it derives significant competitive advantage from extensive coordination among multiple organizational activities, the locations of which are geographically unlimited."*[27]

Fig. 1.4 Types of International New Ventures



Source: Oviatt B. M., McDougall P. P. (1994 p. 59)

Madsen and Servais (1997) generated some proposition regarding the conditions for the rise of this phenomenon and concluded that three main factors that are strictly interrelated can be considered as the driving forces of Born Globals, namely, *new market conditions*, such as the increasing specialization and hence the number of niche markets, the emergence of global sourcing activities and of networks across borders, that, together with increasing homogeneous markets, allow innovative products to spread very quickly all over the world; *technological developments* in the areas of production, transportation and communication, which has removed many of the cost barriers that impeded internationalization; *more elaborate capabilities of people*, including the founder/entrepreneur who starts the Born Global Firm, that steam from an increased mobility and education across borders. Such mobility across nations, languages, and cultures undoubtedly creates a much higher number of potential employees with a competence to communicate with, understand and operate in foreign cultures.[28]

They also argue that a network approach to internationalization processes offers a valuable approach when analyzing such firms. This concept is based on Johanson and Mattsson (1988) attempt to relate the internationalization process of firms to the notion of industrial networks:

[27] Ibidem, p. 59.

[28] Madsen T. K., Servais P. (1997). The internationalization of Born Globals: an evolutionary Process? International Business Review, Vol. 6, No. 6, pp. 565 -566.

> "Instead of regarding the internationalization as a process between a firm and a somewhat anonymous market, they stress the relationships between independent firms forming the network. Due to an informal division of labor among the involved firms, each firm will become dependent on external resources to the extent to which it builds exchange relationships to other firms in the network. Such relationships often take time and effort to establish and develop; especially in long term relationships mutual trust and knowledge imply a high degree of commitment and interconnectedness by different types of bonds. This means that each firm cannot be analyzed separately, but that its state and change aspects must be understood in an interorganizational setting.*"*[29]

Another important contribution of Madsen and Servais (1997) is the importance attached to the entrepreneur. Restating the Uppsala stage model, they argue that the firm's uncertainty regarding new markets can be reduced thanks to the founder's knowledge and international experience, which allows the firm to *leapfrog* some stages. In this way, the learning process is no more gradual but can be applied simultaneously to more markets. In this sense, any differences between traditional exporters and Born Globals comes from differences in the founder's background, as well as in market conditions.[30]

Knight and Cavusgil (2004) focus on the firm's internal capabilities that allow an early internationalization. They define born globals as *"business organizations that, from or near their founding, seek superior international business performance from the application of knowledge-based resources to the sale of outputs in multiple countries."*[31]

Based on the *Resource-Based View*, their study suggests that Born Globals are highly innovative firms whose possession of the foundational capabilities of international entrepreneurial orientation and international marketing orientation engender the development of specific organizational strategies, such as global technological competence, unique products development, quality focus and leveraging of foreign distributor competences. Being young, Born Globals lack a set of tangible resources – finances, human resources, plant, equipment - that older firms have relied upon to become international; however, they leverage a collection of intangible knowledge-based capabilities that engender early internationalization. [32]

More recently, Taylor and Jack (2016) have focused on the ways in which industry specificities impact the internationalization of Born Globals. Their findings, based on the analysis of four Australia-based born global firms can be summarized as follows:

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[29] Ibidem, pp. 573.
[30] Ibidem, pp. 570.
[31] Knight G. A., Cavusgil S. T. (2004). Innovation, organizational capabilities, and the Born-Global firm. Journal of International Business Studies, Vol. 35 , No. 2 , pp. 124.
[32] Ibidem, pp. 124-141.

- High levels of *global integration* motivate a firm to internationalize to gain international customers to survive. The founders' global aspirations are second to the pressure placed on the firms to compete globally in order to survive. On the contrary, in presence of low levels of global integration or competitive pressure, it is the founder's role and global aspiration the primarily motive for the firm to internationalize.

- High levels of *local competition* affect the choice of international markets to improve a firm's position in its domestic market. To gain credibility in the home market, these firms are likely to choose large, well-known markets.

- *Industry specific trends* determine the choice of the entry mode, in the sense that firms are more likely to follow the internationalization pathways of other leading firms, thereby allowing the firm to rely on previously successful strategies as well as compete directly with established competitors.[33]

[33] Taylor M., Jack R. (2016). Born Global Firm Internationalisation: The Influence of Industry Factors. Contemporary Management Research, Vol. 12, No. 3, pp. 289-308.

2. Foreign Market Entry Strategies

2.1 Why and when to enter? Some influential factors

Irrespective of whether the reference theory is the *Uppsala*, *OLI* or *born global* model, once a firm has decided to enter a foreign market, it has to choose the appropriate entry mode. There are six main legal forms of entry – *representative office, licensing or franchising, distribution agreements, joint ventures, acquisition, FDI* (that will be discussed in detail in the next section) - which differ from each other on the basis of two major dimensions, control, and investment intensity. Control means *"authority over operational and strategic decision making"*; resource commitment indicates *"dedicated assets that cannot be redeployed to alternative uses without loss of value."*[34]

The actual decision is contingent upon many external and internal factors, the former composed of the overall *market attractiveness*, *country risks,* and *government requirements*; the latter composed of the intended entry *timing*, the *internal capabilities* of the firm and the *strategic objective*, together with the expected *return on investment* (ROI).

Before examining the modes of entry, it is useful to look into the firm's potential strategic objective and timing of entry, for they might have a major impact on the choice of how to entry a foreign market.

There are four main types of strategic objectives, not necessarily independent of each other:[35]

- *Market development*. A firm may want to entry a foreign country that offers size and growth opportunities. This is perhaps the most common entry objective. China, for its market size determined by the *"middle-class effect",*[36] is a current example of "key country", in which a presence is needed for global long-term competitiveness.

- *Resources access*. An investment in a resource - rich country is based on the presence of a key resource, be it mineral, agricultural or human, that contributes to the competitive advantage of the firm. Again, China perfectly fits in the example of a country that offers low-cost labor force.

- *Learning*. It is the objective of investments in countries where a particular industry is state

[34] Chan K. W., Hwang P. (1992). Global strategy and multinationals' entry mode choice. Journal of International Business Studies, p. 31.

[35] Lasserre, Philippe (2012). Global Strategic Management, Third Edition. Palgrave Macmillan, p. 207

[36] The "middle-class effect" is determined by the emergence of middle classes that triggers the demand for most mass consumer goods, durables and branded products. For instance, in China between 1990 and 1995 the GNP per capita increased by 36 per cent, while the demand for VCRs increased by 158 per cent and refrigerators by 79 per cent. See Lasserre, Philippe (2012). Global Strategic Management, Third Edition. Palgrave Macmillan, p. 181.

of the art and in which a foreign investor gains knowledge by being present. The establishment of joint R&D labs in Texas and R&D centers in the Silicon Valley and Dallas, in the United States, by the Chinese Huawei, company that operates in the telecommunication products industry is a clear example of investments moved by learning objectives.

- *Coordination*. Investments for coordination objectives are directed to hub countries whose location and infrastructure advantages may serve as regional coordination of activities.

Regarding the timing of entry, four phases can be distinguished on the basis of the moment in which entering a foreign country, for whatever objective, starts to be possible or desirable in order to gain a competitive advantage, as well as the type of risk incurred, that is related to a company's aversion or willingness to take a certain amount of risk:

- *Premature phase*. In this phase, the target country lacks purchasing power or demand for a certain kind of product or service so that a significant investment in the country would not generate enough long-term revenues. Representative offices, listening posts or distribution agreements could be possible investments in this phase.

- *Window phase*. A window of opportunity opens when the market takes off but the competitive context is not yet well established. To take a first mover approach in this phase can lead to a strong competitive advantage,[37] although substantial pioneering costs related to consumer's learning and education, as well as operating and investment uncertainties are potential disadvantages. On the other hand, a firm can potentially gain by waiting and adopting a second or follower mover strategy, which allows to take advantage of the window of opportunity while building on rival's experience.

- *Competitive growth phase*. This phase begins when various competitors have entered the market and compete for market share in a high growth situation. Since a new entry in a foreign market in this phase is hazardous, acquisitions or joint ventures allow to access a market without affecting the competitive landscape.

- *Mature phase*. It occurs when competition is well established and acquisition or direct investment with an innovative product is generally the only way to enter.

[37] This hypothesis is supported by empirical empirical evidence, see Luo and Peng (1998).

2.2 How to enter? – Entry modes

Having examined the variables that affect a firm's entry choice, the types of entry modes will be discussed here.

Generally speaking, entry modes can be divided into three main categories: exports, collaborative strategies, and foreign direct investments.

Export occurs whenever a firm based in one country sells goods or services to customers that reside in another country. The level of commitment varies from occasional transactions to the establishment of a foreign agent or distributor. Export is said to be *direct* when a firm's commercialization activities in foreign markets are operated through the firm's own structures, which include *local agent/distributors* as well as *representative*, *technical and procurement office*; while *indirect* exports are operated through the intermediation of third parties – *buyer, broker, export management company, trading company, consortium, piggyback* –.

Collaborative strategies are mid - long term contracts between two or more companies, the most common of which are *licensing* and *franchising*. The difference between these two is that while the former is an arrangement by which the licensor company transfer to a licensee the right to exploit commercially its product and/or technology (where the brand name of the licensor may or may not be included) in exchange for a royalty - usually calculated as a percentage of sales or as a fixed amount per unit sold - the latter entails the right for the franchisee to use the franchisor's brand name on condition that the franchisee adopts a certain kind of operating policies so that it can maintain the quality standards associated with the brand name.

Both *strategic alliances* and *Joint ventures* allow companies with complementary skills to benefit from one another's strengths. They are common in technology, manufacturing, and commercial real estate development, and whenever a company wants to expand its sales or operations into a foreign country. A strategic alliance is a legal agreement between two or more companies to share access to their technology, trademarks or other assets without creating a new company, whereas, in the case of joint ventures, two or more companies invest in a new one that is jointly owned by each of the parent companies. Some governments may require foreign investors to ally with local firms before granting access to the market or resources. Countries such as China, which endorsed wholly owned foreign ventures in March 1992, still ban foreign investments or force foreign companies to share ownership with local firms in strategically sensitive sectors like media, telecommunication, defense or legal

professions.

Foreign direct investments (FDI) includes *mergers and acquisitions* (M&A) and *wholly owned subsidiary*. In a merger, two companies cease to exist as independent legal entities and combine to form a new one, while the acquisition entiles the purchase of one company by another in order to assume control of it. An acquisition occurs whenever a buying company obtains more than 50% ownership in a target company.

The last and most complex internationalization mode is the *greenfield* investment, the one that gives the most control over operations but also the riskiest form of investment, due to the high mobilization of resources required to build a company and its operations in a foreign country from scratch.

Each mode of entry has its advantages and disadvantages and, as previously mentioned in this work, its choice is a function of both the company's strategic objectives, internal capabilities and entry timing, as well as country risks, opportunities, and government policies.

Generally, the appointment of an agent/distributor, the settlement of a representative office and licensing/franchising require low resource commitment and allow a rather quick access to the market; however, the advantage of a low risk is counterbalanced by low returns, and low, if any, market control which increases the risk of technological leakage, in the case of licensing. On the other hand, joint ventures, M&A and greenfield operations require medium to high upfront investments that makes them riskier in both financial and political terms; at the same time, they ensure higher returns and control of the market, reducing the risk of technological leakage.

3. The Internationalization Of Smes

3.1 Theories of family firms

"Family businesses, which bring together the economic and noneconomic realities of organizational life, offer a particularly attractive site for understanding how the confluence of economic and noneconomic considerations affect strategic decisions."[38]

Family firms represent the dominant form of economic organization throughout the world, yet it is recognized that they have received scarce attention, particularly with respect to the development of theories of the firm.

In reviewing the theoretical perspectives in family businesses, Nordqvist et al. (2015) distinguish between:

- Theories borrowed to explain family business: Resource Based View (RBV), Agency Theory, Social Capital Theory and the Corporate Entrepreneurship perspective.
- Existing theories that have a great potential for being modified/extended in the future by using family business evidence: Organisational Identity Theory (Whetten et al. 2014) and theory on emotions in organizations (Brundin and Härtel 2014).
- New theories generated by using unique family business findings: the Socioemotional Wealth perspective.[39]

In this section, the main theories concerning family firms are presented, including the Resource Based View (RBV), Social Capital Theory, Agency Theory and Stewardship Theory, which have been mostly used to explain why family firms need to be examined differently compared with non-family firms, on the basis of some distinctive features that make these firms unique; and the recently developed Socioemotional Wealth perspective, which seems to be able to explain many decisions made within family firms.

The *Resource Based View (RBV)* is a model that sees resources and capabilities within a firm as a source of a competitive advantage that is key to outperform other firms. Beginning with the "theory of the growth of the firm" proposed by Penrose (1955, 1959), this approach was further developed in the 1980s and 1990s by Wernerfelt (1984) and Barney (1991). The framework proposed by Barney, suggests that firm's resources that are valuable, rare,

[38] Chrisman J. J. et al. (2003). An introduction to theories of family business. Journal of Business Venturing, Vol. 18, pp. 442.

[39] Nordqvist M. et al. (2015). Theoretical Perspectives on Family Businesses. Edward Elgar Publishing, pp. 8 – 9. http://www.e-elgar.com/shop/eep/preview/book/isbn/9781783479665/

imperfectly imitable and non-substitutable are the sources of a sustained competitive advantage, an advantage deriving from the implementation of a value creating strategy, whose benefits cannot be duplicated by other firms.

The underlying assumption of this model is that, in order to be so, strategic resources are heterogeneously distributed across firms and immobile. Being firm resources the sum of "all assets, capabilities, organizational processes, firm attributes, information, knowledge, etc. […] that enable the firm to conceive of and implement strategies that improve its efficiency and effectiveness",[40]a resource is strategic when:

- **V**aluable, in the sense that exploits opportunities and/or neutralizes threats in the firm's environment;
- **R**are among both current and potential competitors, which means that is only available to the firm;
- **I**mperfectly imitable, implying that a sustainable competitive advantage exists only if competitors cannot obtain the critical resource or capability that generated it;
- **N**on- substitutable, because when competitors find a substitute they hold the potential of implementing a similar strategy.

The most widely known study in which the RBV is applied to family firms stems from Habbershon and Williams (1999), which conceptualized the term "familiness" as "the unique bundle of resources a particular firm has because of the systems interaction between the family, its individual members, and the business."[41]This means that performance research should assess the impact of such 'distinctive familiness' on the firm's strategic capabilities, rather than assessing how family businesses may or may not have a competitive advantage. In order to do so, resources are divided into four categories: physical capital resources (plant, raw materials, location, cash, access to capital, intellectual property), human capital resources (skills, knowledge, training, relationships), organizational capital resources (competencies, controls, policies, culture, information, technology), and process capital resources (knowledge, skills, disposition, and commitment to communication, leadership, and the team). Once these family business resources are identified, it can be assessed under what conditions they provide a competitive advantage.[42]

Starting from the assumption that family firms have unique characteristics, in their resource

[40] Barney J. (1991). Firm Resources and Sustained Competitive Advantage. Journal of Management, Vol. 17, No. 1, p. 101.
[41] Habbershon T. G., Williams M. L. (1999). A Resource-Based Framework for Assessing Strategic Advantages of Family Firms. Family Business Review, Vol. 12, No. 1, p. 11.
[42] Ibidem

management process model, Sirmon and Hitt (2003) identify five family firm-specific resources – human capital, social capital, survivability capital, patient financial capital and governance structure (which are discussed in detail in section 3.4) – that have the potential to provide competitive advantages over non-family firms (however, a firm's familiness can also create disadvantages). In particular, they argue that managing strategic resources is critical to gaining and maintaining competitive advantages. The model separates resource management phases into three components: resource inventory, which involves resource evaluation, addition, and shedding; resource bundling and resource leveraging. The combination of family firms'-specific resources and the different way in which they are managed compared to the non-family counterpart, results in a potential competitive advantage.

Stemming from the RBV, *Social Capital Theory* addresses the importance of the interaction between individuals or organizations in a social network to explain both differences between firms and in firms' performances. Nahapiet and Goshal (1998) define social capital as "the sum of the actual and potential resources embedded within, available through, and derived from the network of relationships possessed by an individual or social unit",[43]which is composed of three clusters: structural, cogntitive and relational. Structural embeddedness describes the configuration of network ties between people or units in terms of density, connectivity, and hierarchy; the relational embeddedness refers to those assets created and leveraged through personal relationships developed through a series of interactions, such as trust and trustworthiness, norms and sanctions, obligations and expectations, while the cognitive dimension addresses the existence of shared codes and narratives, which provide shared representations/interpretations among parties. From a process perspective, Nahapiet and Goshal (1998) propose that four dynamic factors influence the development of social capital: time (also referred to as stability), in the sense of stable and continuous accumulation of goodwill over time, interaction as a precondition for the development and maintenance of dense social capital, interdependence between the members of the network, and closure, which refers to the existence of strong boundaries that distinguish members from non-members. Network closure facilitates the development of norms, identity, and trust, in other words, the denser the social network, the higher the adherence to norms, which facilitates transactions.

As a resource rooted in relationships, social networks may be used to pursue economic ends.

[43] Nahapiet J., Goshal S. (1998). Social Capital, Intellectual Capital, and the Organizational Advantage. The Academy of Management Review, Vol. 23, No. 2, p. 242.

Social capital's contributions can be derived from both intra- and inter-organizational relationships: internal contributions include the reduction of transaction costs, facilitation of information flows, knowledge creation and accumulation and improvement of creativity, while the increase of alliance success can be seen as an external contribution.[44]

With regard to family businesses, Sirmon and Hitt (2003) conclude that each of the dimensions of social capital is embedded within the family firm, as well as within the interactions the family has with external stakeholders. By increasing the family's social capital, the firm can build more effective relationships with suppliers, customers, and other organizations (ie. financial institutions).[45]

In their exploration of the social capital of family firms, Arregle et al. (2007) state that family social capital "is probably one the most enduring and powerful forms of social capital",[46]because family members are prone to operate more as a team, as they benefit from information, influence, and solidarity provided by social interactions with other members of the family. Contrary to families, the organizational social capital of a business entity has to be created. In family firms, it is the family social capital that affects how organizational social capital is built through institutional isomorphism, organizational identity and rationality, human resource practices, and overlapping social networks.

Firstly, being the family a significant, if not the sole, owner of the firm, it has a strong coercive influence on the firm's development, including its organizational social capital, in setting the firm's behavior as well as in protecting its interests. Secondly, because family members are usually involved in the firm's governance and management activities, they transmit the main characteristics of their family's social capital to the firm's mission, values, and practices and affect the managerial rationalities of the firm. Thirdly, family members affect human resources practices within the firm, in the sense that they are more likely to select and promote employees that share family's values and goals, thus supporting an organizational social capital that is in line with the family social capital. Lastly, family social capital influences the organizational social capital because the firm's network is often initially based on the family's networks. Such overlapping of networks shapes social conventions, habits, traditions and, more generally, the social framework in which the firm operates.[47]

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[44] Arregle J. et al. (2007). The Development of Organizational Social Capital: Attributes of Family Firms. Journal of Management Studies, Vol. 44, No. 1, p. 73.

[45] Sirmon D. G., Hitt M. A. (2003). Managing Resources: Linking Unique Resources, Management, and Wealth Creation in Family Firms. Entrepreneurship Theory and Practice, p. 342.

[46] Arregle J. et al. (2007). The Development of Organizational Social Capital: Attributes of Family Firms. Journal of Management Studies, Vol. 44, No. 1, p. 73.

[47] Ibidem, pp. 79 – 82.

The drivers of social capital are the same for both family and non-family businesses. However, Arregle et al. (2007) found that families tend to be more stable, have more frequent interactions, and are more interdependent because family members are similarly interested in the success of the family firm and tend to be characterized by more dense (or 'closed') networks. All these factors strengthen family social capital, thus contributing to the development of the family organizational social capital.

Being unique to each family firm, family social capital can be a decisive resource, especially in the context of innovations, in the sense that the family's social networks can be used in order to expand, for example, the in-depth knowledge of technologies from other family firms or suppliers.[48]

It should be noticed that only a strong family social capital can lead to unique attributes that drive better performance than non-family competitors. As a matter of fact, family ownership and/or management is not sufficient to create a competitive advantage: a firm owned and managed by a family with a weak social capital is likely to be more similar to a non-family firm. Therefore a strong family social capital is likely to support family firm's uniqueness from a strategic point of view.[49]

Agency Theory and *Stewardship Theory* are two interconnected theories both concerned with the relationship between principal and agent. Jensen and Meckling (1976), describe the agency relationship as a contract under which the principal(s) delegate work to an agent, who acts as a representative of the principal and is supposed to act in the principal's interest. Ideally, in a situation where the principal and agent have the same interests, no conflict of interest exists and no agency costs arise. However, based on the assumption that man is a rational actor who seeks to maximize his/her own wealth, literature often describes the principal-agent relationship as characterized by divergent interests, opportunistic behaviors, and asymmetric information.[50] The divergence between ownership (principal/shareholder) and control (agent/manager) arise from the fact that the principal does not directly manage the company. Managers run the company on a day-to-day basis and can manipulate the information contained in the annual reports, the main source of information for shareholders, thus creating an asymmetry of information; furthermore, managers may want to increase their

[48] Kraiczy N. (2013). Research on family firms – Definition, theories, and performance. *In:* Innovation in Small and Medium-Sized Family Firms, p. 12.

[49] Arregle J. et al. (2007). The Development of Organizational Social Capital: Attributes of Family Firms. Journal of Management Studies, Vol. 44, No. 1, pp. 86 - 87.

[50] Kraiczy N. (2013). Research on family firms – Definition, theories, and performance. *In:* Innovation in Small and Medium-Sized Family Firms, p. 12.

own wealth, or create job security, thus making decisions that are not consistent with the objective of shareholders'wealth maximisation. The principal can limit such divergences by establishing appropriate incentives for the agent and by incurring in monitoring costs designed to control the activities of the agent. Monitoring expenses, incentives (bonding expenditures) and the 'residual loss' ("the dollar equivalent of the reduction in welfare experienced by the principal due to this divergence"[51]) are all agency costs. Jensen and Meckling's theory falls within the so-called positivist line, which has focused mainly on the agency case between owner and CEO of large, public corporations,[52] and has been most concerned with identifying the contract alternatives that can solve the agency problem. Two main propositions are suggested:

1) Outcome-based contracts: by increasing the firm ownership of the managers, managerial opportunism decreases.
2) Information systems: when the principal has information to verify agent behavior, the agent is more likely to behave in the interests of the principal.[53]

The second approach to agency theory is the principal-agent research, which has a broader focus and more theoretical implications. Both positivist and principal-agent streams have a common unit of analysis – the contract between the principal and the agent – and common assumptions about people, organizations, and information. However, the two approaches differ in terms of dependent variables and style. It can be said that they are complementary, because positivists researcher identify various contracts alternatives, whereas principal-agent researchers indicate which contract is the most efficient under varying levels of outcome uncertainty, risk aversion, information.[54]The optimal contract – behavior versus outcome – is determined considering the trade-off between the cost of measuring behavior and the cost of measuring outcomes and transferring risk to the agent.

As a result of information asymmetry, the formal literature distinguishes between two aspects of the agency problem: *moral hazard* and *adverse selection*. The former refers to a situation after contracting where the agent acts in his or her own interests rather than in the interests of the principal; the latter describes a situation before contracting in which the principal is not able to verify the agent's skills or abilities and chooses an agent who is less able, committed,

[51]Jensen M. C., Meckling W. H. (1976). Theory of the firm: Managerial Behaviour, Agency Costs and Ownership Structure. Journal of Financial Economics, Vol. 3, No. 4, p. 308.
[52] Eisenhardt K. M. (1989). Agency Theory: An Assessment and Review. Academy of Management Review, Vol. 14, No. 1, p. 60.
[53] Ibidem
[54] Ibidem

and industrious than the principal expected.[55]In order to control moral hazard and adverse selection, principals have to incur into agency costs, investments in information systems, aimed at controlling agent opportunism.

Although it has been argued that the agency problems outlined by Jensen and Meckling are mitigated in family firms, because it is supposed that family members' interests are more aligned, yet agency relationships in family firms exist (ie. Schulze et al. (2001), for instance, rather argue that private ownership and family management expose firms to agency hazards). Three types of agency relationship can arise in family firms: *family owner vs. external manager*, *family owner vs. external shareholder*, and *family owner vs. family manager*. While the first two cases present similarities with non-family firms and agency theory still applies, the third one has been better explained by the stewardship theory, an extension of the agency theory, which integrates other disciplines such as sociology and psychology.

- *Family owner vs. external manager.* Family firms may decide to employ external managers when capable family members are missing or family members cannot agree on which member should lead the company. In this case, the relationship between principal and agent seems to be similar to non-family firms. However, the strong interest of the family in the firm's success (also due to the fact that very often all the family money is invested in the firm) leads to a close and more effective (because family has a good understanding of its firm) monitoring of the external management, that is likely to curb the opportunistic behaviour of external managers.
- *Family owner vs. external shareholder.* In publicly traded family firms, the family is often the major stakeholder but, in order to raise funds, allows external shareholders to hold minority stakes. In such case, information asymmetry may exist to the detriment of minority stakeholders. In particular, when family business groups control a large number of firms, managers act for the controlling family, but not for shareholders in general. In addition, conflict of interest increases when the firm is also managed by family members.[56]
- *Family owner vs. family manager.* In this case, agency costs may decrease, because family owners, who also manage the firm, ideally act in the interests of the family. This view is supported by *Stewardship Theory*.

[55] Kraiczy N. (2013). Research on family firms – Definition, theories, and performance. *In:* Innovation in Small and Medium-Sized Family Firms, pp. 12 - 13.
[56] Ibidem, p. 14.

Stewardship theory has its roots in psychology and sociology. It postulates a collective-oriented behavior of the agent, who acts as a steward for the organization, making decisions that are in the best interest of the group. Davis et al. (1997) summarize the main differences between agency theory and stewardship theory, concluding that, although agency theory provides a useful way of explaining relationships where the parties' interests are conflicting and can be brought more into alignment through proper monitoring and compensation systems, organizational relationships may be more complex. According to their model, managers *choose* to behave as agents or stewards. In particular, under three main circumstances managers may gain greater utility by accomplishing organizational rather than individual goals:

-Managers whose needs are based on growth, achievement, and self-actualization and who are intrinsically motivated;

- Managers who identify with their organizations and are highly committed to organizational values;

- Situations in which the managerial philosophy is based on involvement and trust and the culture is based on collectivism and low power distance.[57]

Fig. 1.5 Comparison of Agency Theory and Stewardship Theory

	Agency Theory	Stewardship Theory
Model of Man	Economic man	Self-actualizing man
Behavior	Self-serving	Collective serving
Psychological Mechanisms		
Motivation	Lower order/economic needs (physiological, security, economic)	Higher order needs (growth, achievement, self-actualization)
	Extrinsic	Intrinsic
Social Comparison	Other managers	Principal
Identification	Low value commitment	High value commitment
Power	Institutional (legitimate, coercive, reward)	Personal (expert, referent)
Situational Mechanisms		
Management Philosophy	Conrol oriented	Involvement oriented
Risk orientation	Control mechanisms	Trust
Time frame	Short term	Long Term
Objective	Cost control	Performance Enhancement
Cultural Differences	Individualism	Collectivism
	High power distance	Low power distance

Source: Davis et al. (1997 p. 37)

Drawing from Bubolz (2001) and Ward (2004), Davis et al. (2010) support the opinion that stewardship theory is ideal for explaining governance in the family business context because of family business owners' deep emotional investment in the family and because family

[57] Davis J. H. et al. (1997). Toward a Stewardship Theory of Management. The Academy of Management Review, Vol. 22, No. 1, p. 43.

business owners' personal satisfaction (motivation) and reputation are tied to the family enterprise. The results of their research on a sample of 1,100 business employees from both family and non-family businesses, show that value commitment, trust, and agency perceptions explain a significant portion of stewardship variance for family and nonfamily business employees: family member employees were found to perceive significantly higher value commitment, trust, stewardship, and lower agency conflicts in family firm leadership than non-family members.[58]

Socioemotional Wealth Theory is a recent approach that has the potential to become the dominant paradigm in the family business field. Unlike other borrowed theories, which often led to contradictory empirical results, SEW is based on family firms findings and, although may not be unique to family firms, "*is the single most important feature of a family firm's essence that separates it from other organizational forms.*"[59]Gómez- Mejía et al. (2007) developed a general socioemotional wealth model to explain differences in behaviors between family and non-family firms by proposing that "*family- owners' seek utility in the form of preserving socioemotional wealth generated by the noneconomic aspects of family businesses.*"[60] Because socioemotional wealth derives from non-financial benefits, including having the family name associated with the firm, emotional attachment to the firm, and the satisfaction of family members working for the company, the preservation of such wealth justifies decisions that may seem unprofessional to outside observers, such as appointing an inexperienced family member as the CEO of the firm.

In their revision of the concept of SEW, Berrone et al. (2012) propose five major dimensions of Socioemotional Wealth, which they label as FIBER:

- ***F****amily control and influence*. A typical feature of family firms is that family members exert a certain degree of control over strategic decisions. In order to preserve SEW, family owners are more likely to perpetuate control and influence the firm's affairs regardless of financial considerations.
- *Family members'* ***I****dentification with the firm*. There is empirical evidence that, because of the strong identification of the family with the firm, family firms are particularly

[58] Davis J. H. et al. (2010). Is Blood Thicker Than Water? A Study of Stewardship Perceptions in Family Business. Entrepreneurship Theory and Practice, Vol. 34, No. 6, pp. 1093.
[59] Berrone P. et al. (2012). Socioemotional Wealth in Family Firms: Theoretical Dimensions, Assessment Approaches, and Agenda for Future Research. Family Business Review,Vol. 25, No. 3, p. 260.
[60] Kalm M., Gómez-Mejía L. R. (2016). Socioemotional Wealth Preservation in Family Firms. Revista de Aministração, Vol. 51, p. 409.

concerned with maintaining a positive image and reputation; therefore, they show higher levels of corporate social responsibility and community citizenship.

- ***B****inding social ties*. SEW provides kinship ties with some of the same benefits of closed networks with external nonfamily employees, or suppliers, who may be viewed as members of the family. Such ties are likely to generate strong social bonds with the community at large as well. As a result, family firms are deeply embedded in their communities and often sponsor charities events, local sport events, etc.
- ***E****motional attachment*. Because the boundaries between family and firm are rather blurred in family firms, emotional attachment is particularly high in family firms. This dimension is particularly useful in understanding why family members tend to be altruistic to each other, or why conflictual relationships that would lead to the termination of the employment contract in non-family firms are instead preserved in family firms, perhaps in the hope that they will eventually improve.
- ***R****enewal of family bonds to the firm through dynastic succession*. Maintaining the business for future generations is a key purpose for family firms that affects business decisions in that it fosters long-term commitment, even when it requires to forgo an immediate return.

To summarize, the main point of SEW is that when there is high family involvement, firms are more likely to bear the cost and uncertainty involved in pursuing certain actions, because the risks that such actions entail is perceived to be counterbalanced by noneconomic benefits rather than potential financial gains, which explains for both the positive and negative effects of 'familiness' on firm outcomes.[61]

Building upon the theories related to family firms outlined in this section, the relationship between ownership and internationalization, with a particular focus on the extent to which family involvement impacts on the firm's decision to internationalize, will be discussed in the next section.

[61] Berrone P. et al. (2012). Socioemotional Wealth in Family Firms: Theoretical Dimensions, Assessment Approaches, and Agenda for Future Research. Family Business Review,Vol. 25, No. 3, p. 262.

3.2 Relationship between internationalization and corporate governance

Theories of Internationalization have focused on the external environment, the firm's level specificities and the ownership of both tangible and intangible resources as important factors affecting the choice and modes of entering foreign markets, to explain the phenomenon of internationalization. The Eclectic approach identifies the advantages of internalization, location, and ownership to explain the proliferation of MNEs, while stage models such as the Uppsala Model tries to explain the internationalization of SMEs as a gradual process. This approach is unable to explain the phenomenon of the Born Globals, better explained instead by the theory International Entrepreneurship. However, for a long time the effects of governance on internationalization have been neglected; the relationship between family ownership and internalization, in particular, is a recent field of study. Internationalization is a strategic decision depending on resource commitment and, as such, is influenced by the ownership type, in charge of dictating the amount of resources that are to be committed to the firm's internationalization strategy.

Small and Medium Enterprises (SMEs) are fundamental to the world business, as they account for two-thirds of all businesses globally, the 85% of which is composed of family firms. The fact that some of these firms are inert and local, while others are dynamic and international requires a deeper research in the governance structure of these firms in order to understand to what extent certain governance structures encourage a certain degree of internationalization.[62]

In this section, a brief overview of the main findings regarding the relationship between governance structure and internationalization will be given, with a focus on family business.

> "Corporate governance refers to the structures and processes for the direction and control of companies. Corporate governance concerns the relationships among the management, board of directors, controlling shareholders, minority shareholders, and other stakeholders. Good corporate governance contributes to sustainable economic development by enhancing the performance of companies and increasing their access to outside capital."[63]

Such system of practices by which a company is directed and controlled[64] has become a vital issue in managing organizations in the current global and complex environment. Agency theory, Resource dependency Theory, Stewardship Theory, Stakeholder Theory, are based on

[62] D'Angelo A., Majocchi A., Buck T. (2015). External Managers, Family ownership and the scope of SME Internationalization. Journal of World Business, Vol. 51, p. 534.
[63] InternationalFinance Corporation: http://ifcln1.ifc.org/ifcext/corporategovernance.nsf/Content/WhyCG.
[64] OECD Glossary of Statistical Terms https://stats.oecd.org/glossary/detail.asp?ID=6778

the causes and effects of variables, such as the formation of board structure, audit committee, independent non-executive directors and the role of top management and its organizational and social responsibilities.[65]

Much of the research into corporate governance derives from agency theory, which states the separation of ownership and management with conflicting objectives results in principal (owners) – agent (management) problems arising from the dispersed ownership in the modern corporation.[66]

In this view, the board of directors acts as a monitoring mechanism.

Combining the *agency theory* with the *information processing theory*, Sanders and Carpenter (1998) state that firms respond to international complexity through governance. Managerial complexity increases along with increases in a firm's degree of internationalization: as a consequence of the firm's increasing degree of international operations, which results in greater information-processing demand, the size and composition of the board of directors grow. At the same time, they purport that an efficient governance structure that is more appropriate for managing complexity may actually help firms to become more international.[67]

Oesterle et al. (2013) also found an agency theoretical link between a firm's ownership concentration and its international diversification. Managers derive private benefits from pursuing international diversification strategies in order to maximize their own income and prestige; this is in contrast with shareholder's interest in the maximization of firm's value. The agency problem arises when managers over-diversify the firm so that the costs for coordination and control exceed the gains associated with internationalization.[68] To avoid such opportunistic behavior shareholders can either increase managers'ownership participation or monitor the managers; however, the costs of monitoring causes a *free rider* problem in firms with highly dispersed shareholders: small shareholders sell their shares instead of engaging in costly monitoring. Therefore, managers of firms with highly dispersed ownership are more likely to pursue their own interests. Vice versa, the higher the ownership concentration, the less the freedom of managers to pursue their own interests and the lower the degree of internationalization (DOI). However, as the stake of a single owner in a firm grows, the owner becomes risk averse and prefers some more international diversification for

[65] Yusoff WFW., Alhaji I. A., (2012). Insight of Corporate Governance Theories. Journal of Business & Management, Vol. 1, No. 1, pp. 52.
[66] Ibidem
[67] Sanders G. WM., Carpenter M. A. (1998). The Roles of the CEO Compensation, Top Team Composition, and Board Structure. The Academy of Management Journal, Vol. 41, No. 2, pp. 174.
[68] Oesterle M. J. Richta H. N., Fisch J. H. (2013). The Influence of Ownership Structure on Internationalization. Intrnational Business Review, Vol. 22 p.189.

the reason of risk diversification. The soundness of this last assumption is linked to the "identity" of the owners, which has been proved to be a key factor in influencing the relationship between ownership and internationalization: a negative relationship between family ownership and internationalization has emerged from the works of Fernandez & Nieto (2006), while a positive relationship between them exists whereas the main shareholder is a financial or an institutional investor.

The basic assumption of the Resource Dependency Theory is the need for environmental linkages between the firm and outside resources. Directors may serve to link the external resources with the firm to overwhelm uncertainty: they bring resources such as information, skills, key constituents (suppliers, buyers, public policy decision makers, social groups) and legitimacy that will reduce uncertainty, the potential results of which is the decrease of the transaction cost associated with external association. This theory supports the appointment of directors to multiple boards because of their opportunities to gather information and network in various ways.[69]

The studies of Naldi and Nordqvist (2008) and those of Calabrò et al. (2013) both adopt this theory and find a positive correlation between foreign investors and the degree and extent of international operations. It is interesting to note that Naldi and Nordqvist's (2008) findings show that an external CEO and larger top management enhance the scale but not the scope of a family firm's international operations, while external board members enhance the scope but not the scale of international operations.[70] The reason for this may be linked to the different functions of these two organs; the CEO is responsible for the firm's everyday operations, while the Board influences strategic choices such as the entrance in a foreign market.

Calabrò et al. (2013) find a positive relationship (in both family and non-family businesses) between foreign investors' ownership and the level of international sales, as well as a positive relation between the strategic involvement of the board and international sales in non-family businesses. *"Directors with different functional backgrounds, education, and experiences might therefore foster internationalization by connecting the firm to its competitive environment and give the firm information about its domestic and international markets (Zahra et al., 2000)"*[71]

[69] Yusoff WFW., Alhaji I. A., (2012). Insight of Corporate Governance Theories. Journal of Business & Management, Vol. 1, No. 1, pp. 57-58.
[70] Naldi L., Norqvist M. (2008). Family Firms Venturing Into International Markets: A Resource Dependence Perspective. Frontiers of Entrepeneurship Research, Vol. 28, No. 14, pp. 1 – 19.
[71] Calabrò A., et al. (2013). The Influence of Ownership Structure and Board Strategic Involvement on International Sales: The Moderating Effect of Family Involvement. International Business Review, Vol. 22, p.

Furthermore, the paper concludes that CEO ownership negatively impacts on international sales in both family and non-family businesses. In the case of non-family businesses, CEO ownership results in a more risk-adverse behavior aimed at defending his/her own wealth, in accordance with the agency theory; however, in the case of family business, Calabrò et al. argue that the same negative relationship can be explained by what Gómez – Mejía et al. (2011) call *socioemotional wealth*, nonfinancial benefits that family-owners derive from the family firm, which affects managerial decisions, leading to decisions that may seem financially unprofessional (a basic example is the decision to appoint an unskilled or inexperienced family member as CEO). The suggestion for family business owners to facilitate internationalization is to adopt an open governance structure, which admits non-family owners, board members, and CEO.

Adopting a *Resource Based View*, the idea that ownership type influences a firm's resource endowment and risk aversion, which in turn affect the decision to internationalize is supported by empirical findings on a sample of Spanish SMEs examined by Fernàndez and Nieto (2005), who conclude that internationalization is negatively related to family ownership and positively related to corporate ownership. Their study focuses on the "identity" of the owners rather than on the dichotomy concentrated-dispersed, with a focus on the impact of family ownership on internationalization.

Three types of ownership are examined: family, corporate, and family with a corporate blockholder (family firms that have sold part of their equity to another company). Being the family's wealth concentrated in the business, family firms are more risk averse and find it difficult to obtain financial resources and accumulate intangible resources; on the other hand, corporate blockholder can help SMEs to acquire resources and access to financial resources, technologies or distribution channels. The same positive correlation to exports is true in the case of family businesses selling stakes to corporate blockholders. Although the family is kept in charge, the access to the resources granted by the blockholders is dependent on the separation between family and business interests, which is implemented through formal control systems and more effective management systems that favor internationalization.[72]

Building upon the *Stewardship Theory*, which assumes that managers are altruistic and act in the best interest of the owners, and especially its focus on altruism, Zahra's (2003) analysis of

520.

[72] Fernàndez Z., Nieto M. J. (2006). Impact of Ownership on the International Involvement of SMEs. Journal of International Business Studies, Vol. 37, No. 3, pp. 347.

409 U.S. manufacturing firms shows a positive relationship between internationalization and family firm's dimensions of *ownership* and *involvement*. Owner-managers undertake the risk of internationalization to create wealth for themselves and their survivors and are likely to involve their family members in the firm. Thus, the more the engagement in internationalization improves managers' family's employment and involvement, the more likely managers are to proceed with internationalization despite the potential reduction in short-term payoffs.[73]

Family involvement positively affects the intensity rather than the scope of international operations: an increase in the number of family members on the firm's board and their generation in management favors the maximization of revenues from already established foreign markets instead of the pursuit of new markets.

This paper clashes with much of the literature on family firms that generally agree on the negative influence of family ownership on internationalization (see Fernandez & Nieto 2005, 2006).

Sciascia et al. (2010) tried to explain the reasons behind the conflicting results between, among others, Zahra (2003) and Fernàndez & Nieto (2005, 2006) by adopting two complementary theoretical perspectives, *stewardship* and *stagnation*. According to the stewardship theory, family owners' and managers' altruism in pursuing the objectives of the firm stems from their socioemotional attachment to the business, which manifests itself in the strive for continuity and long-lasting benefits for the family members, training, and transmission of values to employees and strengthening of connections with customers.[74]

The stagnation approach, instead, portrays family businesses as characterized by difficulties in growth and survival due to the availability of limited resources, conservatism, and conflicts within the family.[75]

Starting from the assumption that the relationship between family ownership and internationalization is *nonlinear*, the authors adopt the stewardship perspective to explain the positive effects of family ownership on international entrepreneurship, while shifting to the stagnation perspective to explain the negative effect of family ownership. The results, based on the analysis of a sample of 1,035 US family business show that international entrepreneurship is maximized when family ownership is low to moderate. On the contrary,

[73] Zahra A. S. (2003). International expansion of U.S. Manufacturing family businesses: the effect of Ownership and Involvement. Journal of Business Venturing, Vol. 18, p. 507.
[74] Sciascia S., et al. (2010). The role of Family Ownership in International Entrepreneurship: Exploring Nonlinear Effects. Small Business Economics, Vol. 38, No. 1, p. 5.
[75] Ibidem

when family ownership becomes excessive – more than 53% as highlighted by the authors – the effects of stagnation exceed the benefits related to stewardship, hence family ownership negatively affects the firm's international entrepreneurship.

More recently, D' Angelo et al. (2016) have proposed a new theoretical framework based on a synthesis of theories of corporate governance and theories of social capital to understand the ownership conditions under which professional external managers favor internationalization of family SMEs. Social capital theory explains the importance of externally recruited managers to family firms: family SME typically possess strong internal – *bonding* - relationships with other members of the firm, but lack external – *bridging* - social capital that is essential for developing operations in foreign markets such as managerial knowledge and capabilities.

In addition, the authors argue that both theoretical and empirical contradictions in studies regarding the internationalization of family SMEs steam from the decision in the majority of studies to adopt a dichotomous categorization based on family/non-family business;[76] they propose instead a distinction between family-controlled (levels of ownership above 50%) and family-influenced SMEs. The empirical analysis of a sample of 417 Italian manufacturing family SMEs, confirms the positive relationship between the presence of external managers and internationalization, as well as the authors' hypothesis that the effect of the involvement of external managers on internationalization depends on the levels of family ownership (rather than on the distinction between family and non-family businesses), thus explaining the contrasting results among previous empirical research in this field. Specifically, the external manager's contribution to the development of the firm's social capital is positive for family-influenced firms, due to their higher degree of openness towards external capital. Conversely, in family-controlled firm the family and business objective may not be completely separated: the preservation of socioeconomic wealth may become the primary goal and interfere with the scope of internationalization.

This conclusion ties with previous studies reporting that high family ownership mitigates the positive effect of external managers.[77] Therefore, *"it is the combination of external capital with external managers that really works."*[78]

[76] D'Angelo A., Majocchi A., Buck T. (2016). External managers, family ownership and the scope of SME internationalization. Journal of World Business, Vol. 51, p. 535.
[77] Ibidem, p. 543.
[78] Ibidem

3.3 Defining the "Family business"

As noted above, *family business* is a complex and recent field of study; agreeing upon a univocal definition of this concept is not an easy task as well. Different studies have usually given slightly different definitions according to whether a definition was needed for a distinct research purpose or to assist in differentiating family from non-family firms.[79]
Diverging definitions can also be found in some papers cited for this work:

Gallo and Sveen (1991) adopt a conventional definition: *"a business where a single family owns the majority of stock and has total control. Family members also form part of the management and make the most important decisions concerning the business"*[80]and broaden it to include primarily owned family business, firms with a small outside ownership that does not affect the essential characteristics of a family business.

Zahra (2003) defines family business that business that report some identifiable ownership share by at least one family and had multiple generations in leadership positions within those firms; more specifically, belong to the family category private firms in which the family owns more than 50% of the stakes and public companies in which it owns over 10%.

Fernandez & Nieto (2005, 2006) consider firms in which one or more family members occupy managerial positions and divide these firms into "first-generation business" and "second-and- subsequent–generation family SMEs", according to whether the firm is more than 30 years old.

Naldi and Nordqvist (2008) define family firms on the basis of two criteria: a firm in which one or more family members own at least 50% of the firm's shares and a firm that is perceived by the CEO as being a family firm.

Calabrò et al. (2013) combine two dimensions to capture the involvement of the family in the firm: the CEO has to be a member of the owning family and there must be more than one generation actively involved in the business.

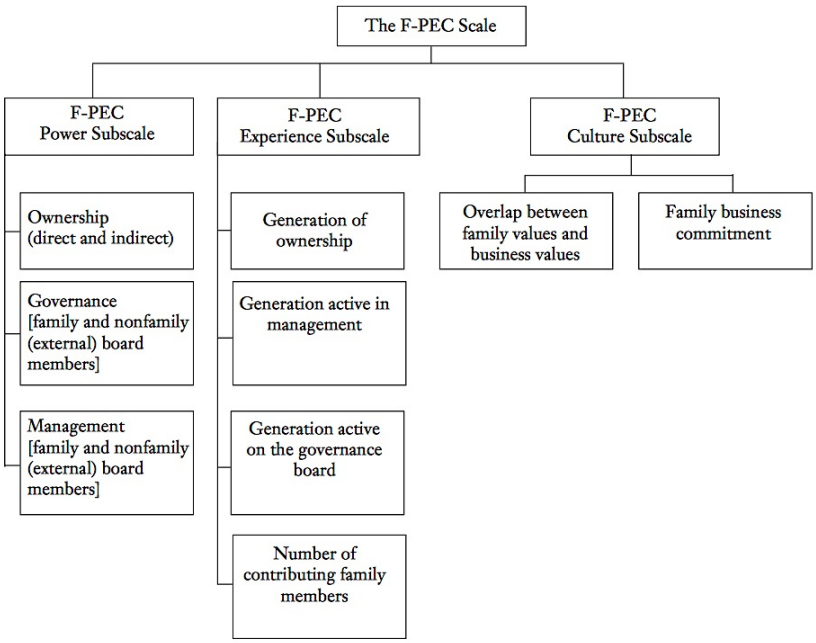
D'Angelo et al. (2016) make a distinction between family-controlled SMEs, with levels of ownership above 50% and family-influenced SMEs, with ownership concentration under 50%.

[79] Astrachan, J. H., Klein S. B., Smyrnios K. X.(2002). The F-PEC Scale of Family Influence: A Proposal for Solving the Family Business Definition Problem. Family Business Review, Vol. XV, No. 1, p. 45.
[80] Gallo M. A., Sveen J. (1991). Internationalizing the Family Business: Facilitating and Restraining Factors. Family Business Review, Vol. IV, No. 2, pp. 181- 182.

Astrachan et al. (2002) developed a model aimed at unifying the definition of *family business* on the basis of different levels of *family involvement*, which makes the classical distinction family/non-family less important: the extent to which family involvement influences the firm is considered more relevant. The authors developed the so-called F-PEC, an index of family influence that derives its name from the three dimensions of family influence considered, namely, *power*, *experience,* and *culture*.

The *power* dimension manifests itself in the extent of ownership, governance and management involvement. It assesses the degree of overall influence or power either in the hands of family members or in those named by the family.

Fig. 1.6 The F-PEC Scale



Source: Astrachan, J. H., Klein S. B., Smyrnios K. X. (2002, p. 52)

The *experience subscale* is related to succession and the number of family members who contribute to the business. It is argued that the level of experience gained from succession is greatest during the shift from the first to the second generation when new rituals are installed and decreases with subsequent successions process. The amount of experience that the business receives from the family is another important dimension that is reflected by the number of family members dedicated to the business.

Culture is the last dimension of the F-PEC scale. It regards the extent to which family and firm share the same values. This aspect, however, is difficult to measure. Firstly, it takes time to anchor specific values in an organization; secondly, the values of an organization might be rooted in family values of former generations but not necessarily manifest in the current

family.[81]

A clear, unambiguous definition of family business is also useful for determining its size and impact on economies. According to the European Family Businesses, based on the best available research, the importance of family business has been equated to:

> − *GDP - in most countries around the world they are 60 - 90% of non-governmental GDP*
> − *Jobs - in most countries around the world they are 50 _ 80% of all private sector jobs*
> − *Start-Ups - 85% of all business start-ups are started with family money*
> − *Job growth - in the Unites States, family business represent more than 75% of net job growth*
> − *Weighting - in most countries around the world, family businesses are between 70 and 95% of all business entities.*[82]

Family firms represent 85% of all SMEs (which, in turn, account for two-thirds of all business sector) in the EU and the USA.[83] According to the International Finance Corporation (IFC), a member of the World Bank, in many countries, family businesses represent more than 70 percent of the overall businesses and play a key role in the economy growth and workforce employment. In Spain, for example, about 75 percent of the businesses are family-owned and contribute to 65 percent of the country's GNP on average. Similarly, family businesses contribute to about 60 percent of the aggregate GNP in Latin America.[84]

Being a crucial sector, that represents a substantial portion of the world's economy, defining it have important implications, particularly for policy reasons.[85]

Early in 1996, Shanker and Astrachan (1996) were not able to answer to a question such as *" [i]f family businesses represent 90% of all US businesses, how much in total taxes do they pay? To what extent are family businesses funding the US government?"*[86] in their attempt to assess family businesses' contribution to the US economy.

[81] Astrachan, J. H., Klein S. B., Smyrnios K. X.(2002). The F-PEC Scale of Family Influence: A Proposal for Solving the Family Business Definition Problem. Family Business Review, Vol. XV, No. 1, p. 50.
[82] European Family Businesses (2012) http://www.europeanfamilybusinesses.eu/uploads/Modules/Publications/family-business-statistics.pdf
[83] D'Angelo A., Majocchi A., Buck T. (2016). External managers, family ownership and the scope of SME internationalization. Journal of World Business, Vol. 51, p. 534.
[84] World Bank Group (2011) IFC Family Business Governance Handbook p. 11. https://www.ifc.org/wps/wcm/connect/6a9001004f9f5979933cff0098cb14b9/FamilyBusinessGovernance_Handbook_English.pdf?MOD=AJPERES
[85] Shanker M. C., Astrachan J. H. (1996). Myths and Realities: Family Businesses' Contribution to the US Economy – A Framework for Assessing Family Business Statistics. Family Business Review, Vol. 9, No. 2, pp. 107 – 123.
[86] Ibidem, p. 117.

Big or small, listed or unlisted, family businesses play a significant role in the EU economy; they range from sole proprietors to large international enterprises.[87]

In 2007 an Expert Group on Family Business was created, bringing together experts nominated by the Member States and some experts from the field with the main purpose to give their input to the Commission on family business relevant issues. The final expert group report managed to bring the 3 accepted elements of what define a family business:

> *1) The majority of decision-making rights are in the possession of the natural person(s) who established the firm, or in the possession of the natural person(s) who has/have acquired the share capital of the firm, or in the possession of their spouses, parents, child, or children's direct heirs.*
> *2) The majority of decision-making rights are indirect or direct.*
> *3) At least one representative of the family or kin is formally involved in the governance of the firm.*
> *4) Listed companies meet the definition of family enterprise if the person who established or acquired the firm (share capital) or their families or descendants possess 25 percent of the decision-making rights mandated by their share capital.*[88]

The International Financial Corporation adopts a less detailed definition: *"a family business refers to a company where the voting majority is in the hands of the controlling family; including the founder(s) who intend to pass the business on to their descendants."*[89]

The above discussion confirms that the definitions of family business mostly concern variables such as ownership, management involvement of the owning family, generational transfer and, more recently, they have broadened to include business culture.[90]

Notwithstanding the efforts of both researchers and governmental institutions, a univocal definition is still missing, while computing family influence with the F-PEC index might not seem an easy task, for it requires time and involves issues that are not easily computable such as culture. However, the *continuum* approach proposed by Astrachan (2002) has been adopted

[87] European Commission: https://ec.europa.eu/growth/smes/promoting-entrepreneurship/we-work-for/family-business_it
[88] European Commission (2009). Final Report of the Expert Group. Overview of Family-Business-Relevant Issues: Research, Networks, Policy Measures and Existing Studies, p. 4.
[89] World Bank Group (2011) IFC Family Business Governance Handbook p. 12. https://www.ifc.org/wps/wcm/connect/6a9001004f9f5979933cff0098cb14b9/FamilyBusinessGovernance_Handbook_English.pdf?MOD=AJPERES
[90] Astrachan, J. H., Klein S. B., Smyrnios K. X.(2002). The F-PEC Scale of Family Influence: A Proposal for Solving the Family Business Definition Problem. Family Business Review, Vol. XV, No. 1, p. 45.

by some researchers and the results recently obtained by D'Angelo et al. (2016) seem to confirm that the involvement approach, instead of an artificial dichotomy family/non-family, better suits the complex field of family firms and even gives an explanation for the existence of antipodal empirical findings, the most contradictory of which are those of Zahra (2003) and Fernàndez & Nieto (2006).

3.4 Characteristics of Family businesses

As previously stated in this work, it is clear that family firms play an important role in the world's economy and that family firms, which have traditionally operated in domestic markets, more often undertake a process of internationalization to face the challenges and catch the opportunities that globalization offers.

Gallo and Sveen (1991), found that family businesses are generally more rigid in their internationalization process than non-family businesses and argue that a successful international implementation rests on some intrinsic factors which may either facilitate or restrain the pursuing of foreign markets. They analyze the characteristics of family businesses and the way in which they may enhance or restrain the company's internationalization process, among which:

- *Strategy and general objectives*. Family businesses are more rigid than non-family businesses in that they are narrowly focused on customer needs in the local market. Since the majority of capital is in family hands, the amount of free capital in the company is limited, making resource allocation more rigid. On the other hand, the typical long-term commitment of family businesses, emphasizes continuity rather than quick profits and may lead to pursue internationalization in order to ensure the continuity of the company.
- *Organizational structure and systems*. Board members are usually selected according to their status and power in the family instead of their professional knowledge and capabilities; admitting expert outsiders might not be easy, for the family does not accept to lose control over operations. However, a strong leader (usually the founder of the company) can guide the company through the complex process of internationalization. Frequently, internationalization is pursued in order to give room to a newly entered family member, especially in the case of new generations.
- *Company culture*. Each family company is influenced by specific assumptions that family members have about the way the business should be run. Culture may be a restraining factor when too much locally embedded, while openness to changes and internationalization can help family members to face the challenges of going abroad.

Kontinen and Ojala (2010) based their literature review on the analysis of 25 refereed journal articles regarding the internationalization of family business, the results of which show that the factors inhibiting the internationalization of family firms are mainly organizational and regard *lack of financial resources, risk avoidance, risk of losing control* and *unwillingness to*

accept outside expertise, while the factors enhancing it include a general *long-term orientation* and *speed in decision-making*. In addition, willingness to use IT, innovation capabilities, plus the ability to distribute power and allocate the resources available allows family firms to be more successful in international operations.[91]

Sirmon and Hitt (2003) consider the institution of the family firm itself, distinguishing five unique characteristics, which provide potential advantages of family firms over non-family firms, namely human capital, social capital, survivability capital, patient capital and characteristic governance structures.

The positive attributes of *human capital* consist of extraordinary commitment; warm, friendly and intimate relationships; the potential for early involvement of children in the firm can deepen firm-specific tacit knowledge. However, the frequent practice of employing family members can lead to hiring unskilled personnel, which retains qualified managers from choosing a family firm.[92]

Basing on strong *social capital*, family firms have developed shared language, norms and a high level of trust which enables building effective relationships with suppliers and customers.

The *patient capital* of family firms is *"financial capital that is invested without threat of liquidation for long period."*[93] While having a patient capital confirms family firm's long-term orientation, however, these firms have limited amounts of external financial capital mainly for two reasons: firstly, they usually avoid sharing equity with non-family investors; secondly, their size normally does not justify bond issues.[94]

Survivability capital "represents the pooled personal resources that family members are willing to loan, contribute, or share for the benefit of the family business."[95]These personal resources are available thanks to the commitment of family members, who offer them in the form of free labor, loaned labor, additional equity investments, or monetary loans.

Regarding governance structure, it is assumed that family firms experience lower governance costs, unless owner does not motivate himself by altruism when running the business.

In conclusion, members of the International Financial Corporation argue that several studies

[91] Kontinen T., Ojala A. (2010). The Internationalization of Family Businesses: A Review of Extant Research. Journal of Family Business Strategy, Vol. 1, No. 2, pp. 109 - 110.
[92] Sirmon D. G., Hitt M. A. (2003). Managing Resources: Linking Unique Resources, Management, and Wealth Creation in Family Firms. Entrepreneurship Theory and Practice, p. 342.
[93] Ibidem, p. 343.
[94] Ibidem
[95] Ibidem

have shown that family-owned companies have outperformed non-family companies in terms of sales, profits, and other growth measures. It is reported that a Thomson Financial study for Newsweek compared family firms to their non-family counterparts on the six major indexes in Europe and showed that family companies outperformed their rivals on all of these indexes, from London's FTSE to Madrid's IBEX. Thomson Financial created an index for both family and non-family firms in each country and tracked them over 10 years through December 2003.

The results showed that family businesses outperformed their counterparts in Germany, where the family index climbed 206% against a non-family 47%; in France, 203% against 76% and also in Switzerland, Spain, Britain, and Italy.[96]

This high performance can be interpreted as the result of the inherent strengths that family businesses have compared to their counterparts such as long- term commitment, high level of trust and the possibility to take quick decisions.[97]

However, the IFC also reports that many family firms fail to be sustainable in the long term: about two-thirds to three-quarters of family businesses either collapse or are sold by the founder(s) during their own tenure, while only 5 to 15 percent continue into the third generation.[98]

This high rate of failure among family businesses can be attributed to a multitude of reasons, some of which are especially relevant to their nature, such as domestic perspective, lack of financial resources due to a more conservative approach to debt, limited managerial capabilities, limited networks.[99]

[96] World Bank Group (2011) IFC Family Business Governance Handbook pp. 12 - 13 . https://www.ifc.org/wps/wcm/connect/6a9001004f9f5979933cff0098cb14b9/FamilyBusinessGovernance_Handbook_English.pdf?MOD=AJPERES

[97] Kontinen T., Ojala A. (2010). The Internationalization of Family Businesses: A Review of Extant Research. Journal of Family Business Strategy, Vol. 1, No. 2, p. 22.

[98] World Bank Group (2011) IFC Family Business Governance Handbook pp. 12 - 13 . https://www.ifc.org/wps/wcm/connect/6a9001004f9f5979933cff0098cb14b9/FamilyBusinessGovernance_Handbook_English.pdf?MOD=AJPERES

[99] Ibidem

Chapter 2 – The Chinese Pharmaceutical Industry

1. Industry Overview

The pharmaceutical industry is a complex and unique industry. Its complexity stems from the fact that pharmaceuticals make a significant contribution to the health and well-being of a population, and government policy exerts a significant effect on the state of the pharmaceutical market.[100] Marketing authorization for all kinds of medicines are given by a country's competent authority: the *Food and Drug Administration* (FDA) in the United States, the *European Medicines Agency* (EMA) for the European Union (in addition, within the EU each country also has its own institution), the *China Food and Drug Administration* (CFDA) in China, just to list a few.

A general *information asymmetry* (i.e. patients do not know which drugs they need nor which drugs are necessarily safe and efficacious), and the presence of *externalities* such as the negative health outcomes derived from ineffective treatments, make strong regulations and effective policies particularly important for the pharmaceutical market.[101]

The massive State intervention and the subsequent impact on both supply and demand is undoubtedly a distinctive feature of the pharmaceutical industry. The supply is subject to various restrictions from the research and trials phases to the production and subsequent commercialization phases, hence the complexity and length of regulatory approval as well as the importance of patent protection and product quality. From a demand-side perspective, it is physicians those who determine the demand; they work as intermediaries, prescibing medications on the basis of the information provided by pharmaceutical companies.[102] Then, pharmacists, or hospitals in the case of China, dispense drugs to patients, while payments can be made by patients themselves or by public or private insurers. The result is a many tiered consumer structure.[103]

There are several instruments through which a State governs both supply and offer. Drug pricing, classification and reimbursement are aimed at controlling public spending and impact on the demand for pharmaceutical products, while regulations regarding patents, drug

[100] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 1

[101] Ibidem

[102] Autorità garante della Concorrenza e del Mercato (1997). Indagine Conoscitiva nel settore farmaceutico, pp. 5-7. www.agcm.it/**indagini-conoscitive**.../3A250FE3093BED4AC12564C3004594A7.html

[103] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 2.

registration, distribution and marketing are aimed at controlling the offer in order to protect public health.

The World Health Organization (WHO) suggests that a national pharmaceutical policy should adhere to three key principles, *access*, *quality* and *rational use*, in the sense that essential drugs should be equitably available and affordable, all medicines should be safe and efficacious and health providers should promote a sound and cost-effective use of medications.[104]

Two main objectives of pharmaceutical policies can be distinguished: *health objectives* and *industrial objectives*. The divergence between these two is an additional source of complexity to the sector: while the main purpose of health policies is to ensure equal access to medications based on need rather than income, industry policies aim at supporting the development of the pharmaceutical industry through fostering R&D and creating an export-oriented industry. Theoretically, an effective pharmaceutical industry is necessary for any country to have drugs to use in its health systems in the first place. However, giving patent protection to innovative products in order to support and encourage R&D operations allows firms to have a monopoly and thus to charge higher prices on their products. This clearly clashes with the health objectives of keeping prices as affordable as possible in order to make them available to ideally everyone.[105]

Another important aspect of the pharmaceutical industry is the degree of internationalization of its companies in order to obviate the limited size of national markets. Being health problems and needs basically the same all over the world, an innovative product could be possibly sold in every market. Entering foreign markets is both an opportunity and a need, for such companies have to recover the huge investments in R&D operations.[106] It takes about 12 years from the identification of a promising molecule in the lab to its commercialisation. Nine out of ten promising molecules are abandoned as they fail the clinical trials on humans.[107]This explains why the pharmaceutical industry is the industrial sector with the greatest budget dedicated to R&D, with a total investment in R&D of $108 billion (intensity of 14.4%) in 2013.[108]

[104] Ibidem, p. 1
[105] Ibidem
[106] Autorità garante della Concorrenza e del Mercato (1997). Indagine conoscitiva nel settore farmaceutico, p. 6. www.agcm.it/**indagini-conoscitive**.../3A250FE3093BED4AC12564C3004594A7.html
[107] IHEST (2012, updated 2015). The Pharmaceutical Industry and China – Q&A, p. 7. http://www.ihest.fr/IMG/pdf/20151008-the_pharma_industry_and_china_ihest_update_final.pdf
[108] Ibidem

1.1. The Chinese Pharmaceutical Industry

> *"China's pharmaceutical environment, characterized by fragmented regulation and perverse market incentives, faces many challenges including problems with drug quality, access and affordability; irrational medicine use; and high drug prices. However, as the second world's largest market by value, there are many opportunities to create a pharmaceutical industry capable of providing affordable quality medicines for its people and the world."*[109]

With a population of 1,382.71 billion people and a GDP growing at a 6.7% and worth RMB 74,412.7 billion ($10,776.38 billion*) in 2016,[110]China is one of the largest and fastest growing economies in the world, accounting for 17.75% of the world economy.[111]

China is also the second largest pharmaceutical market in the world, forecasted to grow from $158 billion in 2016 to $315 billion by 2020,[112] with an annual growth rate of 9.1 percent. Total public and private healthcare expenditure reached $640 billion in 2015 and is expected to almost double to $1.1 trillion by 2020, as the Chinese government rapidly expands universal insurance coverage.[113]

1.1.1. Key Health issues

Health conditions in China have vastly improved since the 1990s: average life expectancy at birth increased from 68 to 72 years between 1990 and 2005 and reached 76 years in 2015 (73 for males and 79 for women),[114] ranking among the highest of developing countries; similarly, both maternal and infant mortality rates have fallen from respectively 53 per 100 000 and 32.2 per 1000 in 2000 to 20.1 and 8.1 in 2015.[115]

In spite of major gains in key health outcomes, China is facing a rapid demographic and epidemiological transition: ageing population, rapid urbanization leading to rapid lifestyle

[109] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 7.

*Calculated at current exchange rate 1 CNY= 0.144819 USD; 1USD= 6.90517 CNY.

[110] National Bureau of Statistics of China (2017). Statistical Communiqué of the People's Republic of China on the 2016 National Economic and Social Development.
http://www.stats.gov.cn/english/PressRelease/201702/t20170228_1467503.html

[111] http://www.tradingeconomics.com/china/gdp

[112] Export.gov (2016). https://www.export.gov/article?id=China-Pharmaceuticals

[113] Pharmafile. Top Pharmaceutical Markets 2016: China.
http://www.pharmafile.com/news/511869/top-pharmaceutical-markets-2016-china

[114]中国统计年鉴（2016）。平均预期寿命。China Statistical Yearbook (2016). Life Expectancy at Birth.
http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

[115]中国统计年鉴（2016）。监测地区 5 岁一下儿童和孕产妇死亡率。China Statistical Yearbook (2016). Mortality Rate of the Maternal and Children Aged under 5 in Surveillance Areas.
http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

changes, as well as significant environmental degradation. These factors are posing new challenges either to the pharmaceutical industry and to health policies.

According to the United Nations (2013), by 2050, nearly 30% of the Chinese population will be over 60, compared with a global trend of 22%.[116]As Chinese people are eating more unhealthy Western food, smoking more (China is home to one third of the world's smokers),[117]and exercising less, chronic diseases are rising in China. The leading causes of mortality in 2015 were cancer (25%), and heart and cerebrovascular disease, which both registered an average of 21,9%, followed by respiratory illnesses (11,93%). There is a slight difference between urban and rural areas: heart disease is the second leading cause of mortality in urban areas (21,98%)[118] and the third in rural areas (21,84%)[119] while cerebrovascular disease is the second leading cause in rural areas (23,17%)[120] and the third in urban areas (20,63%).[121]

In 2013, 28.3% of men and 27.4% of women were overweight (including obese) and 3.8% of men and 5.0% of women were thought to be obese, compared with 6% and 0.6%, respectively, in 1982. Also, 8.5% of the Chinese population was believed to suffer from diabetes and 37% from pre-diabetes in 2010, compared with 2.4% and 3.2%, respectively, in 1994. An estimate of the International Diabetes Federation for 2014 put the number of diabetes suffers at 9.3%.[122]

[116] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, pp. 38-39.

[117]Ibidem, p. 46.

[118]中国统计年鉴（2016）。城市居民主要疾病死亡率及死因构成（2015 年）。China Statistical Yearbook (2016). Death Rate of Major Diseases in Urban Areas (2015). http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

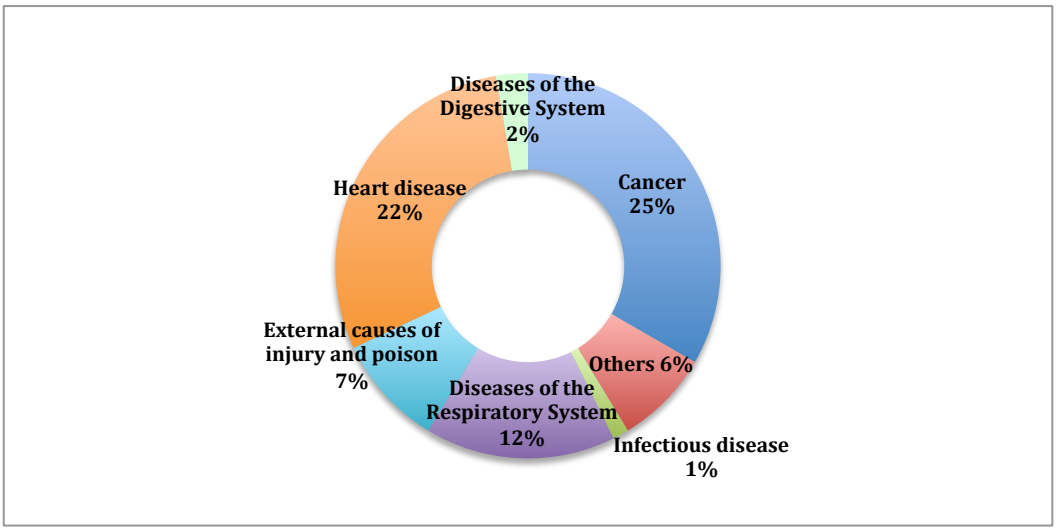
[119]中国统计年鉴（2016）。农村居民主要疾病死亡率及死因构成（2015 年）。China Statistical Yearbook (2016). Death Rate of Major Diseases in Rural Areas (2015). http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

[120] Ibidem

[121]中国统计年鉴（2016）。城市居民主要疾病死亡率及死因构成（2015 年）。China Statistical Yearbook (2016). Death Rate of Major Diseases in Urban Areas (2015). http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

[122] IHEST (2012, updated 2015). The Pharmaceutical Industry and China – Q&A, p. 22. http://www.ihest.fr/IMG/pdf/20151008-the_pharma_industry_and_china_ihest_update_final.pdf

Fig. 2.1 Causes of Mortality in China (2015)



Source: National Bureau of Statistics of China (personal elaboration based on an average between urban and rural areas)

Water and air pollution also heavily affect people's health: a recent 2015 paper from Berkeley Earth estimated that air pollution was responsible for 1.6 million premature deaths, roughly 17% of all deaths in China.[123]

China's distribution of healthcare resources is extremely unequal.[124]Nonetheless, health insurance coverage has improved dramatically, as a result of the health care reform implemented in 2009 aimed to cover all 1.3 billion urban and rural residents with some type of basic medical insurance, improve access and standards for basic medical care, and reduce unaffordable healthcare for all citizens. Three public health insurance schemes that used to operate in Cina – New Rural Cooperative Medical System, Basic Medical Insurance System for Urban Workers, and Basic Medical Insurance System for Urban Non-workers – merged into a unified system in 2010, which is said to cover 95% of the population with basic health care in 2015.[125]

This coverage, although widespread now, only provides the basic benefits and still requires most Chinese to pay high co-pays.[126]

[123]Rohde R. A., Muller R. A. (2015). Air Pollution in China: Mapping of Concentrations and Sources, Plos One. http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0135749

[124] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 6. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

[125] Marketline (2016). Pharmaceuticals in China, p. 12. www.marketline.com

[126] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 6. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

1.1.2. Health care spending and pharmaceutical spending

Health care spending in China has been growing rapidly over the past several years, particularly in light of the 2009 health care reforms. However, at 5–6% of GDP, it is still below the OECD average of around 10% of GDP.[127]

As a consequence of the health care reforms, government spending as a percentage of total health expenditure (THE) increased from 17.9% in 2005 to 30.4% in 2015. Out-of-pocket (OOP) spending, which was at almost 60% of THE in the early 2000s, has gradually been falling since then, as both government and social expenditures have increased, but still remains high at about 29.3% of THE.[128]

It should be noted that both per capita expenditure and the breakdown of spending between government, social and OOP expenditure vary significantly among provinces. The National Health Development Research Center reports that in 2012 the amount of per capita expenditure was 5751 RMB in the capital Beijing, while in the Western province of Gansu, people only spent 1725 RMB per capita. At the same time, social expenditure accounted for 50.5% of THE in Beijing, followed by government expenditure (26.9%) and OOP (22.6%); conversely, OOP expenditure was much higher in Gansu (36.4%), as much as government expenditure (38%), while social expenditure only accounted for 25.6%.[129]

Although health care spending accounts for only about 6% of GDP, China's overall drug spending accounted for around 40% of THE in 2012, a percentage that is higher than OECD average of 20%[130] (i.e. the European average in 2013 was 16.5%),[131]which makes China the world's second largest drug market behind the United States. Most spending still occurs in hospitals and other health care facilities, with far less at retail pharmacies. Government policies are seeking to decrease drug expenditure as a share of health spending and encourage the sale of drugs outside the hospital setting.[132]

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[127] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 62.

[128]中国统计年鉴（2016）。卫生总费用。China Statistical Yearbook (2016). Total Health Expenditure. http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

[129]Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 55.

[130] Ibidem, p. 57.

[131] IHEST (2012, updated 2015). The Pharmaceutical Industry and China – Q&A, p. 20. http://www.ihest.fr/IMG/pdf/20151008-the_pharma_industry_and_china_ihest_update_final.pdf

[132] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 62.

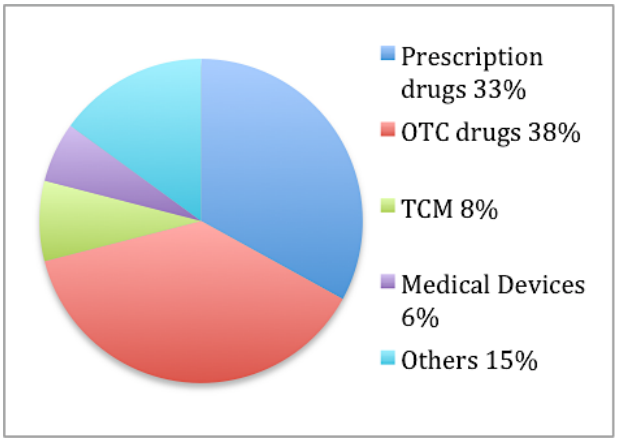
Historically, increases in overall drug spending have been driven by increases in both drug volumes (more prescribing) and drug prices (more expensive drugs). Data from the IMS Health, a health care consultancy, suggest that price growth has been decreasing and that future increases in pharmaceutical expenditure will be driven by continued volume growth.[133]

1.1.3. The Pharmaceutical Market: an Overview

The market of ethical drugs (drugs for which physicians'prescriptions are required) grew by 9.1% in 2015 to reach a value of $97.9 billion* and is forecasted to increse of 48.5% in the period 2015-2020.[134]

OTC sales almost doubled from 2003 to 2009 to approximately $12 billion.[135] With a growth by 6.2% in 2015, the OTC market reached a value of $19,005.3 million**, which is forcasted to increase of 34.3% by 2020. Traditional medicine accounts for 40.6% of the OTC market's total value.[136]

Fig. 2.2 China's pharmaceutical market - market segments (2009)



Source: KPMG (2011)

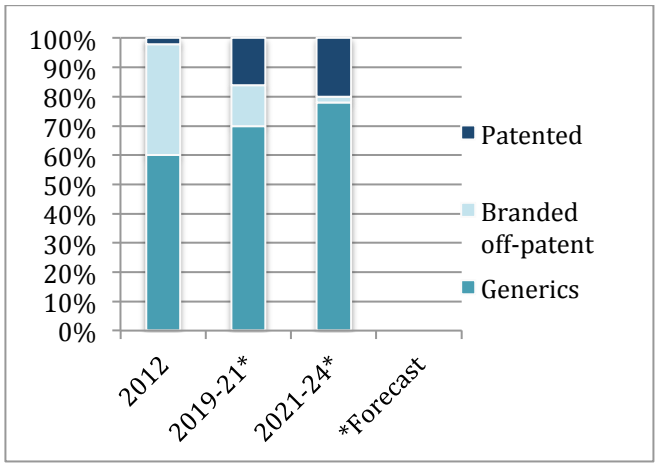
Generic drugs are the backbone of China's pharmaceutical industry, representing over 90% of the Chinese pharmaceutical market.[137]Despite Government encourages innovation, to hold expenditures down in the public insurance plan, the country have continued to rely heavily upon prescription of generics. Furthermore, it is supposed that, with the restricted current

[133] Ibidem
* Market value has been calculated at ex-factory prices (the price at which manufacturers sell the drugs to distributors).
**The market is valued according to retail selling price and incudes any applicable taxes.
[134] Marketline (2016). Pharmaceuticals in China, p. 2. www.marketline.com
[135] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 8. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf
[136] Marketline (2016). OTC Pharmaceuticals in China, p. 2. www.marketline.com
[137] Marketline (2017). Generics in China, p. 7. www.marketline.com

R&D capabilities, the possibility of launching domestic patented drugs in the near term is limited.[138]

Following WTO pressure to oblige China to comply with IP regulations, more and more patented drugs are entering the market. Unfortunately, in spite of a newly introduced IP friendly bill, a stronger legislation demanding full compliance by public authorities and pharmaceutical firms is yet to come.[139] With regards to patented drugs, due to the high confidence that the Chinese consumers place in foreign brands, these are expected to gain market shares on the domestic generic brands. Hence, their sales, which scored a 35.7% CAGR between 2007 and 2010, are forecasted to keep growing,[140] reflecting China's increasing wealth and the expansion of public and private health insurance.

Fig. 2.3 Share of Chinese pharmaceutical sales, %



Source: The Economist (2014)

Due to the demand for pharmaceuticals, especially cardiovascular, respiratory, anti-inflammatory, anti-ulcer and neurological drugs, many foreign drug companies have made significant progress in developing their own manufacturing and distribution networks in China and are dominant players in the Chinese drug market. Currently, the majority of domestic pharmaceutical companies in China is too small to compete with foreign companies. Therefore, almost all Chinese domestic pharmaceutical manufacturers are focused on producing generic drugs.[141] Recent estimates show that the top 20 manufacturers in China only account for less than a quarter of the country's own total pharmaceutical market, which

[138] IMA Life. China's Pharmaceutical Market: a Growing Evolution http://www.ima-pharma.com/mail/article.aspx?idnwl=159&idart=1421

[139] Intellectual Property Watch (2016). Inside Views: China's Pharmaceutical Sector and the IP Puzzle. http://www.ip-watch.org/2016/03/15/chinas-pharmaceutical-sector-and-the-ip-puzzle/

[140] IMA Life. China's Pharmaceutical Market: a Growing Evolution http://www.ima-pharma.com/mail/article.aspx?idnwl=159&idart=1421

[141] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 8.

is dominated, in fact, by country-based foreign drug corporations. As a consequence, many Chinese firms are entering Sino-foreign joint ventures to gain competitiveness in the market.[142]

Tab. 2.1 China Snapshot

Population: 1.38 billion **Urban population:** 56%; **Rural population:** 44% **Population aged 65 and above:** 150 million (10.8%) **Total healthcare expenditure:** 5.9% of GDP **Government healthcare expenditure:** 30.4% of THE **Total pharmaceutical sales:** $108 billion (1% of GDP, 17% of THE) **Generic sales:** $68 billion (64% of total sales) **Patented sales:** $23 billion (22% of total sales) **OTC sales:** $16 billion (16% of total sales)

[142] Intellectual Property Watch (2016). Inside Views: China's Pharmaceutical Sector and the IP Puzzle. http://www.ip-watch.org/2016/03/15/chinas-pharmaceutical-sector-and-the-ip-puzzle/

2. Health Care System In China

China has made great achievements in improving the health conditions of a population that accounts for nearly 20% of the world's total. As previously mentioned, life expectancy at birth has increased from 35 years in 1949 to 76 years in 2015; furthermore, over 95% of both urban and rural dwellers has a basic health care coverage. However, the country is experiencing a demographic and epidemiological transition, which poses many new health challenges: aging population, urbanization and industrialization, emergence of non-communicable diseases and risk factors related to changes in lifestyle and environmental pollution. Since 2009 China has been implementing a new round of important reforms to improve the health care system as well as the pharmaceutical environment. Nevertheless, linking industrial and health policy objectives is not an easy task to achieve.

2.1. Brief History of the Chinese Health Care System

"Citizens of the People's Republic of China have the right to material assistance from the state and society when they are old, ill or disabled. The state develops social insurance, social relief and medical and health services that are required for citizens to enjoy this right. (Article 45)"[143]

2.1.1. From 1949 to 1978: central planning

The health system has gradually evolved into its current form since the founding of the People's Republic of China in 1949, and its growth, particularly with regard to organizational and governance reform, has been closely linked to political, economic and administrative reform on a broader scale.

When the Communist Party took control of China in 1949, it adopted egalitarianism in income distribution and welfare provision. The Government formed a higly centralized planned economy and managed social and economic affairs by using administrative tools. The same top-down administrative system was developed in the health sector.[144]

From the establishment of the Communist Party in 1949 to the economic reforms that started in 1978, there were no private clinics or hospitals in China. The government owned, funded and staffed all health care institutions from small rural clinics to large urban hospitals, and all

[143]中华人民共和国宪法。 Constitution of the People's Republic of China. International Human Rights Treaties & Documents Database. http://www.hkhrm.org.hk/english/law/const03.html

[144]World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, p. 22.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

physicians were employees of the state.[145] To contain public health care spending, the prices of medications and services were set and adjusted periodically by the central government.

A great emphasis was put on preventive medicine, integration of Western medicine and Traditional Chinese medicine (TCM), and rural health. A preventive and epidemic system was established at each administrative level in order to report, monitor, prevent and control infectious diseases, vaccination, food hygiene and environmental and occupational health; a TCM department was established at each Western medicine hospital, toghether with TCM schools, research institutes and a TCM hospital in each province.[146]Given that most Chinese lived in the countryside at that time, rural health was a major concern: many so-called *barefoot* doctors received a short, basic training and staffed the commune-run health centres to solve the problem of physicians undersupply in rural areas at a low cost.

During this period no private insurance existed. In urban areas, the Govenment Insurance Scheme (GIS) and the Labor Insurance Scheme (LIS) covered, respectively, officials and staff (and their dependants) at government agencies, schools, universities and research institutes, and employees (and their dependants) at state-owned factories, with poverty aid programs covering the remaining urban residents. In rural areas, the Cooperative Medical Scheme (CMS) was established and covered about 85% of the rural population in 1976.[147]

Although from 1950 to 1982 huge strides were made in life expectancy, which increased from 42.2 to 64.4 years, and infant mortality, which fell by 75%, from the 130s to the 30s per 1000 births,[148]however, there were severe shortages of doctors and drugs, health professionals' competence was generally poor and the publicly-financed health insurance schemes had low levels of reimbursement, especially in the rural areas.[149]

[145] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 16.

[146] Ma J, Lu M., Quan H. (2008). From a National, Centrally Planned Health System to a System Based On The Market: Lessons From China, Health Affairs, Vol. 27, No. 4, pp. 938 – 939.

[147] Ibidem

[148] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 16.

[149] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, p. 23.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

2.1.2. From 1978 to 2002: market-oriented reforms

The third Plenary Session of the 11th Central Committee of the Communist Party of China (CPC) held in 1978 signed the beginning of the transition from a planned economy to a socialist market economy. During this period, the political, administrative, economic and fiscal systems all underwent huge changes, impacting deeply on the health system and its governance.

Decentralization resulted in more health duties for local government, while more autonomy was given to health providers. Most healthcare institutions became independent business entities financed by their own means. Health service provision gradually became market-driven, while prices of health services were still set by the government. However, the centralization of the fiscal system conflicted with administrative decentralization, impacting negatively on public health financing capacity.[150]

Deng Xiaoping's market liberalization reforms led to a reduction in the central government's share of THE, which fell from 32% to 15% between 1978 and 1999. Conversely, OOP expenditure increased from 20% in 1978 to 59% in 2001.[151]

As the government changed its financing and payment method from a flexible cost-reimbursement to block grants, which were usually much less than the actual operating costs, jurisdictions were encouraged to do whatever they could to generate revenues.[152]

Hospitals regarded drug sales as one of their main source of revenue. State financing, which accounted for about 60% of hospital revenues in 1980s, had fallen to 8.2% in 2003[153]. From the mid-1950s, the government had officially allowed a 15% mark-up on sales of medications, devices and diagnostic testing, so that doctors and hospitals could earn revenue from this mark-up. The 15% mark-up policy, originally aimed at coverig funding shortfalls, incentivized expensive, often irrational, treatment and led to significantly negative consequences for pharmaceutical policy.

In rural areas, China's formerly strong primary care and public health system collapsed: barefoot doctors became either full time farmers or private practitioners. The rural health care

[150] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, pp. 23 - 24.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

[151] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 16.

[152] Ma J, Lu M., Quan H. (2008). From a National, Centrally Planned Health System to a System Based On The Market: Lessons From China, Health Affairs, Vol. 27, No. 4, p. 939.

[153] Sun Q., Santoro M. A., Meng Q., Liu C., Egglestone K. (2008). Pharmaceutical Policy in China, Health Affaris, Vol. 27, No. 4, p. 1046.

insurance programme (CMS) also collapsed and by 1999 only 7% of rural residents had any form of insurance.[154]

In urban areas, instead, the GIS and LIS programs were merged into a new urban employee health insurance programme, which covered all enterprise employess from both state-owned and private enterprises.

Moreover, commercial (private) health insurance plans were introduced in urban and rural areas from the early 1980s. However, in 2003 only 5.6% of the population was covered by commercial health insurance.[155]

The consequeces of the "open door policy" and the subsequent heavy reliance on private financing have caused a series of distorsions in the Chinese health care system, such as unequal access to the health care system because of financial barriers, widening of the gap between urban and rural areas, lack of quality care monitoring systems, lack of health promotion and disease prevention.

According to the World Health Organization, in 2000 the Chinese Health Care System ranked 144th for its performance and 188th for its equity, in a ranking of 191 countries.[156]

A study of the 2003 Third National Health Services Survey highlighted that, when sick, 47% of rural patients and 32% of urban patients chose self-treatment without consulting a physician.[157]

Rural residents, children, seniors, and low-income families are the most vulnerable populations. China's rural population, in particular, has been paying the highest price under health care reform: about 700 million rural Chinese must pay out of pocket for virtually all health services, which potentially results in the deferral of care, untreated illness, financial catastrophe, and poverty.[158] Moreover, being it difficult for many clinics and hospitals in rural areas to make a profit because of limited ability to pay the fees among the rural population, many rural physicians have moved to urban areas, and rural hospitals cannot afford to renovate their facilities, whith a consequent decline in the diversity and quality of health care services in those areas.

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[154] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, pp. 16 - 17.

[155] Ma J, Lu M., Quan H. (2008). From a National, Centrally Planned Health System to a System Based On The Market: Lessons From China, Health Affairs, Vol. 27, No. 4, p. 940.

[156] Brombal D. (2011). Salute e Sanità pubblica, fra diritto e ragion di Stato. http://www.inchiestaonline.it/cina-politica-lavori-diritti/daniele-brombal-salute-e-sanita-pubblica-fra-diritto-e-ragion-di-stato/

[157] Ma J, Lu M., Quan H. (2008). From a National, Centrally Planned Health System to a System Based On The Market: Lessons From China, Health Affairs, Vol. 27, No. 4, p. 941

[158] Ibidem p. 942

In such a profit-driven health care system, preventive medicine were largely ignored because unprofitable. The consequences were disastrous: in 2002, the smoking rate reached 66.9% for males and 3.1% for females; 16% of males and 1.5% of females drank alcohol daily; only 8 percent of the population was regularly carrying out physical activity; 55% of hypertensive patients as well as 66% of diabetics were not aware of their condition.[159]

Between 1980 and 2004 the price for outpatient and inpatient treatments increased 77 times and 116 times, respectively (from 1,6 yuan to 127 yuan for outpatient and from 40 to 4662 yuan for inpatient), against an income increase estimated between 14 and 18 times over the same period.[160]

The outbreak of the Severe Acute Respiratory Syndrome (SARS) in 2003 provided the Chinese government with a valuable lesson on the importance of prevention on one side, and on the need for health system refoms on the other.

2.1.3. From 2003 to 2009: first phase of radical reforms

After SARS, the Chinese Government began to reflect on the issues in the health system, and made great efforts to resolve the problems caused by previous policies. Demographic and epidemiologic transitions, fragmented health delivery system, escalating costs of medical care, increasing financial burden especially for the poor and low quality of health care were all issues that had to be addressed by health reforms.

In order to strengthen health delivery in rural areas, the New Rural Cooperative Medical Scheme (NRCMS) was launched from 2003. The NRCMS would be organized, guided and supported by the Government, and voluntarily participated in by rural people. Government subsidy accounted for about 80% of the total NRCMS fund, and the rest was from individuals' premiums. By the end of 2008, about 91.5% of the rural population was covered by NRCMS; population coverage reached 98% of total rural population by end of 2012, and per capita funding increased from 42 yuan in 2005 to 308 yuan in 2012.[161]

For urban areas, a Urban Employees' Basic Medical Insurance (UEBMI) in which government, employers and individual employees were to share medical expenditures had already been implemented on national scale starting from 1998. Based on the progresses in

[159] Ibidem p. 944.

[160] Brombal D. (2011). Salute e Sanità pubblica, fra diritto e ragion di Stato. http://www.inchiestaonline.it/cina-politica-lavori-diritti/daniele-brombal-salute-e-sanita-pubblica-fra-diritto-e-ragion-di-stato/

[161] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, pp. 169 - 170.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

the coverage and the implementation of UEBMI, in 2007 the Urban Residents Basic Medical Insurance (URBMI) was established for all non-employed urban residents, including children and senior citizens. As for NRCMS, URBMI was jointly financed by the state and individuals with the purpose to minimize the burden of catastrophic medical expenditure. According to the National Health and Family Planning Commission, in 2012, UEBMI and URBMI covered 264 million and 271 million urban employees and residents, respectively, with per capita premiums of UEBMI 2574 yuan and per capita funding of URBMI of 401 yuan.[162]

2.1.4. Developments from the health care reform of 2009

Although the implementation of both rural and urban insurance schemes proved to be efficacious in increasing access to health services, however, there were still doubts about equality of access and financial protection. The high degree of decentralisation of health services, the wide gap between urban and rural areas, and the paradox of prescribing unnecessary and expensive medications to make profits even to people that could barely afford to access the health care system, led the Central Committee of the CPC and the State Council to issue a guiding policy document titled *Deepening the Health System Reform* in March 2009, aimed to achieve universal health coverage by 2020. The main tasks of this round of reforms covered five main areas:

- expand health insurance coverage
- equalize basic public health services
- strengthen primary care
- reform public hospitals
- establish an essential medicine system

All levels of government were allocated RMB 850 billion (approximately US $125 billion) between 2009 and 2011 to implement the reform.[163]

1. The government has been quite successful at expanding coverage rates of the three major insurance schemes, the Urban Employee Basic Medical Insurance (UEBMI) for formal sector urban workers and retirees, the URBMI for other urban residents and the NRCMS for rural residents, so that by 2011 97.5% of rural residents (and 95% of the total population) had access to health insurance. Retired workers of bankrupt state-owned enterprises and

[162] Ibidem, p. 170.
[163] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 13. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

employees of enterprises in difficulty were included in UEBMI and a safety net in the form of the Medical Assistance Fund was established to pay the premium on behalf of the poor people, low-income patients with severe illness, severely handicapped people and senior citizens from low-income families. Medical insurance schemes have been extended to cover outpatient services, as well as 20 catastrophic diseases, including child leukaemia, uraemia and breast cancer.[164]

While coverage rates are quite high, insurance schemes have been extended and payment methods have become more flexible (introduction of capitation, case-based payment, and diagnosis- related groups [DRGs] instead of fee-for-service), the amount of coverage still varies dramatically and many of China's over 260 million migrant workers do not receive health care benefits.[165]Moreover, both reimbursement rates and reimbursement ceilings are much higher in the UEBMI than in the NRCMS, with significant implications for what kind of drugs are reimbursed and the extent to which they are reimbursed across the country.

2. After the successful vaccination campaign against hepatitis B in 2010, the government increased funding dedicated to basic public health activities, including health records, health promotion, vaccination, maternal child health, mental health and NCDs, from 25 RMB in 2011 to 40 RMB per person in 2015.[166] About 40 billion yuan was allocated to this programme, accounting for 6% of the total government health expenditures in 2013.[167] Being it free for all people, this programme is crucial for the vulnerable people who need the services but cannot afford them, and aims at reducing the gap in service coverage between urban and rural areas, wealthier and poorer regions and people.

Access to basic public health services has become more equitable. The state provides all residents with a free package of 41 basic public health services in ten categories, including health record, health education, preventive inoculation, healthcare for children under six, healthcare for pregnant and lying-in women, healthcare for elderly people, treatment for hypertension and type II diabetes patients, healthcare for severe psychosis patients, reporting

[164] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, p. 175.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

[165] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 19.

[166] Ibidem p. 20

[167] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, p. 180.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

and handling of infectious diseases and public health emergencies, and healthcare supervision and coordination.[168]

In addition, the Government has lauched key public health service programmes, such as the prevention and control of AIDS, the provision of folic acid for pregnant women to prevent births defects, the supplementary vaccination against hepatitis B for those under 15 years old, cataract removal for poor patients, and cervical and breast cancer tests for rural women within eligible age.

3. In China, health care services are distributed according to 5 administrative levels: province-level, prefecture-level, county-level, township-level and village-level. According to the China Statistical Yearbook 2016, there were 27,587 hospitals in China in 2015, including 17,430 general hospitals, 6,023 specialized hospitals and 3,267 TCM hospitals; 36,817 township health centers in rural areas and 524 urban health centers and, at the lowest level, there were 208,572 outpatient departments,[169] many of which are a legacy of China's work unit system (i.e. located within and operated by factories, schools etc.).[170] Between 2009 and 2011 alone, some 2200 county hospitals and 33 000 urban and rural primary care facilities were built or renovated.[171]

Most general hospitals are state-run and divided into three tiers on the basis of the services offered and their degree of specialization. Tier 3 hospitals are the largest and most sophisticated hospitals with usually more than 500 beds, tier 2 hospitals are medium-sized (between 100 and 500 beds) and provide general medical services. Tier 1 hospitals are clinics that provide basic medical care but not advanced medical services and have less than 100 beds. Generally, provincial and munucipal hospitals of big urban areas belong to tier 3, municipal hospitals in smaller cities as well as district and county hospitals belong to tier 2, while township hospitals in small towns belong to tier 1.

Until recently, China lacked an effective primary care system, and thus most people sought medical care in hospitals, especially the large hospitals in big cities. Because these facilities are believed to provide the best care, they are usually severely overcrowded and many

[168] The State Council of PRC (2014). Medical and Health Services in China. http://english.gov.cn/archive/white_paper/2014/08/23/content_281474982986476.htm

[169] 中国统计年鉴（2016）。医疗卫生机构。China Statistical Yearbook (2016). Healthcare Institutions. http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

[170] Sinclair J. A. C. (2009). China's Healthcare Reform – Our Prognosis for Multinational Healthcare Players, InterChina Consulting www.interChinaConsulting.com , p.10.

[171] Barber S. L., Borowitz M., Bekedam H., Ma J. (2014). The hospital of the future in China: China's Reform of Public Hospitals and Trends from Industrialized Countries. Health Policy Plan, Vol. 29, No. 3, p. 373.

patients have been unable to gain access to treatment. The government therefore wanted to improve medical care at the grassroots level by establishing a primary care system based on urban community health centres (CHCs) and the improved rural township health centres (THCs).

Primary care is the day-to-day healthcare given by a healthcare provider. It consists of physicians and health care facilities that interact personally with patients and provide for the prevention and treatment of the most common diseases and illnesses. Unlike other forms of care, such as hospital or specialized care, primary care acts as the base of any health care system.[172] A strong primary care system is important in creating equitable access and cutting costs, particularly in China, where people's mistrust in under-funded, and generally poorly equipped and staffed primary care stations have led patient to go to tertiary hospitals for minor issues.

As a result of the reform, the number of both first-tier hospitals and institutions at grass-root level have increased: at the end of July 2016, there were 28,341 hospitals in China, of which, 2,175 first-tier, 7,740 second-tier and 9,029 first-tier hospitals, and 927,598 grass-root level institutions. Between 2015 and the end of July 2016 alone, the number of first-tier hospitals increased of 1,666 units. Conversely, there were 3,998 primary care facilities more than previous year.[173]

In order to reduce the number of outpatient visits at specialized city hospitals, the government has also committed to training primary care staff. In 2012, there were only 109,794 General Practitioners (medical workers with sufficient knowledge in all branches of medicine), or 0.82 per 1000 population,[174] therefore a system under which general practitioners are trained in the regular way has been established; grass-roots medical and healthcare workers are enrolled in training courses for upgrading them to general practitioners; and medical students are specially trained for the needs of central and western urban areas, for which they do not have to pay their tuition fees. A project, known as "ten thousand doctors extending support to rural medical care," has been launched.[175]

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[172] Hou T. (2009). The Chinese Primary Care System: Its Evolution, Challenges and Legal Aspects of Reform. CUREJ – College Undergraduate Research Electronic Journal, Vo. 4, No. 1, p. 5.

[173]国家卫生计生委统计信息中心。2016 年 7 月底全国医疗卫生机构书。
http://www.moh.gov.cn/mohwsbwstjxxzx/s7967/201609/f48e95773590448586a15c55c8007517.shtml

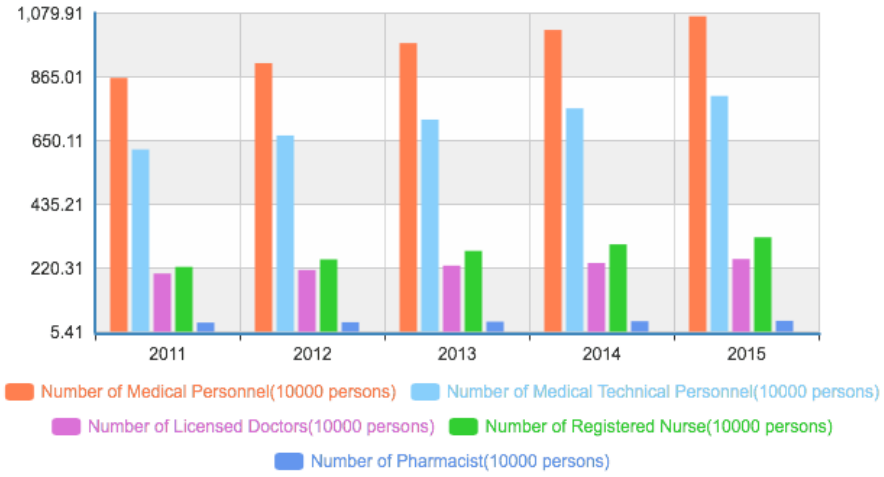
[174] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, p. 119.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

[175] The State Council of PRC (2014). Medical and Health Services in China.
http://english.gov.cn/archive/white_paper/2014/08/23/content_281474982986476.htm

They hope to train 300,000 general practitioners within the next 10 years with a target of 2 or 3 for every 10 000 residents.[176] Policies on establishing twinning partnerships between urban hospitals and rural counterparts have been implemented to reduce the techical gap between urban and rural hospitals, enhancing the service capacity of the latters.

A major reform policy was the introduction of the Essential Drug List at the primary care level. Since then, pharmaceutical price mark-up is no longer a major channel of financing for PHC facilities, compensated instead by public subsidies and service charges, including reimbursement from medical insurance schemes and compensation for public health service.

Fig. 2.4 Medical Personnel



Source: National Bureau of Statistics of China

4. Overutilization of hospitals and underutilization of primary care is a very inefficient mechanism for health care delivery. Public hospitals dominate provision of both outpatient and inpatient care and are financed through the three basic health insurance systems, user charges, and drug mark-ups. Since these state-run hospitals do not receive enough funding from the government to maintain their operations, many of them behave like for-profit institutions and generate profits by prescribing more drugs, more expensive drugs and by encouraging patients to undergo unnecessary expensive medical procedures.

The State Council Reform Office issued guidelines for public hospital reform pilots in 2010. Pilots were chosen to represent the major regions and variations in economic development, in consultation and agreement with local government. The guidance proposed a top-level design composed on'One Aim, Three Domains, and Nine Tasks':[177]the final objective was to

[176] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 21.

[177] Barber S. L., Borowitz M., Bekedam H., Ma J. (2014). The hospital of the future in China: China's Reform of Public Hospitals and Trends from Industrialized Countries. Health Policy Plan, Vol. 29, No. 3, p. 373.

provide accessible and affordable healthcare services for the people. To achieve this purpose a reform is needed in three main domains, namely, organizational arrangements, management systems (governance, compensation and monitoring), and internal management. Improvements in the governance of public hospitals involve the separation of the roles and responsibilities of the bodies involved in hospital supervision and management, as well as exploring the establishment of hospital watchdogs comprised of representatives from health bureaus, medical insurers, the public and relevant experts, and the disclosure of hospital information such as budgets, revenue and expenditure for public monitoring.

A first wave of pilot projects started in 2010 in 17 state-designed cities and 37 province-level districts with the main purposes of removing the 15% drug mark-up from public hospital financing and adopting alternative payment systems including case-based payment method, capitation and global budget. A similar pilot project has been launched since 2012 in more than 300 county-level public hospitals. So far, over 600 counties in 18 provinces, autonomous regions and municipalities directly under the central government have been included in this reform.

In addition, the government announced that it would encourage non-governmental funds to establish both for-profit and non-profit medical institutions. According to the State Council, by 2011, there were 165,000 medical institutions established with non-governmental investment, including 8,437 private hospitals, accounting for 38% of the national total[178]; in 2012 this percentage increased to 42%.[179]More recent data released by the Ministry of Health show that at the end of July 2016 the number of private hospitals had reached 15,470 units, 2115 more than 2015, while there were only 13,318 public hospitals, 447 units less than 2015.[180]

A pilot project has been lauched regarding wholly-owned foreign enterprises, which is a big step from the previous restriction where wholly foreign-owned hospitals and clinics were not allowed in China and foreign investments were only allowed in the form of hospital Joint Ventures with a limit of 70% i foreign shareholding.[181]

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[178] The State Council of PRC (2014). Medical and Health Services in China. http://english.gov.cn/archive/white_paper/2014/08/23/content_281474982986476.htm

[179] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 121.

[180] 国家卫生计生委统计信息中心。2016 年 7 月底全国医疗卫生机构书 http://www.moh.gov.cn/mohwsbwstjxxzx/s7967/201609/f48e95773590448586a15c55c8007517.shtml

[181] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 15. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

A second wave of pilot reforms was announced in 2014 for another 17 cities; meanwhile, about half of China's county hospitals have introduced the Zero Mark-Up policy (ZMU).[182]

5. Drug expenditure has been a major concern in the Chinese health system: in 2008, 51.3% of outpatient spending and 43.5% of inpatient spending were on medicines;[183] drug sales steadily accounted for about 40% of hospital earnings from 2006 to 2011, while government subsidies amounted to only 7-8% of hospitals' budgets.[184]

The possibility to make profits through the 15% mark-up policy has driven expensive and irrational prescribing. Irrational prescribing of antibiotics (contributing to up to 47% of drug sales),[185]for istance, has led to adverse drug reactions, allergic responses, and antibiotic resistance with a consequent loss in the range of effective drugs to fight infections.

To deter irrational prescribing and guarantee a supply of safe quality drugs at affordable prices, an Essential Drug List (EDL) was created in 2009 and updated in 2012. The 2009 EDL contained 205 Western and 102 TCM drugs; the revised version, released in March 2013 included 317 Western and 203 TCM medications. The basic drugs have all been included in the list of reimbursable drugs covered by basic medical insurance; however, coverage largely depends on both local jurisdiction and type of insurance scheme. Inpatient care i salso better reimbursed than outpatient. The EDL has been implemented together with the Zero Mark-Up policy: all retail pharmacies and healthcare facilities are required to purchase and sell these essential drugs without mark-up.

The list of essential drugs is playing an increasing role in China's pharmaceutical system: it is estimated that, by the end of 2020, the EDL will make up to 28% of China's drug market by value (in 2011 it was only 12%).[186]

Together with the EDL, the National Reimbursement Drug List (NRDL) was also revised in 2009. It is a larger list that contains all the drugs listed in the EDL. According to the 2009 version, the NRDL contains 1140 Western and 987 TCM medications divided into class A (349 Western, 154 TCM) drugs that are supposed to be fully reimbursable and class B (791

[182] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 22

[183] World Health Organization (2015). People's Republic of China Health System Review, Health System in Transition, Vol. 5, No. 7, p. 176.
http://www.wpro.who.int/asia_pacific_observatory/hits/series/china_health_systems_review.pdf?ua=1

[184] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 114.

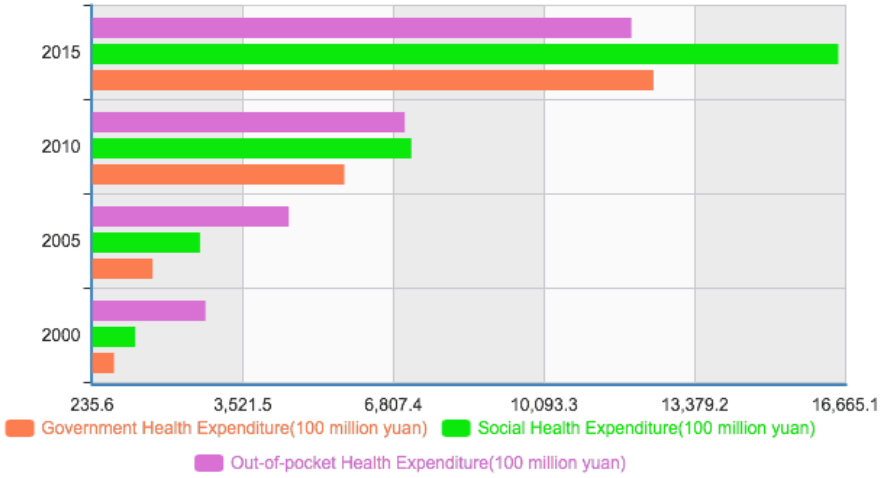
[185] Ibidem p. 103

[186] Ibidem p. 87

Western, 833 TCM) drugs that are considered less essential and have different co-payments depending on the province.

Medications not included in the EDL or the NRDL must be paid for as OOP.

Fig. 2.5 Health Expenditure (% of Government, Social Insurance, and OOP)



Source: National Bureau of Statistics of China

In conclusion, following the 2009 reforms, China has significantly improved its health care system: universal insurance coverage has been achieved, basic health services free of charge for all and a national EDL have both been established. Primary care is gradually being strengthened, while the reform of public hospitals has started.

Nevertheless, variations in coverage among the three different insurance schemes still exist and, with OOP expenditure making up around 30% of THE, there is still the perception that health care and pharmaceuticals are not affordable in China. In addition many essential drugs remain almost unavailable in some poor regions.

The major challenge for China is to provide equal access for its citizens to safe, effective and high quality medications. At the same time, being China one of the largest pharmaceutical markets in the world, reforms in the health care sector must run parallel to those in the pharmaceutical industry. It is clearly stated in the 13th Five-Year Plan that improving the industrial policy environment is a key priority of the Government.

2.2. The 13th Five-Year Plan (2016-2020)

The 80-chapter 13th Five-Year Plan on National Economic and Social Development was ratified by the National People's Congress in March 2016. The document analyzes the decisive stage and sets guidelines and targets for the period 2016-2020; it highlights innovation, coordination, green development, opening up and sharing, with medium-high growth and industrial upgrading as the two major goals. It is the most environmentally-focused five-year plan to date and reinforces the Chinese government's commitment to rebalance the economy to more sustainable growth based on higher-value-added manufacturing and domestic consumption. The 13th Five-Year Plan also broadens the Chinese government's stated commitment to innovation, emphasized in the 12th Five-Year Plan, and to improving citizens' quality of life, an effort that began under the 11th Five-Year Plan through prioritizing the environment, health, education, and social welfare.[187]

Innovation is placed at the heart of China's development strategy in the latest plan and will be an important component of moving Chinese manufacturing up the value-added manufacturing chain and enhancing its future global competitiveness and technological edge. By 2020 the government aims to increase China's global innovation ranking from 18 to 15, as well as the share of research and development (R&D) spending as a percent of GDP from 2.1 to 2.5 (under the 12th Five-Year Plan, overall spending on R&D increased from $105 billion (RMB 706.3 billion) in 2010 to $194.3 billion in 2014 but failed to reach the 2.2% target for R&D spending as a share of GDP by 0.1 percentage points). In addition, the number of patents filed per 10,000 people is expected to increase from 6.3 (nearly double the 12th Five Year Plan target of 3.3) to 12. To enhance the quality of patents together with the quantity, the *13th Five- Year Science and Technology Innovation Plan,* released in August 2016, aims to raise the number of international citations and Patent Cooperation Treaty patents.

The plan also sets goals to increase the number of R&D personnel per 10,000 people employed per year, from 48.5 in 2015 to 60 in 2020 and the share of its total population with scientific degrees from 6.2 percent in 2015 to 10 percent by 2020.[188]

Innovation will be the driving force for the development of emerging industries such as robotics, intelligent systems, precision medicine, environmental protection. Particularly relevant for the pharmaceutical industry is the support of biomedicine and biotechnology in

[187] U.S.-China Economic and Security Review Commission. The 13th Five-Year Plan, p. 3. https://www.uscc.gov/sites/default/files/Research/The%2013th%20Five-Year%20Plan.pdf
[188] Ibidem pp. 7 - 8.

order to foster the development of synthetic biology and regenerative medical techniques. Chapter 23 of the 13th five-year plan highlights the keypoints for the development of the biotech industry as one of the key sectors of the *Made in China 2025* project:

- move faster to facilitate the wide application of genomics and other biotechnologies;

- create demonstrations of network-based biotech applications;

- stimulate the large-scale development of personalized medical treatment, new drugs, bio-breeding, and other next generation biotech products and services;

- promote the creation of basic platforms such as gene and cell banks.[189]

The 13th Five-Year Plan also confirms the Government's efforts to create a *Healthy China* by reducing the cost of medicine, improving rural access to healthcare, and improving medical assistance programs. With an emphasis on prevention, reforms will be deepened to establish a sound basic healthcare system, allow all members of society to have access to basic healthcare services, and get everyone exercising to see that they become more healthy.
The comprehensive reform of all public hospitals will be further implemented to gradually eliminate markups on pharmaceuticals, lower their operational costs, and encourage non-governmental investments. Modern hospital management systems in which public hospitals act as independent legal persons will be established, together with staffing and remuneration systems. Reforms in the fields of pricing for medical services, logistic systems for pharmaceuticals and consumables, and medicine supply are also on the agenda.
Moreover, to foster the research and development of new medicines, newly deveoped medicines will be added to the catalogue of medicines covered by healthcare insurance.
The plan also addresses the improvement of the mechanisms for mediating disputes between them and patients to facilitate more amicable relations.

The *Action Plan for a Healthy China* is structured into 8 areas of action:

1. *Disease prevention and treatment and basic public healthcare services*: increase the range of free basic public healthcare services; increase the capacity to prevent and treat severe, difficult, and complicated diseases including cardiovascular, brain, and vascular diseases, cancer, and chronic respiratory diseases; reduce the rate of mortality due to major chronic diseases by 10%.

[189] People's Republic of China (2016). The13th Five-Year Plan for Economic and Social Development of the People's Republic of China 2016-2020.
http://en.ndrc.gov.cn/newsrelease/201612/P020161207645765233498.pdf

2. *Promote maternal and infant health*: give free vaccines to children within the scope of the national immunization plan; provide free maternal and infant care services; expand the scope of cervical and breast cancer screenings; increase the number of hospital beds for childbirths by 89,000 and the number of ostetricians and midwives by 140,000.

3. *Birth defect prevention and treatment*: screening for 20 complications including Down syndrome, deafness, and thalassemia as well as congenital heart disease in the plan for the comprehensive prevention and control of birth defects.

4. *Strengthen the provision of community-level medical services*: focusing on poor areas in the central and western regions, ensure each county prioritizes the operation of one or two county-level public hospitals (including county-level TCM hospitals), and that the proportion of community-level medical institutions meeting standards reaches over 95%; ensure that community-level medical services can be reached from anywhere within 30 minutes; strengthen and standardize training for 500,000 resident doctors, and ensure the number of general practitioners rises to two for every 10,000 people.

5. *Pass on and innovate traditional Chinese medicine (TCM)*: improve the infrastructure of TCM hospitals; put into effect an action plan to promote the standardization of traditional Chinese medicines and the traditional medicines of ethnic minorities.

6. *Smarter healthcare*: develop regional population health information platforms; expand the use of electronic health records; promote the application of big data in health care.

7. *Popular fitness*: promote fitness guidance services; promote the construction of fitness facilities to see that such facilities can be reached within 15 minutes from anywhere in urban communities;

8. *Food and medicine safety*: improve technical support systems for inspections and testing as well as IT-based oversight systems, build a contingent of professional food and medicine inspectors, and ensure that the equipment of oversight bodies at all levels is up to standard.[190]
The annual government medical insurance subsidy for rural and unemployed urban residents will increase 10.5 percent from around $57 to over $64 per person. The central government has also earmarked $1.9 billion to train general practitioners in order to address the shortfall in the number of Chinese doctors. Through these efforts, the Chinese government is striving to increase the average life expectancy by one year from 76.3 in 2015 to 77.3 in 2020.[191]

[190] Ibidem
[191] U.S.-China Economic and Security Review Commission. The 13th Five-Year Plan, p. 25.

2.2.1. The Five-Year Plan on Food and Drug safety (2016 – 2020)

Two separate five-year plans on food and on drug safety were issued by the State Council on February, 21 2017. The plan on drug safety requires that, by 2020, the quality of drugs should be further improved, the standard of medical equipment raised and the level of supervision enhanced.

The State Council reports that, by 2020, the plan requires the quality consistency evaluation for 289 generic drugs approved by catalog of China's basic drugs should be completed, 3,050 national drug standards and 500 medical equipment standards revised, the updated rate of periodic drug safety report will reach 100 percent and the license holding rate for pharmaceutical practitioners will be over 0.04 percent.[192]

The Government will speed up the establishment procedures to make sure that all phases of medicine production and sales are traceable, and the production and sale of counterfeit medicine will be severely punished. Sample testing will cover all kinds of food, blood products, vaccines and essential medicines to improve risk surveillance and assessment, according to the plans.

The guideline also stated that in order to raise the safety standard of food, medicine, and cosmetics, the quality consistency evaluation for generic drugs should be promoted, reform of the approval procedures for medical treatment should be deepened, an improved regulation system for drug standards should be set up and supervision for drug production should be strengthened. In addition, the pharmaceutical industry should establish an approval system online and further strengthen the national, provincial and city level drug testing system with a focus on major laboratory and coastal testing centers, especially biological products such as vaccines.

Furthermore, the marketing authorization holder (MAH)[193]will be fully implemented in new medicines to encourage their R&D. Related industries and departments should improve medicine approval and prioritize those for rare and major disease with improved drug approval standards. Meanwhile, the reform for medical equipment management by categories will be further promoted and a risk analysis system will also be established.

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https://www.uscc.gov/sites/default/files/Research/The%2013th%20Five-Year%20Plan.pdf

[192] The State Council of the People's Republic of China (2017). China issues five-year plan on food and drug safety. http://english.gov.cn/policies/latest_releases/2017/02/21/content_281475574322127.htm

[193] The MAH is the company in whose name the marketing authorization has been granted. This party is responsible for all aspects of the product, including quality and compliance with the conditions of the marketing authorization.

3. Drug Registration, Pricing And Reimbursement

The China Food and Drug Administration (CFDA) is the primary pharmaceutical regulator, responsible for all drug- related administrative activities, including the registration, production, distribution, use, and market surveillance of drugs, medical devices, foods and cosmetics. It also issues policies on Good Manufacturing Practice (GMP), Good Laboratory Practice, regulations for Good Supply Practice and Good Clinical Practice, and conducts inspections to ensure compliance. In collaboration with the CFDA, the State Administration of Traditional Chinese Medicine is responsible for the management of TCM-related policies. Apart from the CFDA, which also has operating branches at provincial, municipal and county level, responsibility for health care is fragmented across various government ministries, all of which fall under the supervision of China's State Council, the country's highest executive body. The key ministries involved in health care are the National Health and Family Planning Commission (NHFPC), responsible for guidance for health care reform; management of the EDL, including drug selection and tendering; the National Development and Reform Commission (NDRC), which monitors, forecasts and regulates prices of drugs, medical devices and medical services; the Ministry of Human Resources and Social Security, responsible for the National Reimbursement Drug List (NRDL). Other ministries involved in health care include the Ministries of Finance, Civil Affairs, Industry and Information Technology, and Commerce and the Chinese Insurance Regulatory Commission. Non-State Councils, such as the Anti-Corruption Office within the Supreme People's Procuratorate, together with various health and family planning commissions and development and reform commissions at province level also play an important role.

Regulatory fragmentation at the level of central government and between the central and provincial governments can create coordination barriers to policy formulation and implementation leading to dramatic differences in actual policy implementation. This fragmentation also results in uncertainty and delays that can be found in all areas of pharmaceutical policy, including drug approvals, quality standards, and pricing and reimbursement, creating a climate that can be difficult for manufacturers to negotiate.

Corruption is another major problem in China the two scandals related to the head of the State Food and Drug Administration, the predecessor to the CFDA, executed for taking bribes in the drug approval process in 2007 and that of GlaxoSmithKline, which received record fines for bribing government officials and physicians to promote sales of their drugs in 2013, are only two significant examples of a diffused practice in China. This widespread problem has

been addressed by the *"Prohibition on 9 unethical conducts to strengthen morals in the healthcare industry",* issued in 2009 by the NHFPC, which bans physicians from taking kickbacks from patients or companies and, more recently, by the 13th Five-Year Plan. Nevertheless, corrupted practice among officials are difficult to eliminate: in April 2015 Yin Hongzhang, the former deputy director of the regulator's drug testing center, was arrested and has recently been sentenced to 10 years in prison and fined 500,000 yuan ($71,864.89) for having accepted 3.56 million yuan ($511,678.05) in bribes from 2002 to 2015, as well as gifts including ivory products, to help companies in Shanghai, Beijing and other Chinese provinces gain or speed up approvals for vaccines used against SARS and bird flu among others. Yin's sentencing comes as the government has pledged greater scrutiny of vaccines after a scandal broke in 2016 involving nearly $90 million worth of illegal vaccines that were suspected of being sold in dozens of provinces.[194]

In this section the processes related to drug registration, pricing and reimbursement will be discussed. Once a product is registered, pharmaceutical companies are required to apply to the local provincial pricing bureau for pricing approval before the product is sold on the Chinese market. Pricing (how drug prices are determined) and reimbursement (the extent to which insurers pay for drugs) are two key aspects of the Chinese pharmaceutical environment, for they are strictly linked to drug quality, distribution at hospital level, insurance coverage and drugs' accessibility/affordability. Pharmaceutical companies willing to access this market should have a deep understanding of the complex regulatory structure of the healthcare system in China.

[194] Reuters (2017). China jails former drug regulatory official for taking bribes: state media. Health News. http://uk.reuters.com/article/us-china-corruption-health-idUKKBN14O023

3.1. Drug Registration

Drug registration and regulation in China is a complicated and time-consuming process, involving a number of regulatory bodies at various levels of central and local governments. It is very critical for pharmaceutical companies to understand the drug registration system in China and to know how to get the drug approved with China pharmaceutical regulatory authority.

Legislation for the current drug approval pathways in China is set out in the Drug Registration Regulation, promulgated by the CFDA in 2007 and amended in 2013.

In China, drugs are classified as 3 types:

- Chemical Drugs, for which 6 different registration classes exist;
- Biological Drugs, which can be registred as therapeutic biologial product (15 classes) or preventive biologial product – vaccines - (15 classes);
- Traditional Chinese Medicine and Natural Drugs, which include 9 different registration classes.

There are four types of drug applications in China, plus licence renewal:

1. New drug application have to be submitted for :
    - Class 1 to 5 new chemical drugs
    - Class 1 to 14 new therapeutic biological drugs
    - Class 1 to 14 new preventative biological drugs
    - Class 1 to 8 new traditional Chinese medicines and natural drugs
2. Generic drug application can be used for drugs that already have National Standards in China or are listed in the Chinese Pharmacopoeia. Specifically, Class 6 of chemical drugs, Class 15 of preventative biological products, Class 15 of therapeutic biological drugs, and Class 9 of traditional Chinese medicine and natural drugs fall into this category.
3. Imported drug application applies to all drugs manufactured outside of China, even if they are new drugs.
4. Supplemental application are for changes to already-approved drugs. There are a total of 33 kinds of supplements. 17 of these require the CFDA's approval; another 10 situations require approval from the Provincial Drug Authority (PDA), or alternatively can just be filed for record (without approval) with the CFDA. The final 6 situations can be filed for record with the PDA.

5. License renewal. Import Licenses or Drug Product Certificates are valid for 5 years. Renewal applications should be submitted 6 months prior to the product license expiration date together with post-marketing surveillance reports.

CFDA regulation for new drug development is modeled on the U.S. FDA's development pathway. To conduct clinical trials, CFDA requires a clinical trial application (CTA), similar to a U.S. FDA investigational new drug (IND) application. A three-phase clinical evaluation program is required to demonstrate drug safety and efficacy. Developers then submit a new drug application (NDA) for CFDA review, which includes review by the agency's Center for Drug Evaluation (CDE) and National Institutes of Food and Drug Control (NIFDC).

Since 2009, with the purpose to encourage drug innovation in China, a fast-track application process is also available for designated drugs, such as:

- formulations made from plants, animals or minerals that have never been marketed in China or elsewhere;
- newly discovered herbs and their preparations;
- new chemical entities or biological products that have never been launched in any country;
- new drugs to treat HIV, cancer and rare diseases (orphan drugs);
- new drugs to treat diseases which still do not have effective therapeutic methods;
- requisite drugs to treat emergency healthcare events;

Delays in drug approvals are becoming increasingly problematic in China. According to the 2014 CDE annual report, there were 8868 registration applications, of which 7829 were for chemical drugs. This brought the total backlog of applications to 18597 by the end of 2014, an increase of over 4000 from the previous year.[195]As a result, new drugs that are clinically superior to existing treatments or generic medications for drugs that are coming off-patent are not approved in time: estimated review time have reached 10–18 months for a clinical trial application and 12 to 15 months for a new drug application[196].

Antitumor drugs listed in the Chinese market lag behind those in North America and Europe, and Chinese patients with cancer are often unable to receive the most effective treatment, creating a health disparity that disadvantages the Chinese population. An example of these

[195]Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 32.

[196] Ibidem p. 33

delays include the anti-angiogenesis agent *bevacizumab*, which received U.S. Food and Drug Administration (FDA) approval for non–small cell lung cancer (NSCLC) treatment in 2006. However, bevacizumab was not approved for patients with NSCLC in China until 2015.[197]

Reasons for such backlogs are the limited human resource capacity of the CDE (the agency receives nearly 9,000 applications on average every year, despite having a staff of only 120 working in the CDE. In comparison, there are 5,000 staff members in the U.S. FDA's Center for Drug Evaluation and Research who are only responsible for chemical medicine evaluation[198]) and the increadibly high amount of applications for identical molecules, which is a side-effect of China's highly fragmented drug manufacturing industry, where, for example, 35 companies produce the drug *Erythropoietin*[199], a synthesized hormone used a treatment of some forms of anemia.

The CDE reports that for eight compounds (including the very commonly prescribed *esomeprazole*, *atorvastatin* and *clopidogrel*) there are more than 100 different applications. For many other compounds, there are 10 or more identical generics seeking approval.[200]

In addition, after a new drug has been approved, it can still take four to five years to gain placement on a reimbursement list, further delaying clinical uptake.

In August 2015 the State Council launched a significant overhaul of the drug approval and quality process with a goal of clearing the drug approval backlog by the end of 2016 and of having every application approved or rejected within a certain time limit by 2018.[201]To achieve these goals, approval standards were improved by adjusting the classification of drug registration. The definition of "new drugs" has been revised from "drugs which have not been marketed in China" to "drugs which have not been marketed in or outside of China". "New drugs" have been further divided into 'innovative drugs' and 'improved new drugs'.

The definition of "generic drugs" has also been revised from "drugs generic to established national standards", to the new definition "drugs generic to brand-name drugs with similar quality and efficacy". Accordingly, the review and approval of generic drugs will now take

[197] ASCO (2016). The Recent Reform of China's Drug Approval Process. https://am.asco.org/recent-reform-chinas-drug-approval-process

[198] Ibidem

[199]Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 9. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

[200] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 33.

[201]CFDA (2015). Approval system reform for drugs, medical instruments. http://eng.sfda.gov.cn/WS03/CL0757/127120.html

the brand-name (originator) drug as the reference to ensure that the quality and efficacy of the generic drug is consistent with that of the originator drug.[202]

At the same time, the CFDA also promised to accelerate the appraisal and approval process of innovative drugs, including drugs to treat HIV/AIDS, cancer, major chronic diseases, serious infectious and rare disease.

The National People's Congress also started a pilot scheme in 10 provincial regions, including Beijing, Tianjin, Shanghai, Jiangsu, Zhejiang, Fujian, Guangdong, Shandong and Sichuan, for a market authorization holder system for drug manufacturers that would be more in line with that used in developed countries, under which institutions and staff involved in the research and development of drugs will be allowed to apply for the registration of new drugs.[203]

Previously, receiving market authorization was contingent on having a manufacturing facility capable of actually producing the drug., which has limited the ability of R&D organizations such as universities from commercializing the drugs they develop and has led to an excessive amount of manufacturing capacity.

The experiment, started in November 2015, will last for three years, after which the State Council will submit a report to the legislature so that lawmakers will decide whether or not to formally revise the drug licensing system.

[202]Bird&Bird (2016). China: CFDA implements new review and approval system for generic drugs. https://www.twobirds.com/en/news/articles/2016/china/cfda-implements-new-review-and-approval-system-for-generic-drugs

[203]The National People's Congress of the People's Republic of China. Top legislature adopts drug approval reforms to incentivize researchers. http://www.npc.gov.cn/englishnpc/news/Events/2015-11/05/content_1950423.htm

3.2. Drug pricing

Prior to the 1978 market liberalization reforms, almost all drug prices were set by the government in China's centrally planned economy. The Chinese Government has continued to regulate pharmaceutical prices also after market liberalization reforms led to a shift towards a private, market-oriented health care system. From 1992 to 1996, there was an attempt to let the market set drug prices and the pharmaceutical industry grew rapidly. However, to face price increases, corruption and kickbacks, the Government recentralized much of pharmaceutical pricing in 1998.[204]

As a consequence of the "open door" policy, government funding for health care declined precipitously, but hospitals and physicians were allowed to charge a 15% mark-up on the sales of drugs, medical devices and diagnostic tests to recover lost revenue, a practice that incentivized physicians and hospitals to offer more often the most expensive treatments, even when unappropriate.

Moreover, there is evidence that the actual mark-up of medicines in government hospitals in 2005 was much higher, at about 42 percent.[205]With regard to irrational prescribing, an expert group studying a sample of township health centers and village clinics in Chongqing and Gansu determined that, given the clinical indications, less than 2 percent of prescriptions were consistent with best practice, while another study found that 98 percent of outpatients with a common cold were prescribed antibiotics.[206]

The phrase *yi yao yang yi* (以药养医)，*'drugs pay for doctors'* perfectly describes a system where 40% of THE is spent on pharmaceuticals. Much of this money is actually going to pay doctors and hospital costs. Being government-regulated profit margins based on a percentage of the procurement price (because the government lacks the capacity to estimate actual production costs), both physicians and hospitals have strong financial incentives to prescribe and dispense high-price drugs, often causing shortages of low-price medicines.[207]

Bearing the burden for the most widely used drugs, both central and local governments are interested in reducing the cost of drugs. Drug prices are regulated by the National Development and Reform Commission (NDRC) and provincial Pricing Bureaus. Between

[204] Sun Q., Santoro M. A., Meng Q., Liu C., Eggleston K. (2008). Pharmaceutical Policy in China, Health Affairs, Vol. 27, No. 4, p. 1044.
[205] Ibidem
[206] Ibidem
[207] Ibidem

1998 and 2008, authorities issued eighteen price cuts.[208] The government controls the price of drugs reimbursed by the basic medical insurance schemes, as well as of some narcotic drugs. Initial patented drug prices can be freely set by the manufacturers, since drugs can only be listed for medical insurance reimbursement after 2 years of market availability, following which the government controls the maximum retail price. Nevertheless, market competition between enterprises is allowed.[209]

Generally, manufacturers are free to set market prices, unless the drug is included in the Health Insurance Formulary (HIF) or other government-subsidised programme. Until 1 June 2015 the government directly participated in the pricing of reimbursable drugs by setting exact retail prices for selected drugs (so-called government pricing or GP) and maximum retail prices, or price caps for the remaining reimbursable drugs (so-called government-guided pricing or GGP).

Prices were set for each active ingredient and dosage form and were derived mainly from the manufacturers' costs (development, manufacturing, etc.). Local governments could adjust the maximum prices. Some products, considered to have higher quality than their generic forms, were permitted to have prices higher than the maximum retail prices indicated by GGP (i.e.'individual' pricing or pricing 'privilege'). Actual retail prices were set through local tenders. Selected manufacturers were allowed to provide their products to hospitals at prices established through a bidding process (i.e. local procurement prices). As drugs were reimbursed based on their actual price, there was no standardised reimbursement price.[210]

By May 2007, some 1,500 medicines had had their priced fixed by the central government and more than 800 medicine prices had been adjusted by local governments.[211]

Generally, government price cuts hit generic products the most: in 2008 price cuts for generic products made by joint ventures (i.e. original-brand foreign products) had their prices cut by an average of 25%; patented JV products by 20%; and domestic generics by 60%.[212]

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[208] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 51. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

[209] Hu S. et al. (2015). A Case Study of Pharmaceutical Pricing in China: Setting the Price for Off-Patent Originators. Applied Health Economics and Health Policy,Vol. 13, No. 1, p. 14.

[210] Chen Y. et al. (2016). Drug pricing reform in China: analysis of piloted approaches and potential impact of the reform. Journal of Market Access and Health Policy, Vol. 4, p.2. http://doi.org/10.3402/jmahp.v4.30458

[211] KPMG (2011). China's Pharmaceutical industry – Poised for the giant leap, p. 8. http://china.nlambassade.org/binaries/content/assets/postenweb/c/china/zaken-doen-inchina/sectoren/life-sciences/kpmg-china-pharmaceutical-201106.pdf

[212] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 52. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

To address growing healthcare expenditure together with the issue of quality and accessibility to care, in 2009, the new health-care reform started to reduce or eliminate drug price mark-ups and reduce the economic burden of drug expenditure through the establishment of an Essential Drug List.

Currently, medicines sold in China (primarily those included in the EDL and those produced or traded under a monopoly), are subject to price controls and neither hospitals or retail pharmacies are allowed to add markups on drug sales, even if a pharmacy fee is added to each physician's prescription.[213]

A major shake-up occurred in 2010 when a ceiling was imposed on retail prices of about 174 kinds of essential medicines from foreign manufacturers that used to practice independent price fixing since 2000 as a way of encouraging R&D.[214]

Other two rounds of price cuts followed in 2011. The first price cut, in late March, led to an average reduction of 20% in retail prices of 162 molecules and 1,300 dosage forms that dealt with infectious, cardiovascular and circulatory diseases (usually as antibiotics); in September, an average retail price cut of 14% was announced for 80 molecules dealing with hormone, endocrine, and nervous system disorders.[215]

However, while the prices of targeted drugs have decreased by an average of 15–20% and as much as 60%, the total pharmaceutical expenditure has still steadily increased.[216] The fact that physicians can easily evade price ceilings by switching to more expensive antibiotics or prescribing higher doses of medication could explain this phenomenon. Manufacturers could even evade price regulations by registering a "new drug" that was really the same old drug with very minor alterations or even just a changed name.[217] Given this situation, in the autumn of 2014 the NDRC announced that retail price ceilings would be eliminated from 1 June 2015.

[213] KPMG (2011). China's Pharmaceutical industry – Poised for the giant leap, p. 8. http://china.nlambassade.org/binaries/content/assets/postenweb/c/china/zaken-doen-inchina/sectoren/life-sciences/kpmg-china-pharmaceutical-201106.pdf

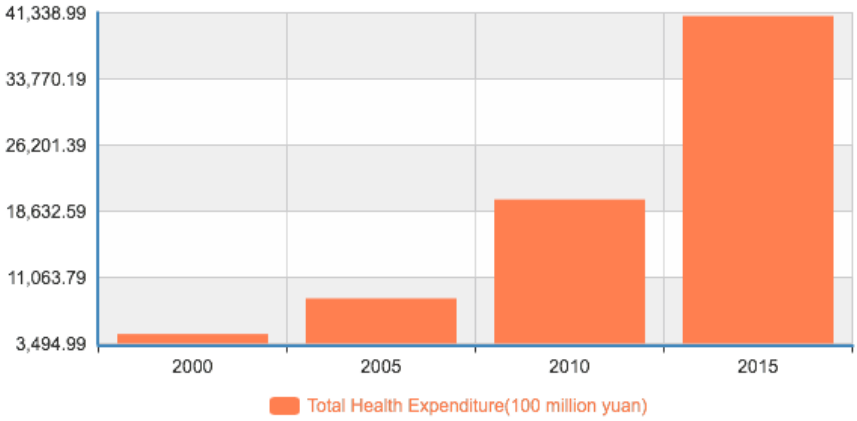
[214] Ibidem

[215] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 52. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

[216] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 79.

[217] Ibidem

Fig. 2.6 Total Health Expenditure



Source: National Bureau of Statistics of China

On May 4, 2015, the National Development and Reform Commission (NDRC) issued the *Opinions on Promoting Drug Pricing Reform* (Fa Gai Jia Ge [2015] No. 904), which required the removal of government pricing controls for most drugs from June 1, 2015. The government no longer administrates the drugs by fixing maximum retail prices. Instead, the prices of drugs are formulated by the market through different means according to the principle of administration by classification. In detail:

- the prices of patent drugs shall be determined by multiple parties in an open and transparent way;

- the prices of blood products outside healthcare list, immunological and preventive drugs within unified state purchase, free state anti-HIV drugs, and contraceptive drugs shall be determined through bidding;

With the exception of narcotics and type I psychotropic drugs, whose price will still be subject to control, manufacturers of all other drugs are entitled to independently decide the prices of such drags based on production cost and market.[218]

The NDRC also issued a *Notice on Strengthening Monitoring of Drug Prices* requiring relevant price authorities to start a six-month long drug price inspection program to strengthen the supervision on drug price and promote the transparency of price information of drug market.

[218] Xu X. (2015). NDRC Issued Opinions and Notice on Drug Price Reform: National Development and Reform Commission. The National Law Review. http://www.natlawreview.com/article/ndrc-issued-opinions-and-notice-drug-price-reform-national-development-and-reform-co

Drug pricing reform is aimed at establishing a more scientific and reasonable drug price formulation mechanism to promote optimization of resource allocation in the healthcare and pharmaceutical industry.

With the current reform, the government is attempting to replace its direct control over the prices of reimbursable drugs with indirect, incentive-driven influence. This new trend indicates that China is considering the adaptation of internal and external reference pricing policies, which are commonly used as an effective pharmaceutical cost-containment tool in OECD countries.[219] However, the analysis of pilot programmes in the cities of Sanming, Shaoxing and in the municipality of Chongqing shows that, the abolishment of GP and GGP for most pharmaceuticals gives manufacturers more freedom to set retail prices only in theory because in practice, prices are expected to continue to be constrained mainly by tenders, hospital budgets and controlled reimbursement levels. Some form of the IRP or ERP policies, commonly used in the OECD zone, are adapted to maintain an indirect influence over drug prices. It should be noticed that, in the case of China, external reference pricing does not result in comparisons with prices of the same drug in foreign countries, as per definition, but rather involves other big and relatively autonomous areas within the same country.[220]Reimbursement caps are instead a form of internal reference pricing based on the classification of drugs according to their perceived quality into patented, off-patent originators and generics. In the city of Sanming, for example, reimbursement caps were placed on 14 molecules felt to have only minor quality differences between domestic generic and imported versions but that exhibited large price gaps. Caps were set at the price of the cheapest domestically manufactured generic – much lower than off-patent originator prices, which led to significant voluntary price reductions from multinational corporations.

[219] Chen Y. et al. (2016). Drug pricing reform in China: analysis of piloted approaches and potential impact of the reform. Journal of Market Access and Health Policy, Vol. 4, p.2.
http://doi.org/10.3402/jmahp.v4.30458
[220] Ibidem

3.2.1. Tendering

The tendering process, established in 2001, is now the main strategy used by governments to price off-patent drugs. Once or twice a year, each province calls for foreign and local manufacturers to submit bids on specific drugs. A tendering committee of pharmacists, local government officials, and NDRC representatives decides which manufacturers may distribute their products in the province.

Tendering is the primary mechanism by which provinces acquire medications for the EDL and is also used for many NRDL drugs. Companies must win tenders to sell that drug within a province and the government mandates that health care institutions must purchase a majority of their medications (around 80% by value) from winning tender lists. Therefore, winning tenders is crucial for the survival of drug manufacturers. Tendering has been successful at lowering EDL drug prices by 25% on average and over 50% in some provinces between 2009 and 2010.[221]

Tendering is carried out separately by each of China's provinces, many of which use different tendering criteria. Many provinces have adopted a 'two-envelope selective tender system' (the so-called Anhui Model), in which the tenderers place the drug quality information, as well as the price, into two separate sealed envelopes. The bidding center then uses the first envelope to select the three highest quality drugs as candidates, and the process is completed by opening of the second envelope to compare their prices. Thus, of the three selected manufacturers, the one offering the lowest price will win the tender.[222] Furthermore, in some provinces, only one company can win a tender for a particular drug while in others there can be up to three winners.

Being price one of the key factors in the decision making process, tendering has received many criticisms related to the fact that, in spite of tendering's ability to lower prices, an excessive emphasis on price over quality can lead to major problems with quality.

Another limit is that tenders are not linked with procurement, so that after tender winners are announced, hospitals must engage with individual manufacturers in a process known as *secondary negotiation*, during which actual drug volumes are specified and hospitals secure a price that is often lower than the listed tender price. Then, hospitals sell drugs directly to patients and can charge a 15% mark-up from what they had to pay. Multiple distributors exist

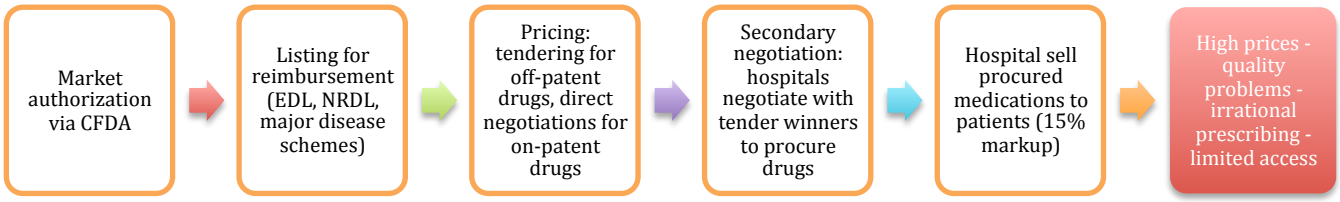
[221] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 80.

[222] Hu S. et al. (2015). A Case Study of Pharmaceutical Pricing in China: Setting the Price for Off-Patent Originators. Applied Health Economics and Health Policy,Vol. 13, No. 1, p. 14.

between the manufacturers and hospital and these all charge mark-ups along the supply chain. The process is slightly different for primary care facilities and pharmacies. Provinces will directly procure for all its primary care facilities from tender winners while pharmacies are able to bypass the tender process and negotiate directly with manufacturers.

Based on these criticisms, China's tendering system is currently undergoing significant changes. In the first half of 2015, both the State Council and the NHFPC released several key policy guidance whose purpose is to emphasize both quality and transparency.

Fig. 2.7 Drug movement from market authorization to patient use



Source: Mossialos et al. (2016)

3.3. Drug reimbursement

There are three major sets of drug reimbursement lists: the national Essential Drug List (EDL); the National Reimbursement Drug List (NRDL), and the Provincial Reimbursement Drug List (PRDL).

The EDL is issued once every three to five years by China's MOH. It includes drugs that are considered "essential" for public consumption, mostly old generic drugs. Drugs on the EDL are 100% reimbursed by the government. Few new or innovative drugs are on the list, though this has changed slightly with the 2013 version. The retail prices for EDL drugs are set by the NDRC.

The NRDL is issued once every four to five years by the Ministry of Human Resources and Social Security (MOHRSS). It is divided into List A and List B.

Drugs on List A are mostly old, generic drugs, many of which are also on the EDL and are 100% eligible for reimbursement. The retail prices for NRDL List A drugs are set by the NDRC.

List B drugs include innovative and premium priced drugs, often for specialized purposes. Provinces have the option to add up to 15% of drugs on NRDL List B. This substitution option is intended to address local needs, especially in regions that have high incidences of rare or unusual diseases. Class B drugs are usually higher priced and the reimbursement percentage for these drugs varies among provinces. Patients' co-payments for class B drugs can be quite high, ranging from 10% - 90%.[223]

List B drugs are officially categorized by active ingredient, not by brand name. The same percentage of the price is always reimbursed, notwithstanding the total price. This system is not very advantageous for the government, which could reduce spending by encouraging the use of generic equivalents. However, the system makes Western versions of drugs much more affordable to many Chinese than they would be otherwise.

Firstly created in 2000, the NRDL was updated in 2004 and 2009. It covers 23 therapeutic classes, from blood system drugs to digestive system drugs to biologics. The majority of drugs fall under the categories of specialist drugs, anti-microbial agents and circulatory system drugs. The current version lists 1,140 Western drugs and 987 Traditional Chinese

[223] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 54. http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

Medicines (TCM). Of these, 349 Western drugs and 154 TCMs are included in list A; the remaining 791 Western and 833 TCM drugs belong to list B.

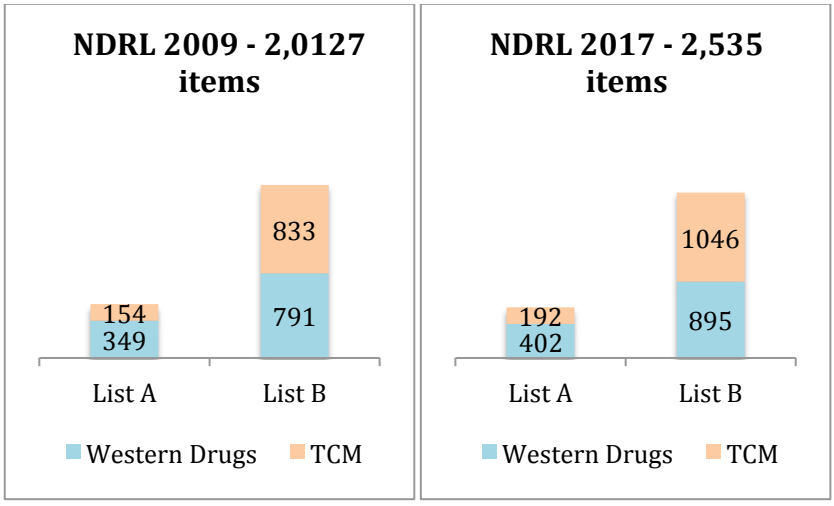
China's provinces can also pay for more drugs, using their own funds. Provincial level governments draw up their own PRDLs for actual implementation of the reimbursement system. List A drugs are fixed nationwide, and provinces may not alter them. List B drugs, on the other hand, may be altered within a limit of 15% to suit local needs. For example, the Beijing government lists 113 more Western drugs and 131 more TCMs than on the NRDL.[224]
Up to the end of 2010, 22 provinces (out of 31) had published their own lists, and of those, 17 provinces published provincial lists with additional medicines. Shandong province and Anhui province have published separate lists for urban and rural areas. In terms of numbers of medicines selected, the provincial selection of the 17 provinces ranged between 76 medicines in Jiangxi and 381 in Shanghai with an average of 179.9.[225]
In terms of reimbursement, there will be a continue move to expand the EDL beyond primary care facilities and county hospitals, and market share is sure to increase. Meanwhile, delays in the updating of the NRDL, have created a drug reimbursement lag that, in combination with the regulatory delays from a backlogged CFDA, means that many new medications have been kept out of patients' reach, because any new drug approved for sale since the last update of the list in 2009 was until now largely to be paid for as OOP by patients. High costs, in particular, are the major obstacle to access the most advanced treatments for many patients. As cancer treatments cost between 50,000 and 100,000 RMB, that is 10-20 times the average per capita income in rural areas (5,000 RMB), and the annual cost required for weekly dialysis, necessary for people suffering from chronicle kidney failure is around 25,000 RMB (5 times the average per capita income), patients often fall into crippling debts or turn to illegal fake treatments.[226]
Inclusion on the NRDL means that a drug is accessible through state insurance schemes, making it affordable to mass market consumers.
Finally, in February 2017 a new list of reimbursable medicines was released. The updated list includes 2,535 among Western and Traditional Chinese medicines, 339 more than the previous version. The number of Western-style medicines included rose by 133 (+11.4%), to

[224]Ibidem
[225]Wang D., Zhang X. (2011). The selection of national essential medicines in China: progress and the way forward. Southern Med Review, Vol. 4, No. 1, pp. 25.
[226]Brombal D. (2011). Salute e Sanità pubblica, fra diritto e ragion di Stato.
http://www.inchiestaonline.it/cina-politica-lavori-diritti/daniele-brombal-salute-e-sanita-pubblica-fra-diritto-e-ragion-di-stato/

1,297, while the number of TCMs rose by 20%, to 1,238 (including 88 ethnic drugs). List A is composed of 402 Western drugs and 192 TCMs, while list B includes 895 Western medicines and 1,046 TCMs.[227]This is the first change in more than seven years and will boost treatments for cancer, kidney disease, hepatitis and haemophilia, such as *tenofovir disoproxil*, a hepatitis B drug sold as Viread by GlaxoSmithKline PLC, and *gefitinib*, a lung cancer drug sold as Iressa by AstraZeneca PLC. However, to be included on the list drug manufacturers are often required to cut their drug's price, as in the case of GlaxoSmithKline's Viread, whose price was reduced by 67% in 2016.[228] Still, price reduction and the inclusion in the NRDL allows most drug companies to make up for any discounts by increased sales volume driven by China's massive population.

The update of the NRDL confirms China's commitment to create a pricing and reimbursement system that is capable of encouraging cost-containment and quality of generics, while simultaneously allowing for innovative new products to be reimbursed.

Fig. 2.8 National Reimbursement Drug List



[227]中国经济网（2017）。掘金新版医保目 http://finance.ce.cn/rolling/201703/06/t20170306_20769844.shtml

[228]Reuters (2017). China updates key drug list in boost for Big Pharma. http://www.reuters.com/article/us-china-pharmaceuticals-idUSKBN1620D7

4. Drug Distribution

A supply chain is the sequence of organizations that are involved in producing and delivering a product or a service. A typical pharmaceutical supply chain consists of primary manufacturing, secondary manufacturing, market warehouse/distribution centers, wholesalers, retails/hospitals and patients.[229]

Before market liberalization, all the pharmaceutical products were distributed by a state-owned company that had the monopoly of distribution to several regional wholesalers, which in turn distributed products to local wholesalers. Such a regulated supply chain lacked a competitive mechanism; however the system allowed greater regulation on both drug quality and price.

The market-oriented reforms implemented after 1978 changed the supply chain of pharmaceuticals dramatically. Firstly, imported drugs reached the Chinese market; secondly, manufacturing firms were allowed to sell directly to hospitals, leapfrogging wholesale stations and drug stores. Meanwhile, bigger distributors could sell drugs to smaller ones. The fact that wholesalers, retailers, hospitals and even manufacturers act as distributors further complicates the competivive and fragmented market of drug distribution in China.

In mature markets, pharmaceutical distribution industry is higly concentrated. 40% of worldwide drug sales occur in the US, a country that hosts only 75 wholesalers, of which the top three have a market share of 85%. In contrast, with over 13,000 pharmaceutical distributors by 2009, China's top three players only had a 22% market share in 2010.[230] It often takes two to three intermediaries to get drugs from the manufacturer to the dispenser and, for some products, there can be as many as six intermediaries in the distribution chain.

One of the main problem related to such a distribution system is the accrual of mark-ups that wholesalers and middlemen charge along the chain, which often means that the price patients pay can be up to ten times higher than the ex-factory price.[231]These mark-ups between ex-factory and hospital price are estimated to amount to an average of 52%,[232] thus contributing to the very high drug prices that most patients cannot afford to purchase.

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[229]Yu X. et al. (2010). Pharmaceutical supply chain in China: Current issues and implications for health system reform. Health Policy, Vol. 97, p. 10.

[230]Tse E. et al. (2012). Changing Landscape of China's Pharmaceutical Distribution Industry, p. 2. http://www.strategyand.pwc.com/media/file/Changing_Landscape_of_China's_Pharmaceutical_Distribution_EN.pdf

[231]Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 98.

[232]Ibidem.

Additionally, there can be wide geographic variation and difficulties with supply chain logistics. Due to a lack of infrastructure and logistical expertise in the rural areas, it has been difficult to establish secure and efficient delivery of drugs to China's rural population. These conditions and a pharmaceutical distribution system that is made up of mainly small, local distributors have made it difficult for regulators to monitor drugs. In April 2015 a 47-year-old woman was arrested for illegal trade of vaccines worth 570 million RMB with the involvement of 300 dealers in 24 provinces since 2010. Involved in the scandal also 13 pharmaceutical wholesalers, including a state-run firm linked to the Hebei Disease Control and Prevention Centre. As reported by the South China Morning Post, the vaccines, produced by licensed manufacturers, were expired or improperly refrigerated and transported at the required cold temperature, making them ineffective.[233]

To reduce drug prices and corruption, the Chinese government is trying to strengthen the distribution system. Early in 2004 the first modern pharmaceutical logistics center was built in 2004 and the first cold chain logistics network was launched in 2007 to provide 36 cities with access to temperature-controlled products.[234]In January 2017, the NHFPC released an explanatory note on a new policy titled "Two-Step Pharmaceutical Procurement System for Public Medical Facilities (Trial) that will reshape the drug distribution system in the country. According to this new policy, drug manufacturers will be forced to work with a single distributor that directly supplies healthcare facilities, eliminating numerous intermediaries in the supply chain. As reported by the Business Monitor International, trials will be introduced in 200 public hospitals of 11 provinces with the aim of expanding to the whole country by 2018.[235]The simplification of a three-tiered pharmaceutical supply chain that listed 13,508 distributors at the end of November 2015[236]is expected to reduce prices and to favor large drug distributors such as Sinopharm, Shanghai Pharmaceutical and Jointown.

The consolidation of the healthcare industry was first put forward in the 12th Five-Year Plan (2011-2015), which called for the establishment of 1 to 3 national distributors with sales over

[233]South China Morning Post (2016). Vaccine scandal: China detains 37 suspects as senior official admits to problems in drug system.
http://www.scmp.com/news/china/society/article/1929384/vaccine-scandal-china-detains-37-suspects-senior-official-admits

[234]Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 10.
http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

[235]BMI Research (2017). Industry trend analysis: 'Two-Step Procurement Policy to Reshape Drug Distribution Landscape.
http://www.pharmaceuticalsinsight.com/industry-trend-analysis-two-step-procurement-policy-reshape-drug-distribution-landscape-mar-2017

[236]Ibidem

100 billion RMB ($15.38 billion) and 20 regional distributors with sales over 10 billion yuan per year ($1.6 billion).[237]Furthermore, the top 100 drug wholesalers should aim to account for more than 85% of the market share, while the top 100 retail drug chains should reach at least 60% of the market share.[238]

To achieve this objective, the major distributors have embarked on strategies of consolidation through mergers and acquisitions to increase their national coverage. Sinopharm, for example, made more than 30 acquisitions in 2010 and 2011 alone.[239]Nowadays, with its medical distribution network composed of 30 distribution centers up to international standards and close to 3,000 retail outlets in 31 provinces, autonomous regions and municipalities, Sinopharm is the largest retailer of medicines, healthcare products and medical equipment.

Distributors are also required to adhere to Good Supply Practice requirements. Issued in 2000, these standards were revised in 2013 and amended in 2016. Basically, the revised standards required: a comprehensive computer information system and an electronic drug monitoring system; a standard documentation for drug selling and drug shipment; to equip warehouses systems that monitor both temperature and humidity; to appoint licensed pharmacists as legal representatives or responsible persons for drug retailing companies. Pharmaceutical companies had a 3-year transition period before compliance became mandatory in 2016, after which all companies not in compliance would be banned from pharmaceutical distribution.

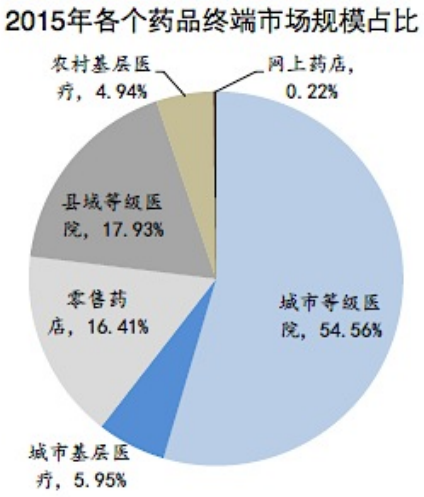
In the new GSP, companies are required to build a track and trace system to enable the traceability of their pharmaceutical products. On 20 January 2017, CFDA published a new notice advising the use of a specific Drug Standard Code of 14 digits to be utilised for drug traceability purposes.[240]

[237]China daily (2011). China issues guideline to strengthen drug distribution. http://www.chinadaily.com.cn/business/2011-05/05/content_12453128.htm
[238]Ibidem
[239]AT Kearney (2012). China's Pharmaceutical Distribution: Poised for Change, p. 6. http://www.atkearney.it/health/featured-article/-/asset_publisher/S5UkO0zy0vnu/content/china-spharmaceutical-distribution-poised-for-change/10192
[240]GS1 (2017). Recommendations on a harmonized implementation of traceability system using GS1 standards in China. http://www.gs1.org/sites/default/files/docs/healthcare/positionpapers/recommendations_harmonised_implementation_china_final.pdf

4.1. Drug dispensing terminals

Approximately 80% of sales are through the pathway manufacturer-wholesaler-hospital-patient. In China, 70–80% of drug sales to the patient are through the hospital in contrast to approximately 20% in developed countries.[241]Prescription drugs on the essential drug list (EDL), which has price controls that allow hospitals and pharmacies to add only a pharmacy fee, are mainly distributed to lower-grade hospitals, retail pharmacies, and community and rural healthcare clinics. On the other hand, prescription drugs on neither the EDL nor the reimbursement drug list are distributed primarily by Grade III (top-tier) hospitals.[242]In the past, most patients' visits took place in hospitals and patients typically preferred hospital pharmacies over retail drug stores for convenience, physician recommendation, non-standardized prescription, and greater assurance of pharmaceutical quality.[243]

Fig. 2.9 Scope of drug dispensing terminals, % (2015)



Source: 中国产业信息 (2016) – www.chyxx.com

The graphic shows the scope of drug sales for each drug dispensing terminal in 2015: pharmacy stores only account for 16.41% of drug sales, while 54.56% of drugs is sold through large city hospitals, followed by county hospitals (17.93%); primary health care facilities in both urban and rural areas account for about 11% sales. The emerging trend of

[241]Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, pp. 97 - 98.
[242] AT Kearney (2012). China's Pharmaceutical Distribution: Poised for Change, p. 2. http://www.atkearney.it/health/featured-article/-/asset_publisher/S5UkO0zy0vnu/content/china-spharmaceutical-distribution-poised-for-change/10192
[243]Yu X. et al. (2010). Pharmaceutical supply chain in China: Current issues and implications for health system reform. Health Policy, Vol. 97, p. 11.

online pharmacy is also shown: just 0.22% of drugs was sold online in 2015, however, this trend is expected to strengthen in the near future.[244]

Although hospitals still derive around 40% of their revenues from drug sales and over 70% of drugs is sold through hospitals, retail pharmacies have been growing in recent years as a consequence of recent reforms aimed at forcing hospitals to make profits through medical services rather than drug sales. Between 2007 and 2014 the number of retail pharmaceutical enterprises increased from 341,000[245]to over 473,000.[246]As these numbers may suggest, the drug retail sector is highly fragmented: in 2010, the top pharmacy companies only captured 22% of the market,[247]that is why the government encouraged the top 100 drug retailers to reach 60% market coverage by 2015.

However, the target was not accomplished: although the number of chain pharmacy stores is increasing more rapidly than the number of mono-pharmacy stores, in 2015, the top 100 drug chain retailers only owned 45.73% of the total number of pharmacy, with 34.8% market coverage.[248]

Online pharmacy is a recent trend and is undergoing unprecedented growth in China. In 2014, online drug sales increased to 3.9 billion RMB, a ten-fold increase from 2011.[249]While as of November 2008 only 21 companies had been licensed as Internet drug traders,[250]525 online pharmacy licenses have been approved as of January 2016.[251]Up to the first quarter of 2016, 610 companies had been licensed as Internet drug traders and 454 online pharmacies existed.[252]

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[244]中国产业信息网（2016）。2016 年中国零售药店数量，市场规模及行业发展趋势预测（图）。
http://www.chyxx.com/industry/201610/455985.html

[245]Yu X. et al. (2010). Pharmaceutical supply chain in China: Current issues and implications for health system reform. Health Policy, Vol. 97, p. 11.

[246] Behrens J. (2016). Pharmacies in the Chinese Market. Bayern, p. 6. http://www.apteka.ua/wp/wp-content/uploads/2016/06/Беренс.pdf

[247]Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 98.

[248]中国产业信息网（2016）。2016 年中国零售药店数量，市场规模及行业发展趋势预测（图）。
http://www.chyxx.com/industry/201610/455985.html

[249]Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of Chinap. 140

[250]Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report, p. 79.
http://www.pacificbridgemedical.com/wp-content/uploads/2015/04/China-Regulatory-and-Market-Access-Pharmaceutical-Report-2014.pdf

[251] Behrens J. (2016). Pharmacies in the Chinese Market. Bayern, p. 9. http://www.apteka.ua/wp/wp-content/uploads/2016/06/Беренс.pdf

[252]中国产业信息网（2016）。2016 年中国医药电商行业现状分析及发展趋势预测（图）。
http://www.chyxx.com/industry/201607/433429.html

This growth follows the update of the pharmaceutical e-retailing guidelines by the CFDA in 2014 that lifted the control over online sales of prescription drugs and lowered the requirements for entering medicine e-commerce.

It has been suggested that competition among hospitals, pharmacies, and online pharmacies could help to decrease drug prices, thus contributing to increased access and affordability for patients. Here again, quality control will be a key issue to be addressed by relevant regulations.

Chapter 3 – Investing in the Chinese pharmaceutical market

1. Investing in China

China's economic and social development during the past three decades has been remarkable. GDP growth has averaged about 10 percent a year, lifting more than 600 million people out of poverty. Driven by market reform and urbanization, China's rapid growth has made it a significant presence on the global stage as the world's largest exporter and the second-largest importer, and it emerged in 2011 as the world's second largest economy.[253]

Regarding social development, the country has achieved nearly universal coverage and gender parity in basic education, has rebuilt its health delivery network, reduced the burden of infectious disease and expanded coverage of health insurance to almost all rural and urban citizens.

Yet, China remains a developing country with a nominal per capita GDP ranking 75 in the world in 2016,[254] and its market reforms are still incomplete.

Despite the challenges that China poses to foreign companies, the country is often regarded as a key market for boosting growth, gain competitive advantage, or ensure long-term survivability.

However, being foreign investments highly regulated, investing in China may be a troublesome issue, especially when it comes to national key sectors such as the healthcare and pharmaceutical industry.

In this chapter, various forms of accessing the Chinese pharmaceutical market will be discussed, from exports and Contract Manufacturing Organizations (CMOs) to more structured investments such as Foreign Invested Enterprises (FIEs). Finally, Contract Research Organizations (CROs) for performing R&D activities will be presented.

[253] World Bank (2012). China – Country partnership strategy for the period FY13-FY16. http://documents.worldbank.org/curated/en/303351468242963292/China-Country-partnership-strategy-for-the-period-FY13-FY16

[254] Statistics Times (2016). List of Countries by Projected GDP per capita. http://statisticstimes.com/economy/countries-by-projected-gdp-capita.php

1.1. Exports of pharmaceuticals to China

China has various inspection and certification requirements for imported goods. The importing of pharmaceuticals, in particular, is subject to customs regulations and complex licensing procedures. It is important for the applicant who wants to enter the China drug market to understand the general registration procedure for importing drugs. There are three initial requirements for import drug registration:

1. Only drugs that have already obtained drug marketing authorization in the producing country where the overseas pharmaceutical manufacturer is located can apply for drug import; however, those that have not yet obtained marketing authorization in the producing country may be approved for importation if confirmed with safety, efficacy and clinical needs by the State Food and Drug Administration.
2. The drug must meet clinical need, comply with safety and efficiency standards and be quality controllable.
3. The foreign pharmaceutical manufacturer must comply with Good Manufacturing Practices (GMP) of both the producing country and China.[255]

If the foreign manufacturer meets these requirements, it must submit relevant dossiers, drug samples, approval documents and both clinical and non-clinical data to the CFDA. Once testing upon three batches of the drug is complete, a Clinical Trial Approval shall be issued and only after the clinical trial is completed the application for Drug Registration can be submitted. Finally, if regulations are conformed to, a Pharmaceutical Product Registration Certificate is issued for the sale of drugs manufactured in Hong Kong, Macau and Taiwan, while an Import Drug License is issued for all manufacturers from all other countries. The Import Drug License is the legal document that grants the foreign manufacturer the right to register, import, sell and use the import drug in China. It should be noticed that only the pharmaceutical manufacturer's representative office, or its registered agent in China can apply for the license.[256]

Generally, for drugs which can be exempted from clinical trials in China, it takes about 9-12 months to obtain the IDL; if clinical trials must be conducted, then it usually takes about 10-12 months for the approval of clinical studies, 12-18 months for clinical trial (3-6 months for

[255] CFDA. Provisions for Drug Registration (SFDA Order No. 28). Chapter VI, Section 1 "Registration of Import Drugs". http://eng.sfda.gov.cn/WS03/CL0768/61645.html
[256] Pacific Bridge Medical (2000). Importing drugs into China: an Update. http://www.pacificbridgemedical.com/publication/importing-drugs-into-china-an-update/

bio-efficacy test) and other 12-18 months for final approval of drug registration.[257] Drugs to be marketed in China for the first time must always be tested before they are marketed or at the time they are imported.[258]

A 'single permit for import of drug' can be applied from the Ministry of Public Health of the People's Republic of China in case of import of drugs that do not have import registration certificates but are of special requirement or short of domestic supply. Such 'permit' is applicable only to the drug, the country, the manufacturer, the quantities, the terms and the Coastal Institutes indicated on it.[259]

China has various inspection and certification requirements for imported goods. Pharmaceutical products must be imported through designated ports of entry and the importer must register and file the import with the drug administration at the port of entry. Currently, there are 19 such ports in China, they are Beijing, Tianjin, Shanghai, Dalian, Qingdao, Chengdu, Wuhan, Chongqing, Xiamen, Nanjing, Hangzhou, Ningbo, Fuzhou, Guangzhou, Shenzhen, Zhuhai, Haikou, Xi'an and Nanning.

Enterprises dealing in drugs must obtain the Pharmaceuticals Operator Licence and the Pharmaceuticals Production Quality Control Standards Certification issued by the food and drug administration.

After the imported drugs have arrived at the port of entry, the importing enterprise has to send them to the local port-of-entry drug laboratory for inspection, to ensure that the drugs are safe and meet the quality standards. After the inspection, drugs meeting the requirements will be issued an Import Drug Clearance Slip and Customs will release the drugs.[260] This process applies to each shipment of import drugs.

Starting from 1 May 2003, the China Compulsory Certification (CCC) mark has been implemented and is required for the importation and selling of medical equipment, including X-Ray Equipment, Haemodialysis Equipment, Electrocardiographs, Implantable Cardiac Pacemakers, Artificial Heart-Lung Machine and Hollow Fiber Dialysers.[261] It is a compulsory safety mark for domestically-manufactured and imported products listed in the CCC Product

[257] RJS MedTech. The procedure for Import Drug SFDA Registration http://www.sfdachina.com/news/info/80-1.htm

[258] CFDA (2001). Drug Administration Law of the People's Republic of China. http://eng.sfda.gov.cn/WS03/CL0766/61638.html#05

[259] MOFCOM (1990). Provisions Governing the Import of Drugs. http://english.mofcom.gov.cn/article/lawsdata/chineselaw/200211/20021100050734.shtml

[260] China Briefing. Certifications for Imported Goods in China. http://www.china-briefing.com/news/2013/10/17/certifications-for-imported-goods-in-china.html

[261] CCC. First Catalogue of Products Subject to CCC Mark. http://www.ccc-mark.com/lists-of-products-subject-to-ccc-mark.html

Catalogue, approved and jointly released by the General Administration for Quality Supervision and Inspection and Quarantine (GAQSIQ) and the Certification and Accreditation Administration (CNCA). The CCC Product Catalogue touches 19 groups of products divided into 132 product categories, including electric appliances, vehicles, safety glasses, and toys, etc. Chinese product certification standards are to a large extent aligned with the European International Standards Organization and American Standard Test Methods. However, China has independent applications for testing procedures that must be conducted in one of the 76 Accredited Testing Labs (ATL) in China, each one designated with specific "product scope" corresponding to one or more product categories.

1.2. Contract Manufacturing Organizations (CMOs)

CMOs offer a wide array of manufacturing services to the pharmaceutical and biopharma industries, ranging from production of small quantities of materials for R&D purposes, larger amounts for clinical study usage to full-scale production for commercial purposes. The global CM market primarily includes solid and liquid dosage forms, injectables, as well as active pharmaceutical ingredient (APIs).[262]

Recently, outsourcing drug manufacture has increasingly become part of pharmaceutical companies'strategy, for:

1) Reducing costs. Increasing R&D costs, the expiration of patent protection on *blockbuster drugs* (drugs with more than $1 billion in annual global sales) and the subsequent increasing competition of generic drugs, and reductions in drug makers' revenue growth due to improved regulations that require higher quality standards and more clinical trials for the approval of New Molecule Entities (NMEs), force most pharmaceutical companies to outsource manufacturing to contain costs.
2) Lower drug development risk. In the past, companies with pending or newly approved drugs had to build expensive dedicated manufacturing facilities. Outsourcing manufacturing to a CMO, the company can avoid such capital expenditures and acquires flexibility to adjust production quantities according to product demand.
3) Adapt to shifting manufacturing requirements. Drugmakers who lack either the financial resources or internal expertise to adapt to specialty manufacturing demands (i.e. biologics, parenteral drugs, transdermal formulations etc.) obviate these problems by outsourcing.
4) Gain access to manufacturing expertise. Drugmakers who lack the requisite personnel, facilities, equipment or expertise to keep pace with best manufacturing practices can leverage the resources and expertise of CMOs.
5) Reduce drug commercialization development times. Outsourcing obviates costly mistakes made by inadequately trained personnel, shortening product development and commercial manufacturing lead times that typically translate into substantial cost savings.[263]

The global CMO market was valued at $26 billion in 2010. One year later, CMO global revenues had reached $31.9 billion, of which China accounted for $1.9 billion. Driven by

[262] Contract Pharma (2012). CMOs and Final Dosage Manufacturing in China. http://www.contractpharma.com/issues/2012-06/view_features/cmos-and-final-dosage-manufacturing-in-china/
[263] Ibidem

increases in the sourcing of biologics and generic manufacturing, it is forecast to reach approximate revenues of $60 billion by 2018.[264] [265]

Pharmaceutical contract manufacturing was officially legalized in China by Article 13 of the Drug Administration Law in early 2001. In August 2003, the SFDA clarified, in the trial version of the "Regulations on Processing Drug for Export", that Chinese drug manufacturers may conduct contract manufacturing for a pharmaceutical company outside China.[266]

Chinese CMOs have emerged as preferred outsourcing partners for many pharmaceutical companies. One of the main drivers is cost savings, thanks to the presence of skilled, often west-trained, low labour wage workforce, which allows to reduce pharmaceutical manufacturing costs by as much as 40%.[267]

However, poor intellectual property right protection, and reports of 81 deaths and 785 serious injuries in the US linked to contaminated heparin sourced from China in 2008 highlighted the importance of quality and safe control, as well as the implementation of tighter controls on IP laws enforcement.[268]As a matter of fact, from its first promulgation in 1988 up to 2004, the Certificate of Good Manufacturing Practice was optional and poor manufacturing practices were widespread, leading to occurrences of medical accidents and legal issues.

Starting from 2004 China began to restructure its regulatory system by expanding the scope of its Good Manufacturing Standards (GMS) to all drug manufacturing plants by 2005, resulting in the shutdown of thousands of unqualified companies. With an increased commitment to international standards, a new version of GMP standards, consistent with WHO GMP, was implemented in 2011, requiring all newly built manufacturing plants to comply with the new requirements, while granting a transition period to already existing plants. The production of blood products, vaccines, injections and other sterile pharmaceutical products in existing drug manufacturers were set to meet the requirements before December 31, 2013; all other manufacturers of pharmaceutical products had time to comply with the requirements of the new GMP version until December 31, 2015.[269]

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[264] Ibidem

[265] Contract Pharma (2012). CMOs and Final Dosage Manufacturing in China. http://www.contractpharma.com/issues/2012-06/view_features/cmos-and-final-dosage-manufacturing-in-china/

[266] Pharmaceutical online (2012). Contract Manufacturing in India and China Backed by Government Policies. https://www.pharmaceuticalonline.com/doc/contract-manufacturing-in-india-and-china-backed-by-government-policies-0001

[267] Ibidem.

[268] PriceWaterHouseCoopers (2009). Investing in China's Pharmaceutical Industry – 2nd Edition, p. 11 https://www.pwc.com/gx/en/pharma-life-sciences/assets/en-pharma_03-26-small.pdf

[269] ECA Foundation (2011). China's New GMP Regulation effective since March 1, 2011. http://www.gmp-compliance.org/gmp-news/chinas-new-gmp-regulation-effective-since-march-1-2011

Despite vast concerns about enforcement of U.S. and European intellectual property (IP) and patent laws in China, the Chinese Government is committed to make conditions more favourable for foreign drugmakers to do business with Chinese CMOs. In particular, the new Marketing Authorization Holder (MAH) program, aimed at allowing research-based organizations and individuals to outsource drug manufacturing to a CMO, while retaining IP rights and marketing authorization status on approved drugs, is likely to significantly impact the global clinical development and manufacturing strategies of multinational pharmaceutical companies operating in China.[270]

Therefore, while many Big pharma companies such as AstraZeneca have already increased their outsourcing orders to Chinese CMOs, with the appealing factors of cost saving, market opportunity, as well as improved IP and GMP standards, China is expected to attract more contract manufacturers in the near future.[271]

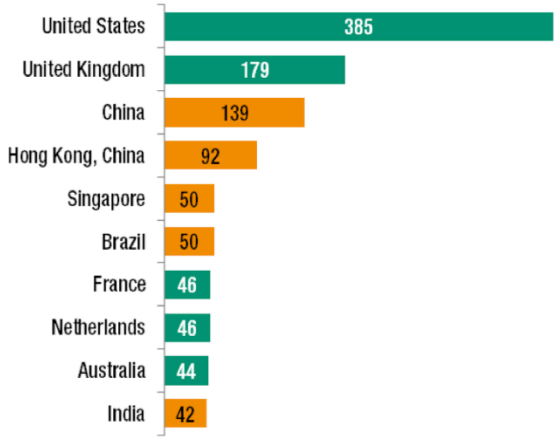
[270] PharmTech (2015). China FDA Reforms Encourage Western Companies to Manufacture in China. http://www.pharmtech.com/china-fda-reforms-encourage-western-companies-manufacture-china-0

[271] PriceWaterHouseCoopers (2009). Investing in China's Pharmaceutical Industry – 2nd Edition, p. 11 https://www.pwc.com/gx/en/pharma-life-sciences/assets/en-pharma_03-26-small.pdf

1.3. FDI Trends

Since the launch of the "open door policy", the country has been attracting foreign investors and still is an attractive market. This is confirmed by the data that UNCTAD released in January 2017 regarding global investment trends: foreign investments in mainland China remained robust rising by 2.3% to a new record of about $139 billion, in contrast with the widespread decline in inflows in developing Asian countries (-22% to an estimated $413 billion).[272]

Fig. 3.1 Estimated FDI inflows: top 10 host economies, 2016 (Billions of US dollars)



Source: UNCTAD (2017)

If in the past China relied heavily on foreign investments to boost growth, in recent years an opposite trend that sees foreign companies relying on the Chinese market to grow and gain competitive advantage has also emerged.

This is particularly true for the pharmaceutical industry, that is betting big on China. Healthcare spending as a percentage of GDP grew from about 2 percent in 2005 to 3.5 percent in 2009 (when the reform of the healthcare system started), to about 6 percent today, accounting for about 4 trillion yuan ($435 billion; 412 billion euros;). Research by Deloitte Analysis (2011) predicts it will top 8 trillion yuan by 2020; by 2030, total Chinese spending on healthcare will reach 16 trillion yuan, 10 percent of that year's expected GDP. As the Government encourages private investments in the healthcare sector, private equity and venture capital funds, insurance companies, and foreign pharmaceutical, hospital and tech companies are flowing into the market. China healthcare mergers and acquisitions surged from $18.8 billion in 2014 to $54 billion in 2015.[273] In addition, China is already the second-

[272] UNCTAD (2017)Global investment trends monitor, No. 25, 1 February 2017. http://unctad.org/en/PublicationsLibrary/webdiaeia2017d1_en.pdf
[273] China Daily (2017). Healthy future.

largest pharmaceutical market in the world, estimated more than $115 billion, with sales predicted to further rise to $315 billion by 2020.[274]

Considering the extraordinary growth opportunities offered by this market, Big Pharma companies are investing heavy sums to achieve two main goals: make China a suitable place for drug discovery, development and manufacturing, and capture as much share as possible of such a booming market.[275]

Investing in China is quite complex, but the Government continues to take liberalisation measures that seek to facilitate foreign investments and increase the transparency of the investment environment. On 3 September 2016, the National People's Congress decided to modify four laws regarding foreign investments, namely, the *Law on Sino-Foreign Equity Joint Venture Enterprises*, the *Law on Sino-Foreign Cooperative Joint Venture Enterprises*, the *Law on Wholly-Foreign Owned Enterprises* and the *Law on the Protection of Investments of Taiwan Compatriots*. Among others, the change replaces to a large extent the requirement to obtain approval for the establishment and changes to foreign invested enterprises by a nationwide filing system. Under the existing, more than 30-years old, approval regime, foreign investors must apply for the prior approval from China's foreign investment approval authority, the Ministry of Commerce (together with its local offices and counterparts, MOFCOM) for the establishment of any foreign-invested enterprises (FIEs), and for any subsequent changes in and to such FIEs on a case-by-case basis, which often interfered with the parties' freedom of agreement on commercial terms – especially in the case where the FIE is a Chinese-foreign joint venture – and certainly always delayed the transaction.[276] Indeed, in reviewing an FIE application case, MOFCOM officials have and do routinely exercise wide discretionary powers in blue-penciling provisions of the application documentation in both the initial establishment of and any subsequent changes to the FIE, that leads to back-and-forth negotiations with the MOFCOM officials for such application documentation which delay the transaction.[277]

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http://europe.chinadaily.com.cn/epaper/2017-02/17/content_28234229.htm

[274] Ibidem

[275] FierceBiotech. Top 10 Big Pharma investments in China. http://www.fiercebiotech.com/special-report/top-10-big-pharma-investments-china

[276] Reed Smith (2016). China amends its Foreign-Investment Laws, officially reforming its more than three-decade-old Foreign Investment Approval Regime. https://www.reedsmith.com/China-Amends-Its-Foreign-Investment-Laws-Officially-Reforming-Its-More-Than-Three-Decade-Old-Foreign-Investment-Approval-Regime-09-22-2016/

[277] Ibidem

Tab. 3.1 Top 10 Big Pharma investments in China (US$ billion)

Company	Investment	Details
Pfizer (辉瑞)	$9.4	$145 million invested in branded generics and JVs; 1 global Biotech Center,
Roche （罗氏）	$9.2	$410 million invested in R&D and diagnostics; 1 manufacturing plant, 1 R&D center, 1 global drug development center, 1 cooperation department.
Merck & Co. (MSD 默沙东)	$8.12	$1.5 billion invested in vaccines, diabetes, JVs; 10 operatig areas , 1 manufacturing plant, 1 R&D center.
Novartis (诺话)	$8.08	$1.25 billion invested in R&D and Active Pharmaceutical Ingredients (APIs)
Johnson & Johnson (强生)	$6.84	3 R&D organizations in China, and an Asia Pacific Innovation Center (APIC) recently opened in Shanghai to connect innovations from China and the region to the global market
GlaxoSmithKline (GSK)	$6.09	$63 million invested in vaccines and JVs
Sanofi （赛诺菲）	$5.94	$90 million invested in diabetes
AstraZeneca （阿斯利康）	$5.3	$200 million invested in branded generics and CRO collaboration
Eli Lilly （礼来）	$4.88	$80 million invested in diabetes and branded generics
Bristol-Myers Squibb （百时美施贵宝）	$3.56	1 pharmaceutical plant in Shanghai that manufactures antibiotics, cardiovascular, analgesics and metabolics

Source: Grimes & Miozzo (2015); FierceBiotech

Following the Amendments that took effect last October, the existing approval system has been replaced by the so-called "negative list plus filing-for-records", based on which, the establishment and administration of corporate changes of FIEs in "industries that are not subject to special administration measures for entry" will no longer be subject to the prior approval by MOFCOM. Instead, a filing-for-records with MOFCOM for the establishment and changes will be required.[278] However, the MOFCOM approval will still be required for foreign investment made into sectors that fall within the "negative list" issued by the State

[278] Ibidem

Council, which groups items that require "special administration measures for entry".[279] Therefore, according to this new system, the *Catalogue for the Guidance of Foreign Investment Industries* will divide industries into (1) encouraged, for which only filing-for-records procedures with the local MOFCOM office will be required, and (2) negative list, which groups encouraged items subject to limitations on foreign equity ownership, restricted items and prohibited items, for which MOFCOM prior approval is still required.[280]

The so-called FIEs are the sole forms of investment that also allow to carry out manufacturing activities in China. They include:

- Wholly Foreign-Owned Enterprises (WFOEs – 外商投资企业), limited liability companies wholly owned by the foreign investor(s).
- Sino-foreign Joint Ventures (JVs – 中外合资企业), business arrangements in which the participants create a new business entity or an official contractual relationship and share investment and operation expenses, management of responsibilities, profits and losses.[281] JVs are sometimes the only form of investment allowed for selected industries that are controlled by the Government (ie. building and constructions). Otherwise, foreign companies may consider appropriate to engage in a JV when the Chinese partner owns an extensive distribution network, have access to critical resources, a high percentage of market share, or a strong brand. Sino-foreign JVs can take the form of Equity Joint Ventures (EJVs - 中外合资经营企业) or Cooperative Joint Ventures (CJVs - 中外合作经营企业).
    - Equity Joint Ventures (EJVs - 中外合资经营企业) are limited liability companies for the establishment of which foreign partner(s) shall contribute a minimum of 25%. According to the *Catalogue for the Guidance of Foreign Investment Industries,* in some specific industries the Chinese party is required to have control over the JV, in which case the foreign party is not allowed to own more than 49%.
    - Cooperative Joint Ventures (CJVs - 中外合作经营企业) is a more flexible form of investment, in which there is neither a minimum contribution requirement, nor a limitation regarding the contribution made by the investors

[279] Baker McKenzie (2017). Draft 2016 Foreign Investment Catalogue – China continues opening Sectors to Foreign Investors.
http://www.bakermckenzie.com/en/insight/publications/2017/01/draft-2016-foreign-investment-catalogue/
[280] Ibidem
[281] Path to China (PtC). Joint Venture Registration in China (2017). http://www.pathtochina.com/reg_jv.htm

to be expressed in a monetary value (as in the case of EJV). Furthermore, the parties involved can agree upon whether to operate as separate legal entities (and bear liabilities independently), or as a single business entity. A cooperative venture may also be registered as a limited liability entity, resembling an EJV in operation, structure, and status as a Chinese legal entity.[282]

- Foreign Invested Commercial Enterprises (FICEs - 外商投资商业企业), which can have the form of either a WFOE or a JV, are allowed to conduct the following commercial activities:
    - Import/export
    - Retailing of goods and related services to individual persons from either a fixed location or through television, telephone, internet, mail order and vending machines.
    - Franchising of a business model or brand directly, or passing it to other local companies
    - Wholesaling of goods and related services
    - Commission agency activities

  Since a FICE is not allowed to engage in selling pharmaceutical products, agricultural chemicals, chemical fertilizers, processed oil, grains, vegetable oil, edible sugar and cotton, if a foreign investor wants to establish more than 30 retail stores in China and distribute the products mentioned above, the FICE is required to have the form of a JV in which the foreign party owns a maximum of 49%.[283]

Merger and acquisition is a new trend in China: the actual use of foreign capital in the mode of merger and acquisition was $16.82 billion, with an increase of 181% year on year and a proportion rising from 5.6% in 2014 to 14.7% in 2015.[284]

Generally, the scale of foreign capital attraction is increasing rapidly, as well as the actual use of foreign capital. Between January and November 2015, China set up 23,648 foreign-invested enterprises, with an increase of 11% year on year. Foreign capital attraction in the free trade pilot sites in Guangdong, Tianjin and Fujian also obtained remarkable achievements,

[282] Ibidem
[283] EU SME Centre (2012). Establishment of a Foreign Invested Enterprise in China. http://www.ccilc.pt/sites/default/files/eu_sme_centre_guideline__establishment_of_fie_in_china_jul_2012.pdf
[284] MOFCOM (2016). 2015 Business Review IV: Foreign Capital Volume Creates New High while Reform and Opening up Measures Rapidly Push Forward. http://english.mofcom.gov.cn/article/zt_businessview2015/news/201602/20160201261310.shtml

with 5,159 foreign-invested enterprises set up in total, doubling its increase year on year. The actual use of the foreign capital also increased of 7.9% year on year. In particular, the actual use of foreign capital of service industry reached $69.58 billion, with an increase of 18.8% year on year, accounting for 61% of the national total; for high-tech manufacturing industry it was $8.54 billion, with an increase of 11.7% year on year.[285]

[285] Ibidem

1.4. Catalogue for the Guidance of Foreign Investment Industries

The catalogue for foreign investments is a key instrument for regulating foreign investments in China. Firstly promulgated in 1995, it was periodically updated in 1997, 2002, 2004, 2007 and 2011. The current version -the sixth edition- promulgated in 2015, groups industries in three categories, according to whether foreign investments are encouraged, restricted or prohibited. Industries not appearing on the list are to be considered as permitted.

In the 2015 version, a total of 423 projects is listed, of which 349 are encouraged. The number of projects under the restricted category has been reduced from 79 to 38, while the remaining 36 are prohibited. Projects requiring the invested enterprises adopting the form of Sino-foreign equity/cooperative joint ventures (EJV/CJV) have decreased from 43 to 15. Projects requiring majority shareholding by Chinese parties have decreased from 44 to 35.[286] The 2015 Version mainly lifts restrictions on manufacturing industries and service industries, including logistics, retail/wholesale, e-commerce and finance.

Focusing on the medical and pharmaceutical industry, the list of the **encouraged** projects includes:

1. Planting and cultivation of traditional Chinese medicines.[287]
2. Production of drugs and drug compounds, with particular concern for drugs concerned with cancers, cardio, cerebrovascular and nervous system diseases, which have been ranking high among the main causes of mortality in China in the last few years as a result of the epidemiologial transition that the country is experiencing. The development of new drugs and the use of new technologies is also encouraged. In detail, the catalogue lists the following pharmaceutical projects:

> 52. Production of new type compound medication or active composition medication (including bulk drug and preparation);
> 53. Production of amino acids: tryptophan, histidine, and methionine with fermentation method;
> 54. Development and production of new anti cancer medication, new cardio-cerebrovascular medication and new nervous system medication;
> 55. Production of new drugs with bio-engineering technology;

[286] MinterEllison (2015). China's Foreign Investment Industries Guidance Catalogue -2015 version-. http://www.minterellison.com/files/Uploads/Documents/Publications/Alerts/Alert%20-%20China%20New%20FDI%20Catalogue%20-%20March2015.pdf

[287] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录(2015 年修订), section I Farming, Forestry, Animal Husbandry and Fishery Industries, point 6.

56. Production of new type bacterin for AIDS, HCV and contraception as well as cervical carcinoma, malaria and hand-foot-and-mouth disease;
57. Exploitation and production of marine drug;
58. Drug preparation: production of new formulation using new technologies of sustained-release, release, targeting and percutaneous absorption;
59. Exploitation and production of new type of pharmaceutical adjuvant;
60. Production of antibacterial raw material drug for animal use (including antibiotics and synthetic chemicals);
61. Production of new products of antibacterial drug, insect repellent, pesticide, anticoccidial drug for animal use and new formulation;
62. Exploitation and production of new diagnosis reagent;
324. Biological engineering and bio-medical engineering technique and development technique of biomass energy. [288]

3. Manufacturing of specialized medical equipment and new technologies for the enhancement and control of drug quality:

165.Manufacturing of electronic endoscopes;
166. Manufacturing of fundus cameras;
167.Manufacturing of key components of medical imaging equipments (high magnetic field intensity and superconducting magnetic resonance imaging equipment, X-ray digital tomography imaging equipment, and digital color ultrasonic diagnostic equipment);
168.Manufacturing of Medical Ultrasonic Transducer (3D);
169.Manufacturing of boron neutron capture therapy equipments;
170.Manufacturing of image-guiding intensity-modulated radiation treatment system;
171.Manufacturing of Hemodialysis, Blood Filter;
172. Manufacturing of full-automatic biochemical monitoring equipment, blood cells analyzer with five classifications, full-automatic chemiluminescence immune analyzer and high-throughputDNA sequencing system;
173.New techniques of quality control of medicine products and new equipment manufacturing;
174.New analytical techniques and extraction technologies, and equipment development and manufacturing for the effective parts of national medicines;
175.Manufacturing of multi-layer co-extrusion water-cooled film mold-blowing equipment for non-PVC infusion bags for medical use.[289]

4. Scientific research in the field of biological engineering and biomedical engineering.[290]

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[288] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录(2015 年修订), section III Manufacturing Industries, subsection (XI) Medical and Pharmaceutical Products Industry.

[289] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录(2015 年修订), section III Manufacturing Industries, subsection (XVIII) Special Equipment Manufacturing.

[290] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录(2015 年修订), section VIII Scientific Research and Technical Services, point 324.

5. Investments in service agencies for the elderly, the handicapped and children, as well as retirement organizations.[291]
6. Pharmaceutical wholesale and retail trade industry is also encouraged, including the development of chain distribution in rural areas and the joint distribution of general goods, logistics and related technical services such as low-temperature distribution of special drugs.[292]

Investments in medical institutions moved from permitted (in the 2011 version) to **restricted** and limited to EJVs or CJVs.[293]However, wholly foreign owned hospitals have been implemented on a pilot scheme in Beijing, Tianjin, Shanghai, and in the provinces of Jiangsu, Fujian and Guandong.[294]

In order to protect Chinese cultural heritage, some investments in the field of Traditional Chinese Medicine are **prohibited**, including:

> 7. Processing of traditional Chinese medicines that have been listed as the Regulations on Conservation and Management of Wild Chinese Medicinal Material Resources and Rare and Endangered Plants in China;
> 8. Application of preparing technique of traditional Chinese medicines in small pieces ready for decoction, like steam, frying, moxibustion, calcining, and production of the products of secret recipe of traditional Chinese patent medicines.[295]

Development and application of human stem cells and gene diagnosis therapy technology are also prohibited.[296]

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[291] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录 (2015 年修订), section XI Public Health and Social Work, points 346, 347.

[292] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录 (2015 年修订), section VI Wholesale and Retail Trade Industry, points 315, 316.

[293] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录 (2015 年修订), section XII Public Health and Social Work, point 34.

[294] MinterEllison (2015). China's Foreign Investment Industries Guidance Catalogue -2015 version-. http://www.minterellison.com/files/Uploads/Documents/Publications/Alerts/Alert%20%20China%20New%20FDI%20Catalogue%20-%20March2015.pdf

[295] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录 (2015 年修订), section III Manufacturing, subsection (I) Medical and Pharmaceutical Products Industry.

[296] Catalogue for the Guidance of Foreign Investment Industries (Amended in 2015). 外商投资产业指导目录 (2015 年修订), section VIII Scientific Research and Technical Services Industries, point 20.

In order to further open up to foreign investments, on 7 December 2016, China's NDRC and MOFCOM jointly revised the 2015 Catalogue and released a draft 2016 version, soliciting public comments until 6 January 2017. On top of the significant liberalization in 2015, the revised Catalogue reduces the number of restricted items from 93 to 62, and relaxes restrictions on market access of foreign capital in services, manufacturing and mining sectors.

It will include a ‘Negative List’ grouping those industries subject to restrictive measures, and a list of encouraged projects. Foreign investors will have to consult the Negative List in order to determine whether their investments are subject to MOFCOM approval under the new FIE recordal system.

2. Is China transforming into a hub for pharmaceutical innovation?

Over the past 10 years, the overall growth in global R&D investments is being driven by substantial increases in Asian countries, which accounted for 42.3% of all global R&D investments in 2016, and especially in China, whose R&D investments increased by more than 10% per year for many years. Currently, China R&D growth rate is in the 7% growth rate range (which is still more than twice that of the US and most European countries) and accounts for 20.1% share of total global R&D.[297] The US continues to be the country with the largest investments in R&D, as in the past 50 years, however, a slowing rate has been recorded in the past few years. Nowadays the US share of global R&D exceeds that of China by only 5.6 points percentage.

According to the Industrial Research Institute (IRI), for the next five years and beyond, technological demands will be driven by biopharmaceuticals, automation and robotics, artificial intelligence, cloud computing, autonomous transportation systems, unmanned aerial systems and advanced military and weapons systems. Most countries, and especially Japan and China, are facing an increasing rate of aging populations that directly impact global demographics, which is also likely to drive technological demands, economic and R&D funding hurdles, and possible future research staffing issues on a global basis.[298]

With regard to the Chinese pharmaceutical industry, there are many doubts as to whether the country can actually foster pharmaceutical innovation, due to the huge backlog in the pharmaceutical registration process and the failed attemps to speed it up, the predominance of generic pharmaceuticals and Government's pressure on drug prices. Currently, the country's pharmaceutical manufacturers allocate only 1% of total costs to R&D; in comparison, Japan, France, and Germany dedicate 25%, 12% and 3%, respectively.[299] Also, when innovation happens, many new pharmaceuticals may never reach the market, if companies are unable to have their drug listed on the reimbursement list. Bribery scandals, a copycat business environment, and doubtful integrity of published research also contribute to the scepticism about China's innovation potential.

[297] The Industrial Research Institute (2017). 2017 R&D Trends Forecast: Results from the Industrial Research Institute's Annual Survey, Research-Technology Management, Vol. 60, No. 1, p. 18.
[298] Ibidem p. 19.
[299] Euromonitor International (2016). Pharmaceuticals: China wishes to Transform into a Hub for Innovation – Is it possible?
http://blog.euromonitor.com/2016/06/pharmaceuticals-china-wishes-to-transform-into-a-hub-for-innovation-is-it-possible.html

However, it is evident that the Chinese Government gives priority to innovation, as China's innovative pharmaceutical companies have relatively easy access to capital and receive growing direct investments from the government. The overall government spending on R&D has been rising at a CAGR of 14% over 2009-2015 – representing the highest growth among other major pharmaceutical producers.[300]

As the world's second largest pharmaceutical market, China is rapidly progressing as a hotspot for global innovation. Most Big Pharma companies have established their research units in China: Roche started operations in Shanghai in 2004, followed by Pfizer and Sanofi-Aventis in 2005, GlaxoSmithKline (GSK) and AstraZeneca in 2007, Novartis in 2008, and both Eli Lilly and Johnson & Johnson in 2009; Merck, Novo Nordisk and Bayer choose to settle their R&D centers in Beijing.

However the innovative output is low, as only 1.78% of the 9543 patents granted by the United States Patent and Trademark Office (USPTO) between 2004 and 2014 by the top big pharma companies had Chinese citations, and only 1.44% involved Chinese inventors.[301] It seems that, notwithstanding the positive developments in both business and regulatory environment, the objective of developing China as a major pharmaceutical R&D hub, is likely to be achieved in the long-term with a view to developing a significant market share in the coming 10–20 years, as growth opportunities in other markets decline. For the time being, the country still lacks leadership and management skills and is likely to continue to depend for some time on significant contributions from foreign companies to help develop its own pharmaceutical industry, to provide medication for a rapidly growing middle class with the ability to pay and to provide treatments for increasing numbers of people suffering from untreated or misdiagnosed diseases such as cancer, diabetes and hypertension.[302]

2.1. R&D and IP protecion

Ding et al. (2011) analyzed China's evolution from pure imitation to independent innovation and showed that the Government's relevant policies played a key role. Intellectual property policies, in particular, have shaped drug R&D environment in such a way that the dates when different patent laws came into force can be used to delimit four phases in the evolution of pharmaceutical R&D in China:

[300] Ibidem
[301] Grimes S., Miozzo M. (2015). Big Pharma's Internationalization of R&D to China. European Planning Studies, Vol. 23, No. 9, pp. 1878/1882.
[302] Ibidem

- *Pure imitation phase (1949-1984).* Before 1985 China had no patent law to protect IP rights of pharmaceutical products, so drug manufacturers simply imitated patent drugs from foreign companies.

- *Innovative imitation phase (1985-1993).* In 1985 the first patent law came into force but did not prohibit the imitation of the molecular structure of existing drugs. This, added to the fact that most Chinese companies lacked both capital and technology, led to the production of drugs that had the same molecular structure of the originals but showed some innovative features mainly in delivery methods and preparation formulations.

- *Imitative innovation (1993-2008).* To comply with the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIP) and prepare for entering the WTO in 2001, China amended its Patent law in 1993 and in 2000, and legally defined 'new drug' for the first time in its Provisions for Drug Registration, offering Data Exclusivity Protections to any applicant who obtained approval for production or distribution of a drug containing any new chemical entity. During this period drug innovation was focused on the development of "me-too" drugs, isomers[303] obtained by modifying the chemical structure of existing drugs, such as changing acid or basic group. Despite the high volume of new drug approvals occurred in the period, China's real drug innovation capabilities remained limited due to the practice of registering a new drug by simply changing some chemical components. When applying the new drug standards of the USA, China had only 2 New Chemical Entities between 2000 and 2008, while the USA had 193 in the same period. For this reason the SFDA (current CFDA) implemented the New Provision for Drug Registration in 2007, raising the requirements for drug approval, which greatly reduced the number and improved the quality of new drugs.

- *Independent Innovation (2008-present).* The National Intellectual Property Strategy Compendium issued by the State Council in 2008, sets the objective of making China a country with high levels of IP properties' creation and protection by 2020. The 2008 patent law marked the shift towards a more comprehensive and stronger drug patent protection, making it difficult to imitate existing drugs. In addition, to foster innovation in the Chinese pharmaceutical industry, a special project, Major New Drug Creation, was lauched under the 11th Five-Year Plan with the aim to develop a series of innovative drugs for 10 major diseases such as malignant tumors and cardiovascular diseases with a budget of about US$1 billion. The funding for this project are estimated to increase to about $4.3 billion by 2020.[304]

[303] Compounds with same atomic weight but different composition.

[304] Ding J. et al. (2011). From Imitation to Innovation: A Study of China's Drug R&D and Relevant National Policies. Journal of Technology Management & Innovation, Vol. 6, No. 2, pp. 1-13.

As already mentioned in chapter 2 of this work, innovation is placed at the heart of China's development strategy in the 13th Five-Year Plan, which positions biomedicine as a key emerging industry and will be an important component of moving Chinese manufacturing up the value-added manufacturing chain and enhancing its future global competitiveness and technological edge. The main targets for 2020 are: (1) to increase China's global innovation ranking from 18 to 15, as well as the share of R&D spending as a percent of GDP from 2.1 to 2.5; (2) increase the number of patents filed per 10,000 people from 6.3 to 12; (3) increase the number of R&D personnel per 10,000 people employed per year to 60, and the share of its total population with scientific degrees from to 10%.

2.2. CROs and Technological Parks

As Big Pharma's traditional R&D model has entered a period of crisis due to the increasing costs of the innovation process, talent shortages and mounting competition from generic drug companies following the so-called "patent cliff",[305] China is being increasingly integrated into the global pharmaceutical value chain in order to both reduce the costs of drug development and to seek new forms of innovation. Between 2004 and 2007, multinationals increased their R&D sites by 6% and of these new sites, 83% were located in either China or India.[306]
China, in particular, has become a major center for developing APIs and also for clinical trials. However, due to concerns about the regulatory environment as well as safety and quality issues, big pharma has been reluctant to offshore the high end of this activity to China.
Clinical trials can account for between 40% and 60% of total costs of drug development, and estimates of savings in China vary from 67% to 80% of the costs in the US or Japan,[307] which, together with China's large pool of human subjects for clinical trials, can be exploited to attract foreign investments and gain access to basic science and venture capital.

Chinese CROs (Clinical Research Outsourcing) have evolved to be the most active component in the Chinese pharmaceutical R&D arena.[308]The first CROs were set up by the foreign Quintiles and MDS Pharma Service in 1996. Since then, more than 300 CROs were established in China, which mainly provide preclinical and clinical research services for MNCs, local companies, as well as other organizations such as universities and academic

[305] A colloquialism to denote the potential sharp decline in revenues upon patent expiry of one or more leading products of a firm, since these products can be replicated and sold at much cheaper price by generics'manufacturers.
[306] Grimes S., Miozzo M. (2015). Big Pharma's Internationalization of R&D to China. European Planning Studies, Vol. 23, No. 9, p. 1876.
[307] Ibidem, p.1885.
[308] Shi et al. (2014). Contract Research Organizations (CROs) in China: integrating Chinese Research and Development capabilities for global drug innovation. Globalization and Health, Vol. 10, No. 78, p. 5.

institutes. In recent years, to compete against global giant CROs such as Quintiles, Covance, PPD, ICON and Parexel, the industry of Chinese CROs was consolidated through M&A of small CROs, giving rise to local key players such as WuXi AppTec, Tigermed, and VenturePharm. These local giants rely on unique connections with local universities, academic institutes, hospitals and domestic pharmaceutical companies, and receive a noteworthy sum of governmental funding.

Chinese CROs are playing an increasingly important role in integrating Chinese pharmaceutical R&D capabilities into the global drug industry. Nowadays, they are the most efficient channel for foreign organizations to obtain and use the emerging pharmaceutical innovation capabilities in China; simultaneously, they contributed to reshape the R&D of the national pharmaceutical industry, thanks to their interactions with both research institutions and pharmaceutical companies.[309]

China's effort to innovate the country and to catch-up, if not overtake, the US has also brought many innovation hubs, or high-tech parks, to life. As reported by the State Council, the country's altogether 146 high-tech innovation zones contributed to 12 percent of the national GDP, with Beijing's Zhongguancun, Shanghai's Zhangjiang and Shenzhen's Nanshan, among others technology hubs, competing for the future "Chinese Silicon Valley".[310]

Beijing's Zhongguancun Science Park was the first special area to be formally established in 1992. Nowadays, it is the largest and most important center of innovation in China. Home to 6,157 high-tech enterprises (a tenth of the nation's total) by the end of 2015, it launched as much as 33.4 startups on average on daily basis in the first quarter of 2016 only. Zhongguancun is leading in biotechnology and biomedicine, accounting for 20% of all new patents in the field of biotechnology in China in 2013.[311]

Shanghai's Zhangjiang Hi-Tech Park was initially designed to be China's "Silicon Valley" and "Drug Valley" upon its establishment in 1992. In 2013 it was listed as the most competitive high-tech innovation zone to Silicon Valley.[312] As a "Drug Valley", Zhangjiang has been dedicated to biological technology development. More than 300 drugs are under research, half of which are innovative. One in every three new drugs in China, as well as 25%

[309] Ibidem
[310] State Council (2016). China's High-Tech Innovation catching up with Silicon Valley http://english.gov.cn/news/top_news/2016/08/05/content_281475409885715.htm
[311] Alberto Forchielli (2016). Chinese Innovation Hubs. http://www.albertoforchielli.com/2016/09/19/chinese-innovation-hubs/
[312] State Council (2016). China's High-Tech Innovation catching up with Silicon Valley http://english.gov.cn/news/top_news/2016/08/05/content_281475409885715.htm

of new patents in this field in China, come from this tech park.[313]Foreign MNCs play an important role in pharmaceutical research. Up to date, 133 MNCs have invested in R&D operations in Shanghai.

Innovation hubs usually develop in urban communities that are home to universities, research centers, wealthy investors. These, together with national and local government policies and funds are all fundamental factors in creating a favorable environment for fostering innovation and for startups to emerge. The most common source of funding for innovative startups is Venture Capital (VC), and all major innovation hubs in China can count on VC investors such as Sequoia Capital, IDG Capital Partners and SB China Capital (the top 3 VC firms in 2015 according to Forbes). Private VCs are complemented by state-controlled venture funds: in August 2016 the State Council has approved a $30.19 billion venture capital fund to invest in innovative technology and industrial upgrading projects to be financed by China Reform Holdings Corp Ltd, China Postal Savings Bank, China Construction Bank Corp and Shenzhen Investment Holdings.[314]

Beijing has been the city that secured the most venture capital funding both in terms of number of deals and capital, followed by Shanghai. In 2015, 677 deals were signed in Beijing, for a total value of around $20 billion. In Shanghai, on the other hand, $12.2 billion were raised through 365 deals.[315]

As suggested by the rising number of strategic mergers and acquisitions, the rapid growth of Chinese innovation-oriented drug companies (like Zai Lab), and increased activity of Chinese drug developers in the stock market, there is a rising confidence in the Chinese pharmaceutical innovation potential. The deals between Eli Lilly and Innovent, the partnership between AstraZeneca and WuXi AppTec, the raising of $158.4 million in an initial public offering on NASDAQ by BeiGene (drug developer), as well as the imminent IPOs of Jiangsu Hansoh and Simcere on Hong Kong Stock Exchange are signals that innovation activities are expected to intensify in the near future.[316]

[313] Alberto Forchielli (2016). Chinese Innovation Hubs. http://www.albertoforchielli.com/2016/09/19/chinese-innovation-hubs/

[314] Reuters (2016). China launches $30 bln State-controlled Venture Capital Fund. http://www.reuters.com/article/china-funds-idUSL3N1AZ1SX

[315] Alberto Forchielli (2016). Chinese Innovation Hubs. http://www.albertoforchielli.com/2016/09/19/chinese-innovation-hubs/

[316] Euromonitor International (2016). Pharmaceuticals: China wishes to Transform into a Hub for Innovation – Is it possible? http://blog.euromonitor.com/2016/06/pharmaceuticals-china-wishes-to-transform-into-a-hub-for-innovation-is-it-possible.html

Chapter 4 – Assessing the attractiveness of the Chinese pharmaceutical market

In order to choose the target country and the most appropriate method of entry, companies need to assess the *attractiveness* of that country, either in absolute terms or relative to another country. The so-called '*country attractiveness analysis*' is preliminary to the choice of the form of entry, generally known as '*entry strategy'*.
Theoretically, a country is attractive if, in investing in it, foreign investors "*get a return that is equal to or higher than their risk, adjusted weighted cost of capital.*"[317]Thus, the evaluation of a foreign investment is usually based on the trade-off between opportunities and risks.

Based on the proposal of Laserre of evaluating a country's attractiveness through the analysis of its components, namely (1) market and resource opportunities, (2) competitive context and (3) country risks, in the first part of this chapter, I will attempt to assess the overall 'attractiveness' of the People's Republic of China in macroeconomic terms. Firstly, a PESTLE analysis of the pharmaceutical market will be presented, and then, the issues likely to affect the ease of doing business in China will be discussed to give a bird's eye view of the whole environment in which a potential foreign investor would operate. Secondly, an assessment of market (in terms of demand) and resources (in terms of natural, human and infrastructure/support industries) opportunities will be made, with a particular focus on issues that are relevant for pharmaceutical companies. Finally, the level of competition in the main segments of the pharmaceutical industry will be assessed and some implications for family firms will be outlined.

[317] Lasserre, Philippe (2012). Global Strategic Management, Third Edition. Palgrave Macmillan, p. 174.

1. Assessing China's Macroeconomic environment

1.1. PESTLE Analysis of the Pharmaceutical Market in China

PESTLE, acronym of Political, Economic, Social, Technological, Legal and Environmental, is a useful tool for companies to assess which macroenvironmental aspects are likely to impact operations in a foreign country.

Political factors include tax policies, fiscal policy, trade tariffs etc. that may affect the business environment to a great extent; economic factors include inflation rate, interest rates, foreign exchange rates, economic growth patterns etc. and also accounts for the FDI (foreign direct investment) depending on certain specific industries who're undergoing the analysis; social factors refer to cultural trends, demographics, population analytics etc; technological factors refer to automation, R&D, and the amount of technological awareness that a market possesses; legal factors take into account both the legal environment of the foreign country and company-specific policies. Consumer laws, safety standards, labor laws etc. are examples of legal factors; environmental factors include all those aspects that influence or are determined by the surrounding environment, such as climate, geographical location, weather etc.[318]

In thise section, the key factors that favoured the rapid growth of the pharmaceutical industry and those that will continue to drive this growth in the next years are summarized.

Political analysis

With over 70 million members in the country, the Communist Party of China is the largest political party in the world.[319] It has governed China for over 60 years and remains secure in its position as the country's sole political party. People who criticize the Government are often punished severly for "inciting subversion", while home confinement, abductions and brutal physical torture are used against activists. According to Amnesty International, between July and October 2015, targeted crackdown on 245 lawyers and activists took place.[320] Besides, scandals involving education, healthcare and police sectors have roiled the opinion of the public against the Government in most of 2016, representing a wide spate of social crisis.

[318] Pestle Analysis. What is a PESTLE Analysis? A Tool for Business Analysis. http://pestleanalysis.com/what-is-pestle-analysis/

[319] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, p. 16. www.marketline.com

[320] Ibidem, p. 18.

Furthermore, there has always been heavy censorship of the media and the internet, especially social media. Topic such as the Tiananmen Square protests, Falun Gong, protests in the ethnic minority provinces of Tibet and Xinjiang, other sensitive subjects and, since 2010, even the word "freedom" are censored.

Recent directives require online writers to register with their original names and restricted the use of Virtual Private Networks (VPN's), which many Chinese (but also foreigners living in China) depend upon to gain information that are blocked otherwise, or to access social networks and websites that are otherwise censored in mainland China, such as Facebook, Instagram and Google and its tools. Therefore, it comes to no surprise that in its Freedom on the Net 2015 report, Freedom House, a US based non- governmental organization (NGO), ranked China worst abuser of internet freedom with a score of 88 (where 0 indicates most free and 100 least free).[321] For a country that aims at positioning itself among the most innovative countries of the world, this lack of freedom of expression is counter-productive and is likely to have its effect on innovation and creativity in the long term.

The country has strong geopolitical influence, especially in Africa, which surpassed the US as China's largest trading partner and gave China access to oil reserves. China's sphere of influence is also spreading in South and Southeast Asia, where the Chinese Government is financing ports, pipelines, roads, naval bases, as well as public investments. Furthermore, being a permanent member of the United Nations, China has great power over UN decisions and its global policymaking bodies.

While, internally, the outbreak of ethnic violence due to the Islamic separatist movement among Turkic-speaking Muslim Uighur ethnic group poses a high political risk to the country, Chinese claims on over 90% of the resource-rich East China Sea and the South China Sea have fuelled maritime and territorial disputes with Japan, Vietnam, Philippines, Taiwan, Malaysia and Brunei. Tensions in the area are further complicated by the intervention of the USA, which has deployed its naval assets to see to it that the access to waterways is not impeded for its allies. Furthermore, there are concerns about the newly elected President Donald Trump, who during his campaign has labelled China as a "manipulative power", stating that the country is hell bent on the destruction of the industrial sector in the US. His rhetoric might lead to a rift in the Sino-US relations.

On the other hand, China signed a total of 58 economic deals amounting to $50 billion with Russia. The two countries hope to remain friends and align themselves to challenge the

[321] Ibidem, p. 19.

international system led by the USA. However, the election of Trump, who is said to have been strongly supported by Russian President Putin may change this scenario.

Furthermore, the "One Belt, One Road initiative" (一带一路) proposed by president Xi Jinping that focuses on connectivity and cooperation thanks to improved infrastructure connectivity and enhanced economic and trade cooperation between the PRC and Eurasia, will strengthen the influence of China. At the same time, in a phase of economic slowdown, countries located along both the land-based silk road and the oceangoing maritime silk road will benefit from this ambitious project. Strategically located at the intersection of these two roads, Italy could build closer investment and trade ties through the initiative. The two countries may cooperate in technological innovation in Internet Plus and other technology-related sectors, and align their thoughts and plans to grow their manufacturing sectors. China may also strengthen cooperation with Italy in environmental protection and renewable energy, agriculture and food safety, sustainable urbanization, medical and health, and aviation and aerospace sectors to strengthen China's industrial restructuring and future developments.[322]

After more than three decades of high-speed growth and industrialisation, the Chinese economy has now begun to enter a phase of medium-high growth that drives China towards a 'moderately prosperous society'. As China progresses from the early stages to the relatively advanced stages of industrialisation, a gradual economic transformation is shifting its industrial structure towards the middle to high end of the value chain.

Two aspects outlined in the 13th Five-Year Plan are particularly relevant for the pharmaceutical industry, which was also one of the 7 key industries in the 12th Five-Year Plan:

-The commitment to ensure equal opportunity, social security, and access to high-quality education and healthcare for all.

-The intention to shift from a manufacturing, export-driven economy, to an innovation-driven economy.

These two objectives can be achieved by developing China's biopharmaceutical industry, an important part of the bioscience industry that has been highlighted among the strategic emerging industries of the country. Biopharmaceuticals include sub-industries such as synthetic pharmaceuticals, modern traditional Chinese medicine (TCM), biopharmaceuticals and medical devices. As the precision of medical technologies is improving rapidly and the

[322] ChinaGoAbroad (2016). China to strengthen economic cooperation with Italy via the "One Belt, One Road" Initiative. http://www.chinagoabroad.com/en/article/20467

ageing population in China continues to grow, the Chinese biopharmaceutical industry is poised to sustain rapid development throughout the 13th FYP period.

Government's purpose is to double the industry's scale through the broad application of genomics and other biotechnologies, networked application demonstration, and the scaling up of new products and services, including personalised treatment and innovative pharmaceuticals. Innovation will be strengthened through collaboration on key R&D projects, the commercialisation of pharmaceuticals, advances in medical devices, and the modernisation of TCM. Industry and organisational structure will be optimised through cross-sectoral mergers and restructuring, trans-regional shifts, and the development of concentrated industry clusters.[323]

The Chinese Government also puts great emphasis on improving people's livelihood. As a consequence, the strong growth of the healthcare industry will be the main driver of an improved quality of life. Within the industry, composed of medical treatment, pharmaceuticals, health supplements, health management services and aged care, the pharmaceutical sector occupies the largest share. China will spur rapid industry growth by driving innovation in and upgrading of pharmaceuticals and medical device technologies, optimising the organisational structure of the industry, and cultivating new, more intelligent development approaches. As China promotes the 'Healthy China' strategic plan, both the medical services sector and the wider healthcare industry as a whole are set to flourish. Given China's immense and fast-growing ageing population, recent technological breakthroughs, the 'Internet Plus' movement and healthcare system reform, estimates show that the value of the country's healthcare industry will top RMB 8 trillion by 2020.[324]

From all these directives foreign Pharma MNCs will still have a huge opportunity in China as the government supports the opening up approach for this R&D focused industry. Cooperation schemes and incentives would be at foreign companies hand, especially the highly innovative enterprises.

In general, projects listed in the 'encouraged' category are usually eligible for preferential treatment. The principal incentives include a 15% preferential tax rate applicable to new high-technology enterprises (HNTE) and a 50% super deduction for qualifying R&D expenditure. The rules governing qualification of an enterprise as an HNTE have been revised to lower

[323] KPMG (2016). The 13th Five-Year Plan - China's transformation and integration with the world economy, p. 15. https://assets.kpmg.com/content/dam/kpmg/cn/pdf/en/2016/10/13fyp-opportunities-analysis-for-chinese-and-foreign-businesses.pdf

[324] Ibidem, pp. 59/60.

certain thresholds for a company to be recognized as an HNTE, streamline the application process and update the list of state-encouraged high-new technologies.

Effective from 1 January 2016, two individual income tax incentives were extended nationwide to stimulate technological innovation. The incentives allow the payment of individual income tax to be deferred for qualifying employees and individual shareholders of HNTEs with respect to stock awards or the capitalization of undistributed profits/reserves. Furthermore, a geographically-based incentive focuses on new HNTEs established in or after 2008. This incentive (in addition to the 15% rate that applies to all new HNTEs) is a two-year tax holiday, followed by three years of tax levied at a 12.5% rate. The 15% preferential tax rate also is granted to qualified high-tech service enterprises in 21 specified cities between 1 July 2010 and 31 December 2018, and encouraged businesses in certain regions, including Western China, Hengqin (Guangdong), Pingtan (Fujian) and Qianhai (Shenzhen), between 1 January 2011 and 31 December 2020.[325]

However, serious problems that may hinder the sound development of the industry still exist, such as exaggerated claims of medicinal efficacy, imitation, and counterfeiting.

Economic Analysis

The second world largest pharmaceutical market has very strong economic fundamentals. China has been registering strong economic growth over the past three decades, and, by the end of August 2016 had accumulated $3.19 trillion of foreign exchange reserves, useful to mitigate external shocks from the global macroeconomic environment.[326] The services sector is becoming a major driver of growth to the Chinese economy: contribution to GDP increased rapidly, from 31.36% in 1990 to 46.80% in 2015.[327] China's structural shift from export led growth to consumption led growth and transition from manufacturing dominated economy to services dominated economy may bring further economic growth and prosperity. Deregulation in the finance, education and healthcare is likely to boost the development of the service sector.

After joining the WTO in 2001, China instituted a series of changes to its trade regulations to conform to WTO standards. Various economic sectors and certain industries gradually have been opened to foreign investment. Although the economy previously was dominated by

[325] Deloitte (2016). Taxation and Investment in China 2016, p. 4. https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Tax/dttl-tax-chinaguide-2016.pdf
[326] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, p. 20. www.marketline.com
[327] Ibidem, p. 23.

state-owned enterprises (SOEs), domestic private enterprises and foreign investments have become the main driving force of economic development.

China has set up a number of special economic zones (SEZ), economic and technological development zones (ETDZ), export processing zones and bonded warehouse zones to attract domestic and foreign investment and export activities. Various preferential policies, covering tax, foreign exchange, customs, investment, employment, etc., are provided to qualified enterprises or industries in these areas. The Shanghai Pilot Free Trade Zone (Pilot FTZ) was launched in September 2013 with the aim to deepen reform and introduce policy innovations to establish advanced rules on trade and investment. Three new Pilot FTZs in Fujian, Guangdong and Tianjin were launched in April 2015.[328]

The top three foreign direct investment concentrated industries are manufacturing, real estate and leasing and commercial services.

The country has abolished most price controls, with market forces now determining the prices of the majority of products traded. In general, prices remain controlled only for goods and services that are deemed essential, such as pharmaceuticals.

Investment conditions in China have improved due to the vast consumer demand for pharmaceuticals, the lower labor costs and the changes resulting from economic reform, especially thanks to improvements in the Patent Law. The lack of Chinese pharmaceutical R&D, in particular, has left gaps in the market that are currently filled by Foreign Pharma companies, where the local demand stimulation drives Pharma growth as China still suffers from an important shortage in healthcare facilities and solutions for an ageing population that requires a better allocation of healthcare resources.[329]

One of the main current challenges is overcapacity in the Chinese heavy industry sectors, including automotive, coal, iron, cement, steel and ship building, which impacts on the country's growth and may lead to a burgeoning of bad loans in industries facing overcapacity.

Major risks to the financial stability stem from the real estate slowdown driven by a significant oversupply in smaller cities and in the northeast region, especially affected by a steep fall in property prices; the rapid growth of shadow banking, a system of credit intermediation that involves entities and activities outside the regular banking system, including trust funds, leasing companies, credit guarantee companies and money-market funds; and the increase in local government debt. Although a $300 billion debt swap plan that

[328] Deloitte (2016). Taxation and Investment in China 2016, p. 1. https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Tax/dttl-tax-chinaguide-2016.pdf

[329] Chitour H. L.(2013). Big Pharma in China – The Driving Forces behind their Success – A Qualitative Analysis. Chinese Studies, Vol. 2, No. 4, p. 172. http://dx.doi.org/10.4236/chnstd.2013.24028

allows local governments to convert their debt to low interest bonds was carried out in June 2015, the magnitude of the Chinese debt (237% of GDP in the first quarter of 2016) may have implications for the whole world and casts doubt over the long term growth of the country.[330]

Social Analysis

As already mentioned in previous chapters, major improvements have been recorded in life expectancy, infant mortality, poverty and inequality. In addition, healthcare improvement is one of the main objectives of the 13th Five-Year Plan, together with the expansion of the social safety net by increasing Government's health expenditures.

With around 6 millions people migrating to urban areas in search for better employment conditions, who generally live a marginalized life, rapid urbanization has become an important issue in contemporary Chinese society. Fuelled by huge gaps in terms of economic development and regional GDP per capita between provinces, especially between the industrialized East and Southeast and the impoverished, mainly rural North and West regions, urbanization has put increasing strain on urban infrastructure, aggravating congestion and pollution. To foster a uniform development of various provinces, since 2015, the Government has launched a "Go West" Plan that gives tax incentives to encouraged industries investing in the Western regions.

Gender imbalance is a serious problem: it estimated that by 2020, the number of men aged between 20 and 45 will exceed the number of women of the same age by 30 million.[331] As gender imbalance could lead to an increase in sexual violence, human trafficking and crime, which will destabilize the society, the Government has banned sex selective abortions and has allocated cash incentives to girl-only families.

An increasingly ageing population resulting from the one-child policy remains one of the main concerns of the Government, as it increases the need for finances to be spent on health expenditure. Furthermore, China may lose its cost competiveness, as the increase in elderly population puts a strain on the large pool of young workers with relatively low wages on which the country relies.

The combination of rapid urbanization with the fast pace at which the Chinese population is ageing also helps driving the growth of Pharmaceutical companies in the Mainland. These two factors generate a number of healthcare issues such as the increasing burden of diabetes, cardio-vascular diseases related to obesity and sedentary lifestyles of a rising number of urban

[330] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, pp. 26-27. www.marketline.com

[331] Ibidem, p. 29.

Chinese population. In addition, the ageing population also means a rise in degenerative diseases such as dementia and Alzheimer. China will also have to deal with the consequences of their astonishing growth rate in the last two decades by dealing with the effects of this development on the environment and its devastating consequences on public health, most prominently the appearance of "Cancer villages" throughout the mainland with an alarming rate of cancer incidence where heavy polluting industries are concentrated.

Furthermore, the continuously expanding middle-class is now increasingly aware of the health risks to which they and their children are exposed, that is why research has shown that for health products this population tends to spend more and more on internationally recognized brands especially after the numerous food scandals of contaminated baby milk powder in 2008.[332] This creates a major opportunity for multinational companies such as Pharma companies who entered the Chinese market as they are known for the safety and high-quality of their products. Therefore, this class tries to select carefully the products they consume and are quickly reactive to the health problems they are facing and are ready to take the necessary measures to counteract the disease.

For diabetes for example, this urban middle-class is more receptive to preventive measures and more likely to be diagnosed at earlier stages to be able to manage the disease and the treatment in an optimal manner.

Technological Analysis

The country's R&D pacts with more than 150 countries across the world have increased China's international influence in the field of science and technology. As the Government wishes to make China an innovative-driven country, R&D expenditure, as well as human resources in R&D sector have increased rapidly over the last decade. The strong growth in innovation is confirmed by the consistent rise in the number of patents acquired by China, the highest among the BRICS countries.

China has about 3,677 R&D institutions, while the number of researchers per million people doubled between 2000 and 2012 and is likely to increase, as China produces the second largest number of graduates in science and engineering after India. It should be noticed that an increasing number of Chinese graduates leave the country to study or to perform research despite the country providing researchers incentives such as offers of funding, advanced laboratory apparatus, housing allowance, facilities of employment for spouses and school

[332] Chitour H. L.(2013). Big Pharma in China – The Driving Forces behind their Success – A Qualitative Analysis. Chinese Studies, Vol. 2, No. 4, p. 173. http://dx.doi.org/10.4236/chnstd.2013.24028

admission for their children. Brain drain of talented graduates is a major concern, as only 41% of the 2.64 million Chinese students who went to study abroad have returned to the country.[333]

The country has modernized its infrastructures by building Pharma clusters for young Chinese biotech and Pharma companies such as Zhangjiang Park in Shanghai and Zhongguancun Park in Beijing to help these enterprises in their innovation endeavors by being in contact with major Pharma companies such as Eli Lily and Novo Nordisk, who have established their R&D headquar- ters in these cities. More and more Big Pharma are forming partnerships with promising local firms to help offset the consequences of their own pipelines drought. The new R&D model in the Pharma industry has also helped to seal a great deal of strategic partnerships between academia and private Pharma companies, in an effort to boost drug research using local talents, (whether educated in China or returning from overseas), who are in charge of R&D in Pharma laboratories across the country. This helps nurture the local talent pool, by having access to the latest technologies that multinational Pharma companies offer, along with the biotech incubators across the country in biotech parks in Shanghai, Beijing or more recently in Tianjin. In addition, Chinese Government has introduced a series of strict reforms for the local firms to comply with International Good Manufacturing Practice (GMP) and Good Laboratory Practice (GLP) standards, which has led to the disappearance of small Pharma firms that couldn't afford the upgrade. These drastic upgrade measures enforced by the Chinese government, have reshaped the industry's structure in the country with the emergence of high technology reliant Pharma manufacturers with state of the art facilities to manufacture high-end Pharma products rather than small, local fragmented manufacturers of low -end pharmaceutical products.[334]

Legal Analysis

One of the main concerns regarding the Chinese legal system is the influence that burocrats and senior officials exert over judges, which results in preferential rulings. Therefore, being biased, the Chinese legal system is perceived as generally ineffective and unfair.

With the objective of expanding the healthcare coverage to the entire population by 2020 while containing healthcare expenditures, a series of reforms have been put into practice that are reshaping the healthcare sector in China. Among these, the introduction in April 2009 of the so-called "Anhui model" (see chapter 2). This new set of laws and regulations represents

[333] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, p. 32. www.marketline.com
[334] Chitour H. L.(2013). Big Pharma in China – The Driving Forces behind their Success – A Qualitative Analysis. Chinese Studies, Vol. 2, No. 4, p. 174. http://dx.doi.org/10.4236/chnstd.2013.24028

an aggressive tendering system enforced by the Chinese government that resulted in the slash of drug prices by at least 30% of key drugs (part of the essential drugs list). Both foreign and local pharma companies raise the concern of the government's attempt to cut prices through tendering to compete on prices and the resulting decrease in quality of the drugs produced to cut on manufacturing costs. Although this reform has resulted in the shrinkage of the profit margin of these companies, they are still profitable, and this reform would eventually be profitable in the long term for Foreign Pharma as it will drive demand up, resulting in growth through the increase of sales volume.

Intellectual Property Rights and Patent Protection.

To many foreign companies, China remains attractive as the world's largest potential market for pharmaceutical products. As such products rely heavily on the protection of intellectual property rights, it is essential for foreign companies in this field to adopt a combination of IP protection methods to formulate a strategy for their products in China. To this end, China has aligned its legislation with the minimum WTO requirements of the Trade-Related Aspects of Intellectual Property (TRIPs) protocol, which contains general standards for the enforcement of intellectual property rights, and has revised both its Patent and Trademark Law, adding administrative penalties and criminal liabilities to civil liabilities. As a result, the country has established a relatively comprehensive legal system in relation to IPR protection where intellectual assets are protected by way of patents, trademarks, copyrights, and trade secrets.

However, weak enforcement of IP laws is the major obstacle to China's objective of transforming into an innovative country. The International Intellectual Property Alliance (IIPA) successfully campaigned for China to be added to the United States Trade Representative's (USTR) Priority Watch List, which is the category for US trading partners with the most serious IPR violations. As a result, China is subject to Section 306 monitoring as of 2016.[335]

Therefore, with most of China's legal framework meeting international requirements, the next step for China is to shift its focus to implementation and enforcement.

Labor Law.

China has been and still is a very attractive outsourcing country mainly due to cheap labor costs compared to the West. The minimum wage varies with the geographical location. Each province or municipality must set a minimum wage but total labor costs can be as much as five times higher than basic wages in some companies, with a range of benefits and subsidies

[335] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, p. 38. www.marketline.com

making up the balance. For example, the minimum wage in Shanghai was RMB/month 1.120 in 2013, while it reached RMB/month 870 in Chongqing. For skilled factory worker the average salary would be around 500 USD per month which was 3 times more than what he could earn working in Jiangxi province.[336] However, since the 2010 labor strikes following the Foxconn scandal,[337] labour costs began to rise all over China: as a result, the minimum wage in Shenzhen increased of 20% starting from March 2011, while the amount of minimum wage in Beijing doubled within a 6 months period.[338]

In particular, wages are increasing fast where enterprises struggle to retain their employees. Multinational Pharma companies have started a fierce battle to attract and retain the growing, yet sometimes still insufficient, talent pool in China, where highly skilled employees in the field are still cheaper to hire than their Western counterpart due to the costs of living in China being still lower than in Europe or the US.

Environmental Analysis

The increase in manufacturing without adequate ecological or pollution control norms has resulted in acid rains that have damaged forests and watersheds in parts of Asia and even in the USA. High levels of environmental pollution are caused by China's primary energy source, that accounts for 73% of total energy production in 2015, while clean sources of energy such as nuclear, renewable and hydroelectricity together accounted for a mere 27%.[339]

Around 70% of rivers and lakes in China are polluted and roughly 50% of river and lake water is deemed unfit even for human consumption. It is also alarming that more than 80% of groundwater, which accounts for around one-third of the country's water resources, is polluted in the populated plains of China, which means that it is drinkable only after proper treatment or, in the worst case, it cannot be drunk even after being treated. Water contamination is linked to higher incidences of cancer along waterways and the riverside near pharmaceutical, power and chemical plants.

Soil is also contamined mainly from arsenic and other heavy metals, due to excessive mining, industrial waste dumping and irrigation using polluted water.[340]

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[336] Chitour H. L.(2013). Big Pharma in China – The Driving Forces behind their Success – A Qualitative Analysis. Chinese Studies, Vol. 2, No. 4, p. 171. http://dx.doi.org/10.4236/chnstd.2013.24028

[337] Foxconn Technology Group is known as the world's largest electronics contract manufacturer, producing hardware for big technology brands such as Apple, HP, Samsung etc. In 2010, 18 of its workers attempted suicide and 14 of them died. This event attracted the attention of media and raised a wave of criticism against the violation of human rights from the community.

[338] Ibidem.

[339] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, p. 40. www.marketline.com

[340] Ibidem, p. 41.

Air, water and soil pollution constitute a serious threat to the health state of the Chinese population and is responsible for increased healthcare costs. Outdoor air pollution, for example, has become a major concern for public health. It has been estimated that the total health cost associated with outdoor air pollution in urban areas of China in 2003 was between RMB 157 and 520 billion, accounting for 1.2% - 3.3% of China's gross domestic product.[341]

The incidence of esophageal squamous cell carcinoma (ESCC), which is the eighth most common malignancy worldwide, is highest in China. The incidence of ESCC is high in Shexian county (Anhui province), and environmental factors, particularly nitrogen-contaminated drinking water, are the main suspected risk factors. Another recent study on the association between pollution and cancer incidence in Guangdong province has demonstrated the correlation between long-term environmental exposure to both cadmium and lead and an increased risk of mortality from all types of cancers. There is a clear association between water, soil or air contamination with pollutants such as heavy metals toxins or bacteria pose a serious threat in the long-term by considerably increasing the cancer exposure for the population in addition to genetic malformations for new born and other pollution related affections such as Asthma. The government estimates to roughly 400 'cancer villages' throughout the Chinese territory and has recently acknowledged the need for an urgent and effective strategy to control the phenomenon.[342]

Since the Kyoto Protocol was ratified for the second time in 2011, the Government has been highlighting its growing concern about environmental issues. Environmental protection is part of the economic strategy of the 13th Five-Year plan; in the end of 2015 China promised to reduce power sector emissions intensity by 60–65% from 2005 level by 2020 and environmental protection laws are slowly becoming more stringent in China.[343] In September 2016 the G20 meeting was held in the city of Hangzhou. Ahead of it, the country ratified its Paris climate change agreement.

The environment deterioration is likely to create new opportunities for the Pharma industry and the most profitable sectors include R&D, manufacturing and marketing for drugs set to cure or alleviate pollution related diseases symptoms. Sectors such as Oncology drugs already represent one of the most promising market segments in China. The Chinese gastric cancer

[341] Chitour H. L.(2013). Big Pharma in China – The Driving Forces behind their Success – A Qualitative Analysis. Chinese Studies, Vol. 2, No. 4, p. 175. http://dx.doi.org/10.4236/chnstd.2013.24028
[342] Ibidem.
[343] MarketLine (2016). China In-depth PESTLE insights. Country Profile Series, p. 40. www.marketline.com

drug market also was expected to grow from $250 million in 2010 to $469 million in 2015.[344] China's demand for lung cancer treatment drugs has grown at a fast pace in the past decade as well.

As environmental issues will not be solved in the short term, more people will be affected by water, air and soil pollution. With the healthcare coverage expansion and improved patient spending power, demand for cancer treatment drugs and targeted therapies will continue to growth in the next years.

[344] Chitour H. L.(2013). Big Pharma in China – The Driving Forces behind their Success – A Qualitative Analysis. Chinese Studies, Vol. 2, No. 4, p. 175. http://dx.doi.org/10.4236/chnstd.2013.24028

1.2. Ease of doing business

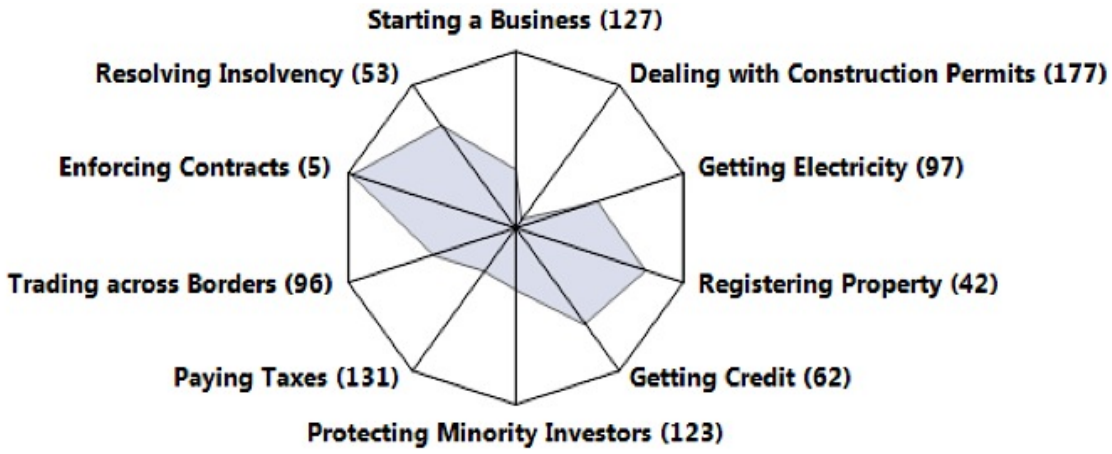
In a series of annual reports, the World Bank ranks 190 economies on the basis of business regulations that make business opening and operation more or less easy and the protection of property rights.

The *Doing Business* report, in particular, analyses and tracks changes in quantitative measures of regulations affecting various phases of setting up and running a business, including: starting a business, dealing with construction permits, getting electricity, registering property, getting credit, protecting minority investors, paying taxes, trading across borders, enforcing contracts, resolving insolvency and labor market regulation. Furthermore, an economy's distance to frontier score is indicated on a scale from 0 to 100, where 0 represents the worst performance and 100 the frontier.

According to the *Doing Business* report 2017, with a change of 2 positions compared to 2016, China ranks 78 out of 190 for overall ease of doing business. This slightly positive change is also reflected by the *Distance to Frontier score (DTF),* in which the country gained about 1.42 points, from 62.86 in 2016, to 64.28 in 2017. Although this result is higher than the East Asia and Pacific regional average of 61.97, China still lags behind countries such as the USA, which ranks 8 with a DTF of 82.45 and Japan, which ranks 34 and scored a DTF of 75.53.

However, taken alone, the overall ranking does not tell much. Therefore, a breakdown of the 10 components of the aggregate ranking is useful to give a deeper insight into the business regulatory environment in China, the number of procedures required, delays and costs, while comparisons with previous years may show if and where improvements (or worsenings) have been recorded.

Fig. 4.1 Rankings on *Doing Business* topics – China



Source: World Bank (2017)

Globally, China stands at 127 in the ranking of 190 economies on the *ease of starting a business*. For entrepreneurs, it is slightly more difficult to start a business in China compared to the Asia –Pacific region, while the gap widens when comparisons are made with Russia and the USA. Generally, it takes almost one month (28.9 days) and 9 procedures to start a business in China, with a cost of equal to 0.7% of income per capita (costs are the same for both men and women). To ease and make starting a business less costly, two reforms were applied in Beijing and Shanghai that eliminated minimum capital requirement and the requirement to obtain a capital verification report from an auditing firm. Furthermore, a single form to obtain a business license, organization code and tax registration has been introduced.

Although China simplified the process of *obtaining a construction permit* by centralizing preconstruction approvals, dealing with construction permits still requires 22 procedures, takes over 8 months (244.3 days) and costs 7.0% of the warehouse value, therefore standing at 177 in the ranking with a DTF of 48.52, far below the regional average of 69.96 and the USA, which scored 75.74 points.

Getting electricity there requires 5.5 procedures, takes almost 5 months (143.2 days) and costs 390.4% of income per capita, lagging behind regional average of around 3 points DTF and, in general, performing worse than USA, Russia, and Japan.

China performs better than other Asia-Pacific countries and scores a DTF very close to the USA (76.15 against 56.72 for the Asia-Pacific region and 76.8 for USA) when it comes to *registering property*, an activity that takes 19.5 days, requires 4 procedures and costs 3.4% of the property value.

With regard to the *ease of getting credit*, China stands at 62 in the ranking of 190 economies. China's collateral and bankruptcy laws are not as better designed to facilitate access to credit as those of Russia, India and USA; although China records a low score on the strength of legal rights index, a high score (8, as for USA) in the depth of credit information index, indicates the availability of more credit information, from either a credit registry or a credit bureau, which facilitate lending decisions. As a matter of fact, the country improved its credit information system by: introducing credit information industry regulations, which guarantee borrowers' right to inspect their data, while in the cities of Beijing and Shanghai payment histories from utility companies started to be reported, and credit scores started to be provided to banks and financial institutions.

Protecting minority investors matters for the ability of companies to raise the capital they need to grow, innovate, diversify and compete. Effective regulations define related-party transactions precisely, promote clear and efficient disclosure requirements, require

shareholder participation in major decisions of the company and set detailed standards of accountability for company insiders.[345]

By aggregating various minority investor protection indices, such as the extent of corporate transparency, shareholder rights index, disclosure index, and director liability index, China ranks 123 globally for strength of minority investor protection, recording a DTF score of only 45, below the regional average of 52.07, and a gap of about 20 points from India, which has a DTF of 73.33.

The *paying taxes indicator* is based on how much taxes and mandatory contributions the business must pay, how these taxes are filed and paid, how much time taxpayers spend preparing, filing and paying three major taxes (profit taxes, labor taxes -including mandatory contributions- and consumption taxes) and how much time taxpayers spend complying with postfiling processes and waiting for these processes to be completed.[346] Although steps have been made to make paying taxes faster, easier and less costly for businesses, such as the unification of tax regimes for domestic and foreign enterprises, the clarification of the calculation of taxable income for corporate income tax purposes, and the introduction of an electronic system for filing and paying taxes in Beijing and Shanghai, the country ranks 131.

In a globalized world, export and import activities are increasingly important for companies. However, excessive burocracy or inadequate infrastructures can hinder trade operations. Globally, China stands at 96 in the ranking on the *ease of trading across borders*, which is based on indicators such as the time and cost to complete export and import in the two largest business cities, Beijing and Shanghai. With regard to the DTF, China scores 69.13 points, slightly better than Asia-Pacific regional average of 68.08, but lags far behind the USA, which record a DTF of 92.01.

Efficiency in resolving commercial disputes through the courts is essential, for it encourages entrepreneurs to involve in new business relationships, because they perceive that they can rely on the courts for protecting their economic rights.[347]In this respect, China performs very well, even better than the USA. Indeed, since China amended its civil procedure code to streamline and speed up all court proceedings*, contract enforcement* takes 452.8 days (about 15 months) and costs 16.2% of the value of the claim, which makes China rise in the ranking and gain the 5th place.

Recovering debts is fundamental for creditors, therefore, fast and cheap insolvency

[345] World Bank (2017). Doing Business 2017: Equal opportunity for all. Economy profile 2017 China. Washington DC: World Bank, p. 93.
[346] Ibidem p. 104.
[347] Ibidem, p. 116

proceedings are fundamental and result in the speedy return of businesses to normal operation and increase returns to creditors. China stands at 53 in the ranking of 190 economies when considering the time, cost and outcome of the most likely in-court insolvency procedures. According to data collected by *Doing Business*, *resolving insolvency* takes 1.7 years on average and costs 22.0% of the debtor's estate. The average recovery rate is 36.9 cents on the dollar. Considering DTF benchmark, China performes better than its Asia-Pacific counterparts, with a score of 55.82 against a regional average of 40.33. Here again, there is a quite wide gap between China and the USA (89.19) and China and Japan, which ranks second, with a DTF of 93.34.

Labour market regulation is the eleventh dimension considered in the creation of the ease of doing business index. Specifically, data on the flexibility of regulation of employment (related to the areas of hiring, working hours and redundancy), as well as measures of several aspects of job quality, such as the availability of maternity leave, paid sick leave and the equal treatment of men and women at the workplace are collected. Unlike all previous dimensions considered, the report on labour market regulation neither present rankings of economies, nor include the topic in the aggregate distance to frontier score or ranking on the ease of doing business. However, to make the data comparable across economies, the World Band assumes that the worker is a full-time cashier in a supermarket or grocery store, age 19, with one year of work experience, and the business is a limited liability company (or the equivalent in the economy).[348]

It emerges that, a minimum wage of $349 per month is applicable in Shanghai and a minimum wage of $274.1 is applicable in Beijing, with a ratio of minimum wage to value added per worker of 0.4 in Shanghai and 0.3 in Beijing.

The minimum number of working days per week is 6 days, with no restrictions on night work (nonpregnant and nonnursing women can work the same night hours as men), weekly holidays or overtime work. There are no permiums for night work in Beijing, while a premium of 34% of hourly pay is granted in Shanghai, while in both cities a premium of 100% of hourly pay is granted for work on weekly rest days and a 50% premium is granted for overtime work.

The maximun lenght of probationary period is 6 months and dismissal due to redundancy is allowed by the law. Notification to a third-party, such as a government agency is required if one or more workers are dismissed; however, in case of dismissal, there is no need for third-

[348] Ibidem, p. 133.

party approval.

With regard to job quality, although there is no gender discrimination in hiring, remuneration is not equal for work of equal value. Maternity leave is mandated by the law, although minimum length of maternity leave may vary (ie. 128 days in Shanghai; 98 days in Beijing), 100% full wages are granted on maternity leave. Unemployment protection is granted after a minimum contribution period of 12 months.

When comparing China's labour market regulation with OECD countries, a striking gap appears concerning labour costs: minimum wages in the USA are 5 times the minimum wages in China ($ 1,687.97 in Los Angeles; 1519.17 in New York), while in Italy it is equal to $2,083.94. Other differences mainly concern premiums. For example, in the USA no premium is granted for both night work and work on weekly rest days, while a 50% premium is granted on overtime work; on the other hand, in Italy a 15% premium per hour is granted for both night work and overtime work, while there is a 30% premium for work on weekly rest days.[349]

[349] World Bank (2017). Doing Business 2017: Equal opportunity for all. Washington DC: World Bank.

2. Assessing market and resources opportunities in the pharmaceutical industry

Professor Michael Porter (1998) has argued that countries can build competitive advantages that make them attractive for business development in certain industries. He distinguishes four major drivers of national competitive advantage, which constitute the so-called 'country diamond':

-Natural endowment (natural, human, capital, physical, technological and administrative or scientific resources)

-Quality of the demand (whether customers are demanding on quality, fostering the competitiveness of the firm serving them)

-Vigorous competition (whether competitors stimulate each other)

-Presence of supporting industries (whether there is a pool of qualified product and service suppliers that enhance the quality and competitiveness of firms operating in this country)[350]

Starting from this concept, in this section the resource opportunities of China in the pharmaceutical industry are analyzed.

2.1. Market opportunities

Correlations of macroeconomic data on social, demographic and institutional indicators (such as GDP, socio-economic and age distribution, as well as government spending) with some measures of consumption of certain products, allow a broad assessment of the potential size of the market, while forecast GDP growth gives a crude estimate of the anticipated size of the market.[351]

Based on the latest edition of The World Medicines Situation on medicine expenditures of the World Health Organization, and on official Chinese data available in the Chinese Statistical Yearbook, a broad assessment of the pharmaceutical demand will be made.

Although data collected by the World Health Organization refer to 2006, this is the only report that allows expenditure comparisons between countries. As a matter of fact, data on pharmaceutical spending have usually been limited to that generated by the pharmaceutical industry, principally to serve their own marketing purposes and in most cases these data have a limited coverage, both geographically and in terms of content.[352]

[350] Lasserre, Philippe (2012). Global Strategic Management, Third Edition. Palgrave Macmillan, p. 189.
[351] Ibidem, p. 178.
[352] World Health Organization (2011). The World Medicine Situation 2011, p. 2.

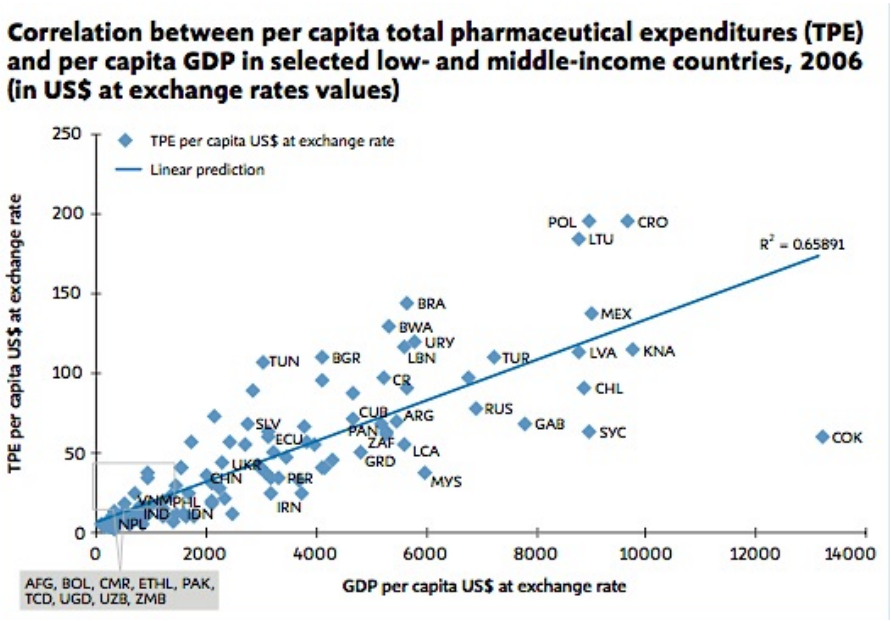
Data on total pharmaceutical expenditures for 2006 confirm that pharmaceuticals account for an important share of all expenditure on health. This proportion varies considerably between high- and low-income countries; pharmaceutical spending as a share of total health expenditure ranges from a mean of 19.7% in the high-income countries to a mean of 30.4% in the low-income countries (Table 1.1). On average, poorer countries spend proportionally more of their health budget on medicines than the wealthier countries.[353] As previously mentioned in chapter 2, China's overall drug spending accounted for around 40% of THE in 2012,[354]a percentage that is higher than OECD countries average.

Spending on medicines is positively correlated with total health spending, especially in low and middle-income countries. Indeed, the higher the per capita health expenditure, the higher the per capita pharmaceutical expenditure.

In 2006, world pharmaceutical spending represented 1.5% of global GDP, ranging from 1.41% in high-income countries to 1.63% in lower middle-income countries. In both poor and rich countries, there is a positive correlation between GDP and TPE in per capita terms, suggesting that in general the larger the per capita GDP, the larger the amount spent on pharmaceuticals.[355] However, data show that, within the same country, middle-low and low income groups tend to spend a larger share of GDP on pharmaceuticals, although total health expenditure is higher in upper-middle and high income groups than in lower-middle and low income groups.[356]

[353] Ibidem, p. 6.
[354] Mossialos E., Ge Y., Hu J., Wang L. (2016). Pharmaceutical policy in China: Challenges and Opportunities for Reform. London School of Economics and Political Science and Development Research Center of the State Council of China, p. 55.
[355] World Health Organization (2011). The World Medicine Situation 2011: Medicine Expenditures, p. 8.
[356] Ibidem

Fig. 4.2 Correlation between TPE and GDP



Source: World Health Organization (2011)

Fig. 4.3 TPE and THE as a percentage of GDP by income group, 2006

	Total pharmaceutical expenditure						Total health expenditure	
Income group	N	Population (thousands)	Mean (%)	Median (%)	Minimum (%)	Maximum (%)	N	Mean (%)
High	46	1 011 957	1.41	1.40	0.30	2.70	49	11.3
Upper middle	37	812 489	1.45	1.30	0.40	2.70	54	6.4
Lower middle	44	3 379 873	1.63	1.45	0.40	3.80	47	4.4
Low	34	1 114 890	1.62	1.50	0.40	3.60	41	5.3
All countries	161	6 319 210	1.52	1.40	0.30	3.80	191[a]	9.8

Source: World Health Organization (2011)

China's "middle-class effect"

With its fast growing GDP, a vast and rapidly ageing population that is facing an increasing rate of chronic diseases, and high pharmaceutical expenditure, China became the second largest pharmaceutical market in 2015 and is expected to become the first by 2020, as a result of a fast growing, increasingly wealth middle class.

As more than 75% of China's urban consumers will earn $9,000 to $34,000 per year by 2022,[357] China's middle income consumers, and their changing lifestyles and behaviours, will play a significant role in China's shifting emphasis from investment and export driven growth towards consumption driven growth, with important implications for the healthcare and the pharmaceutical industry. A report on China's middle income consumers of the China-Britain Business Council (2013) shows that healthcare has become a big concern for Chinese citizens. China's middle income consumers are typically younger compared with most developed markets, well educated, and their higher standards of living greatly contribute to personal health awareness among the urban middle income population. They see health as a priority and view Western hospitals and foreign-trained doctors as the preferred choice for medical check-ups, vaccinations and preventive care. If in the past spending on private healthcare would be seen as a luxury, nowadays it is regarded a standard cost of living for the new middle income consumers. China's growing urban middle income population is demanding customer-friendly healthcare, higher quality services and the opportunity to receive patient-centred healthcare.[358]

When asked which are the most important aspect they consider most important for private health care, price is only at the fourth place, after technical qualification, doctor's attitude, and facility & environment. Moreover, with growing purchasing power and a preference for Western brands, Chinese middle class are likely to drive the consumption of patented drugs from Western pharmaceutical companies.

In 2012, 54% of China's urban households were considered "mass middle" class, meaning they earned between US$9,000 and US$16,000 per year. But by 2022, thanks to a growing number of higher-paying high-tech and service industry jobs, 54% will be classified as "upper

[357] McKinsey Quarterly(2013). Mapping China's middle class. http://www.mckinsey.com/industries/retail/our-insights/mapping-chinas-middle-class

[358] China-Britain Business Council (2013). China's Middle Income Consumers, p. 26. http://www.cbbc.org/cbbc/media/cbbc_media/KnowledgeLibrary/Reports/Sector%20Profile/CBBC-China-s-Middle-Income-Consumers.pdf

middle" class – meaning they earn between US$16,000 and US$34,000 a year, while the low income group will decrease from 29% in 2012 to 16% in 2022.[359]

Tab. 4.1 China's Middle Class as a % of Urban Households

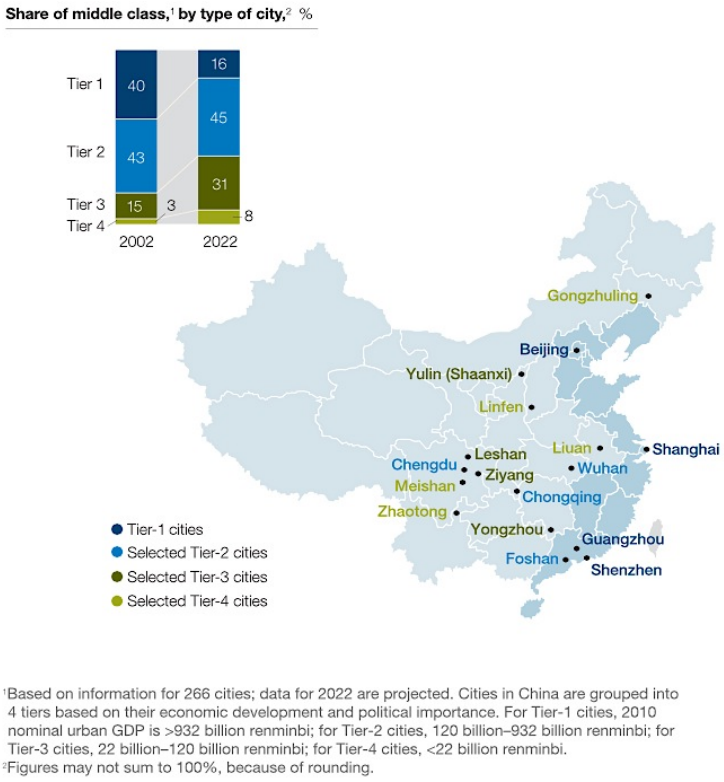
	2012	**2022**
Poor <$9,000	29%	16%
Mass Middle $9,000-$16,000	54%	22%
Upper Middle $16,000-$34,000	14%	54%
Affluent >$34,000	3%	9%

Source: Business Insider (2016)

Middle-class growth will be stronger in smaller, inland cities than in the urban strongholds of the eastern seaboard.[360]In 2002, 40% of China's urban middle class lived in first-tier cities like Beijing, Shanghai, Guangzhou and Shenzhen; as middle class growth will be far greater in the smaller cities of the north and west, this percentage is forecast to fall to 16%, while the share of upper-middle-class households in third-tier cities should reach more than 30 percent by 2022, up from 15 percent in 2002,[361]as shown in fig. 4.4

[359] Business Insider (2016). China's Middle Class is Exploding. http://www.businessinsider.com/chinas-middle-class-is-exploding-2016-8?IR=T
[360]McKinsey Quarterly(2013). Mapping China's middle class. http://www.mckinsey.com/industries/retail/our-insights/mapping-chinas-middle-class
[361] Ibidem

Fig. 4.4 Share of middle class by type of city (%)



[1]Based on information for 266 cities; data for 2022 are projected. Cities in China are grouped into 4 tiers based on their economic development and political importance. For Tier-1 cities, 2010 nominal urban GDP is >932 billion renminbi; for Tier-2 cities, 120 billion–932 billion renminbi; for Tier-3 cities, 22 billion–120 billion renminbi; for Tier-4 cities, <22 billion renminbi.
[2]Figures may not sum to 100%, because of rounding.

Source: McKinsey (2013)

Additionally, China's household debt-to-GDP ratio of 40% is less than half the American household debt-to-GDP ratio, and is much lower than those of other developed countries.[362] Higher incomes, low debts, and an increasing consumption-oriented young generation will create new market opportunities for both domestic and international companies also in the pharmaceutical sector, as an increasing number of health-conscious consumers will be willing to spend an increasing amount of their income on sophisticated treatments.

Table 3 summarizes China's main macro indicators, relevant for an overall assessment of the Chinese pharmaceutical market potential.

[362] Business Insider (2016). China's Middle Class is Exploding. http://www.businessinsider.com/chinas-middle-class-is-exploding-2016-8?IR=T

Tab. 4.2 China's macro indicators for overall market assessment

Economic	Demographic	Institutional
GDP RMB 68,551 trillion $ 11,008 trillion GDP (PPP) $ 19,815 trillion	Population 1,382.71 mln - Urban 56,1% - Rural 43.9%	Government healthcare spending RMB 124,752,800,000,000 (30.45% ot THE) R&D expenditure as % of GDP: 2.10% Manufacture of medicine: -Number of enterprises 7,392 -R&D Institutions 2,781 - Full time R&D personnel 128,589 - R&D projects 21,761 - Patent applications 16,020 -Inventions 10,019 - New products 22,106 - Expenditure on new products development RMB 42,794,850,000 -Sales revenue of new products RMB 473,626,750,000 Manufacture of Medical Equipments and Meters -Number of enterprises 5,062 -R&D Institutions 2,164 - Full time R&D personnel 83,521 - R&D projects 11,907 - Patent applications 24,260 -Inventions 9,135 - New products 14,430 - Expenditure on new products development RMB 27,672,380,000 -Sales revenue of new products RMB 217,925,830,000
GDP per capita RMB 49,992 $ 8,027.7 GDP per capita (PPP) $ 14,450.2		
GDP growth rate 6.7%		
Income distribution: -low income RMB 5,529 -lower-middle-income RMB 12,899 -middle-income RMB 20,924 -upper-middle income RMB 31,990 -high income RMB 59,259	Natural growth rate 5.86% per 1000 Age distribution: - 0-15 year 17.7% - 16-59 year 65.6% - 60 and above 16.7% (of which 65 and above 10.8%)	
Disposable income per capita RMB 23,821 (+8.4%) -Urban areas RMB 31,194.8 -Rural areas RMB 11,421.7		
Saving Rate (% of GDP) 49%		
Exports RMB 13,845.5 bln (-1.9%)		
Imports RMB 10,493.2 bln (+0.6%)		
Investment rates		
Per capita healthcare and medical expenditure RMB 1164.5 - Urban households RMB 1443.4 - Rural households RMB 846.0		

Source: China Statistical Yearbook; World Bank; Statista (2016; 2017)

2.2. Natural, human and support industry resources

Natural resources

Pharmaceuticals are derived either from natural resources, or from synthetic chemistry. Some medicines are semi-synthetic, using a natural resource that is then modified by chemical reactions (ie. Aspirin). The genetic diversity in the world's plants, animals, and microbes can be a rich resource for potential medicines. Examples of drugs whose active ingredients were first isolated from environmental sources include penicillin, aspirin, and the anti-cancer drug *taxol*. There are probably many more potential drugs available in the biodiversity of rain forests, deep oceans, and other biomes. Besides its chemical raw material, the pharmaceutical development also requires the use of water, energy, and other components in order to produce drugs. Industrial use of water accounts for 20% of global usage, varying from country to country, from less than 5% to around 7%, depending on how industrialized the country is. The pharmaceutical industry uses water both in manufacturing processes and in cleaning equipment. The latter accounts for 60 to 80% of water usage in a pharmaceutical manufacturing plant.[363]

China is one of the twelve countries in the world with richest biodiversity. Due to its vast land area, it has various and complicated types of ecosystems that house more than 30,000 higher plant species (making China ranking third in the world, following Brazil and Colombia), and over 6,000 vertebrate species, which account for 13.7% of the world's total.[364]

As most of the second industries, in particular pharmaceutical manufacturing, uses biological resources and their products directly as raw materials, and more than 50% of medicinal components in the world come from animals and plants,[365] China has the advantage in the production of all kinds of biological resources, especially in Chinese medicine. Additionally, the Catalogue of Foreign Investments encourages the research, development and production of therapeutic agents from marine natural products. At the same time, the availability of vast, low-cost water and energy resources attract pharmaceutical manufacturers.

However, as the country faces serious threats to biodiversity, which can lead to serious consequences, such as worsening health problems, higher food risks, increasing vulnerabilities and fewer development opportunities, the activities of pharmaceutical firms

[363] Encyclopedia.com. Pharmaceutical Development Resources.
http://www.encyclopedia.com/environment/energy-government-and-defense-magazines/pharmaceutical-development-resources

[364] Ministry of Environmental Protection of China (2014). China's Fifth National Report on the Implementation of the Convention on Biological Diversity, p. 16.
https://www.cbd.int/doc/world/cn/cn-nr-05-en.pdf

[365] Ibidem, p. 15.

may be limited in protected areas, for preserving water resources, for example. Biodiversity conservation is strategically important for China's long-term socio-economic development, well-being of the present and future generations and building an ecological civilization in China and implementing initiatives such as *Beautiful China*.[366] At the end of 2010, the State Council of China launched the "National Plan for Major Function Zones", according to which the country's land is divided into four major function zones: land for priority development, land for key development, land for limited development and land prohibited for development. 25 key ecological function zones have been included in national-level land zones prohibited for development. Within these zones, large-scale and intensive industrial and urbanization development activities are limited so as to allow for environmental protection and ecological restoration and to enable ecosystems to provide ecological goods. National-level nature reserves, world cultural and natural heritage sites, national-level scenic zones, national forest parks and national geological parks have been also included in national-level land zones prohibited for development, where industrial and urbanization development activities are banned to protect natural and cultural heritages and rare animal and plant genetic resources of China.[367]

Under China's 13th five-year development plan, ecological civilisation and ecological security are prioritised as key issues for the country's sustainable development. Supported by the Ministry of Science and Technology of China, China has recently launched 37 National Key Research and Development Programmes on "Ecological restoration and protection in the typical ecological fragile zones" to be implemented from July 2016 to December 2020.[368]

Human resources

With a population of over 1.3 billion people, China is a vast reservoir of human resources. In the past, multinationals looked to China mainly for its low cost labor to manufacture goods primarily for Western countries, making China one of the preferred locations for concentrating labor-intensive, low value-added production.

By the end of 2015 China's total population had reached 1.37462 billion, which contained an economically active population of 800,910,000 persons, 4.01 million more than in 2014; the number of employees had reached 774.51 million, of whom 42.4% were employed in the

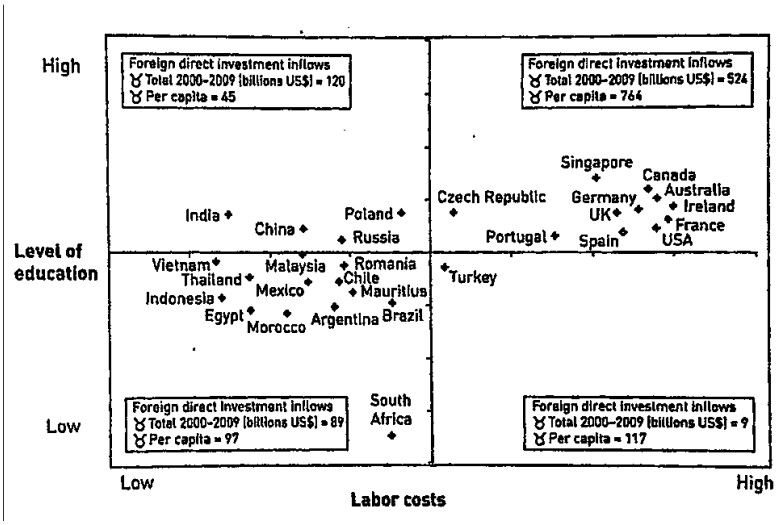
[366] Ibidem, p. 1.
[367] Ibidem, p. 2.
[368] Asia-Pacific Network for Global Change Research (2017). China Launches National Key Programmes for Ecological Restoration and Protection in its Ecological Fragile Zones.
https://www.apn-gcr.org/2017/01/10/china-launches-national-key-research-and-development-programmes-for-ecological-restoration-and-protection-in-its-ecological-fragile-zones/

tertiary industry, while 28.3% and 29.3% were employed in the primary and secondary industry, respectively.[369]

China gives priority to education in its development strategy, and has established a comparatively complete national modern educational system. In 2000, 9- year compulsory education was made universal throughout the country, and illiteracy among people between the ages of 20 and 50 was basically eliminated. The development of national education has remarkably raised employees' educational level.[370]

In 2015, the number of students graduating from compulsory education reached 93.0 percent of the total enrollment and the gross enrollment rate in senior high schools reached 87.0 percent, while the post-graduate education enrollment reached 1.911 million students with 645 thousand new students and 552 thousand graduates. The general tertiary education enrollment was 26.253 million students with 7.378 million new students and 6.809 million graduates. Vocational secondary schools had 16.567 million enrolled students, including 6.012 million new entrants, and 5.679 million graduates.[371]

Fig. 4.5 Cost of labor and level of education in service industry



Source: Laserre (2012, p. 186)

369 中国统计年鉴（2016）。就业基本情况。China Statistical Yearbook (2016). Employment. http://www.stats.gov.cn/tjsj/ndsj/2016/indexeh.htm

370 Beijing Review (2010). China's Human Resources. http://www.bjreview.com.cn/document/txt/2010-10/13/content_303463.htm

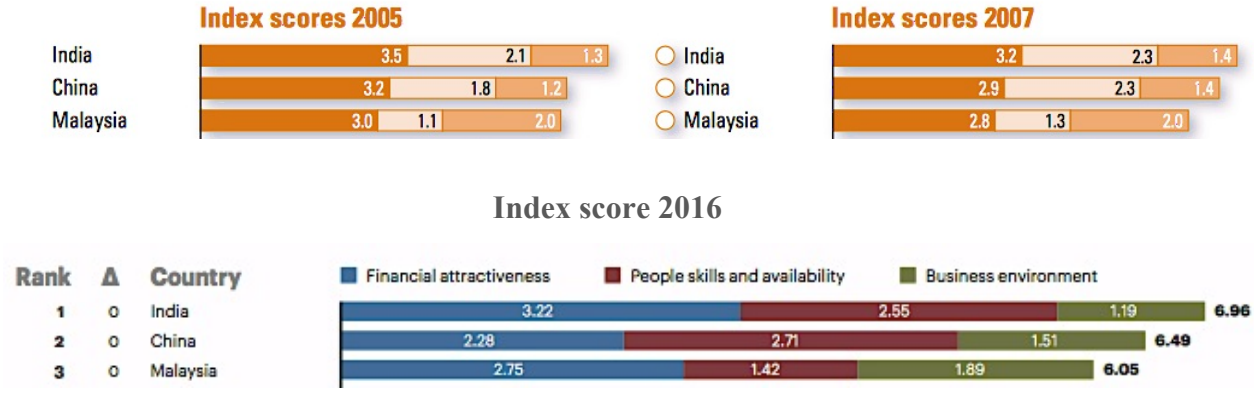
371 National Bureau of Statistics of China (2016). Statistical Communiqué of the People's Republic of China on the 2015 National Economic and Social Development. http://www.stats.gov.cn/english/pressrelease/201602/t20160229_1324019.html

The country has a large pool of skilled scientists. There are about 128 universities and colleges of medicine and pharmaceutics, complemented by 53 tertiary vocational- technical colleges. There are about 666 institutes dedicated to science and technology. In total, as of 2007, there were over 1.6 million science and engineering graduates (including undergraduate, masters and PhD students) and about 7.7 million enrollments for doctoral and masters study programmes.[372]

As China is highly committed to innovation and industrial upgrading, the number of talented and highly qualified personnel is likely to increase in the near future. The 13th Five-Year plan sets goals to increase the number of R&D personnel per 10,000 people employed per year, from 48.5 in 2015 to 60 in 2020 and the share of its total population with scientific degrees from 6.2 percent in 2015 to 10 percent by 2020.[373]

Every year, A.T Kearney, a global management consulting firm, publishes the *Global Services Location Index* to rank top 50 countries in the most attractive offshoring destinations on the basis of 3 main criteria, namely Financial Attractiveness, People Skills & Availability and Business Environment. The 2016 Global Services Location Index, the 7th edition of the GSLI, was released on 10th January 2016. As in previous years, India and China continue to lead the Index. Their decline in labour cost advantage through the years, has been offset by improved, more available talent and enhanced business environments, confirming that, in the fast-developing service sector, the key to maintaining and enhancing long-term competitiveness lies in skills development, infrastructure investment and regulatory environment, rather than in attempts to control wages.

Fig. 4.6 Global service location index – Top 3 countries



Source: A.T. Kearney

[372] PWCH (2008). The changing dynamics of pharma outsourcing in Asia, p. 23. https://www.pwc.be/en/pharma/the-changing-dynamics-of-pharma-outsourcing-in-asia.pdf

[373] U.S.-China Economic and Security Review Commission. The 13th Five-Year Plan, p. 3. https://www.uscc.gov/sites/default/files/Research/The%2013th%20Five-Year%20Plan.pdf

Although India continues to be the most attractive offshore location with a score of 6.96 and the talent of its engineers to develop products attracted Chinese companies such as Huawei - the world's fourth largest smartphone vendor that set up its first overseas R&D center in Bangalore in 1999, where it currently employs 2,700 engineers - China, with a score of 6.49, is closing in on India, thanks to major gains in educational skills and cultural adaptability. The country surpasses India in terms of people skills and availability and business environment, while it is the gap in terms of financial attractiveness that determines India's first place in the rank. However, following the renminbi's recent drop in value against the U.S. dollar and the progresses in improving governance and liberalizing financial markets, China's financial attractiveness is likely to increase. Yet, the U.S.-China Business Council's 2014 China Business Environment Survey found that nearly half of companies expressed reluctance to invest in R&D in China because of weak enforcement of (IP) rights, while 40% say air pollution makes it difficult to attract expatriate staff to work in China, and causes an increased amount of sick leave.[374]

However, the actual situation seems to be different: despite China's huge population and improvements in education, some of the most acute challenges of doing business in China are associated with finding and keeping people. Additionally, as Chinese society is ageing, the number of workers aged between 20 and 24 in 2030 will be less than 60% of those in 2010.[375]

The biggest problem consistently cited by most companies operating in the country is lack of available talent.[376]Notwithstanding the increasing number of graduates, the distribution of talent is uneven and smaller cities face a lack of good English skills. Softer skills, such as people management skills, communication skills, especially in terms of international communication are also challenging. Retaining the best people is also challenging: top performers are often offered large salary increases by competitors and according to research by Hays only 20% of people stay with a company for five years or more.[377]

[374]A.T. Kearney (2016). Global Services Location Index, p. 5. https://www.atkearney.com/documents/10192/7094247/On+the+Eve+of+Disruption.pdf/49fa89fa-7677-4ab8-8854-5003af40fc8e

[375] HR (2017). Winning the War for Talent in China. http://www.hrmagazine.co.uk/article-details/winning-the-war-for-talent-in-china

[376] Ibidem

[377] Ibidem

Tab. 4.3 China Labor

Employed persons 776,030,000	Unemployed persons 982,000
Unemployment rate 4.02%	Job vacancies 4,335,000
Labour costs 103.40 index points	Minimun wages RMB/month 2,190
Wages RMB/year 62,029	Wages in manufacturing RMB/year 55,324
Retirement age women 50	Retirement age men 60

Source: Trading Economics (2017)

Infrastructure and support industry resources

The third type of resources that can be of interest to foreign investors, and especially to investors in the pharmaceutical industry, is the quality of logistic infrastructures, as well as the availability of supporting industries and services.

China leads the world in infrastructure investments, a top priority for the Government, which has long recognized that a modern economy runs on reliable roads and rails, electricity, and telecommunications.

Over the past 20 years, 8.5 percent of China's GDP has been invested into infrastructure—twice the level of India and more than four times that of Latin America. China's stock of infrastructure as a percentage of GDP is well above the global average, but still ranks only 42nd in a survey of factors contributing to global competitiveness. Some 70 new airports, 43,000 kilometers of new expressways, and a major expansion of port facilities are planned to be ready by 2020, while 22,000 kilometers of additional rail track were to be completed by 2015. Not surprisingly, five of the top ten global construction and engineering companies (by 2010 revenues) are Chinese.[378]

From the late 1990s to 2005, 100 million Chinese benefited from power and telecommunications upgrades. Between 2001 and 2004, investment in rural roads grew by a massive 51% annually. And in recent years, the government has used substantial infrastructure spending to hedge against flagging economic growth.

China's leadership has charted equally ambitious plans for the future. Its goal is to bring the entire nation's urban infrastructure up to the level of infrastructure in a middle-income country, while using increasingly efficient transport logistics to tie the country together.[379]

[378] McKinsey & Company (2013). Ten Forces Forging China's Future. http://www.mckinsey.com/global-themes/asia-pacific/ten-forces-forging-chinas-future

[379] McKinsey & Company(2013). Chinese Infrastructure: The Big Picture. http://www.mckinsey.com/global-themes/winning-in-emerging-markets/chinese-infrastructure-the-big-picture

According to the World Bank (2016), China's logistics sector has grown over 20 percent a year and is now the largest logistics market in the world. However, the country lacks a well-developed logistics network. In particular, connectivity, technology penetration and modern warehousing have been lagging.[380]

With regard to the pharmaceutical industry, in a country with a huge rural population (700-800 million) lacking in key infrastructure and logistical expertise, it is difficult to ensure that drugs are delivered to patients in a timely, safe and cost- effective manner. In addition, increasing demand, especially in the farther West, puts a strain on the country's logistic infrastructure. Enabling the supply chain to actually get the medicines, medical devices and health care to people outside the tier 1 and tier 2 cities is a major challenge for logistics providers, as the need for a better, secure, traceable, temperature-controlled transportation model increases.[381]

Inefficiencies are exacerbated by the high degree of fragmentation in the logistics industry. With more than 13,000 logistics enterprises, this fragmentation is a major contributor to the unusually high transportation costs of pharmaceutical products, whose distribution continues to be dominated by major state-owned distributors such as Sinopharm, Shanghai Pharma and China Resources that controlled about 20 percent of the market in 2014.[382] Thus far, many of the small, local distributors have lacked both the scale to automate and the logistical expertise of distributors in developed countries. In addition, this lack of scale has meant that manufacturers seeking to distribute their products on a national basis need to bring in multiple distributors to help their products reach the retailer. One current challenge is the lack of a comprehensive product tracking system set up between the various distributors. Consequently, product traceability is hard to guarantee, and when problems arise, product recalls can be extremely difficult to manage. The complexity of the supply chain has also left it vulnerable to the entry of counterfeit products, a substantial threat to the pharmaceutical industry. The need to use multiple distributors can also risk interruption of the cold chain and negatively affect product quality.[383]

The introduction of the Standards of Good Supply in 2000 and their periodical revision in 2013 and 2016; the latest update of the Catalogue for Foreign Investments, which encourages

[380] World Bank (2016). World Bank helps China improve logistics infrastructure. http://www.worldbank.org/en/news/press-release/2016/04/29/world-bank-helps-china-improve-logistics-infrastructure

[381] JOC (2014). China's logistics sector struggles to meet pharma demand. http://www.joc.com/international-logistics/logistics-providers/chinas-logistics-sector-struggles-meet-pharma-demand_20140606.html

[382] Ibidem

[383] PWHC (2009). Investing in China's Pharmaceutical Industry – 2nd Edition, p. 18 https://www.pwc.com/gx/en/pharma-life-sciences/assets/en-pharma_03-26-small.pdf

pharmaceutical wholesale and retail trade industry, including the development of chain distribution in rural areas and the joint distribution of general goods, logistics and related technical services such as low-temperature distribution of special drugs; and the expansion of the US-based Cardinal Health, suggest that pharmaceutical logistical infrastructures are improving and will continue to improve, as collaboration between global logistics services providers and China-based pharma distributors will be the future trend that will benefit both parties, as well as the Chinese pharmaceutical market as a whole.

In addition, the NDRC and the MOH jointly launched a rural health service system enhancement plan, in which RMB 36 billion will be invested over the next three years, to support construction of 2,176 county- level hospitals nationwide. As of now, RMB 31.4 billion in funds are in place to upgrade and build 1,877 countylevel hospitals, with additional funds set aside for construction of 29,000 township hospitals, and the upgrade of another 5,000. The infrastructure improvements and covered treatment of underserved populations are expected to boost the pharmaceutical market in China's rural and suburban areas.[384]

[384] Deloitte (2011). The next phase: Opportunities in China's pharmaceutical market, p. 12. https://www2.deloitte.com/content/dam/Deloitte/ch/Documents/life-sciences-health-care/ch_Studie_Pharmaceutical_China_05052014.pdf

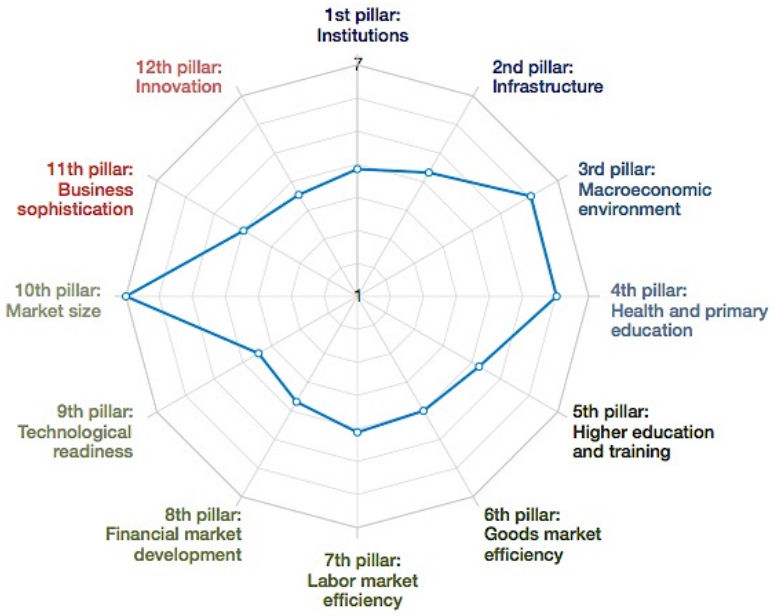
2.3. Global competitiveness index

Based on data from internationally recognized organizations, such as the International Monetary Fund (IMF); the World Bank; and various United Nations' specialized agencies, including the International Telecommunication Union, UNESCO, and the World Health Organization, since 1979, the World Economic Forum publishes the Global Competitiveness Report, which ranks countries on the basis of a competitiveness index. Since 2005, this index integrates 114 macroeconomic and micro/business indicators of competitiveness, grouped into 12 pillars: institutions, infrastructure, macroeconomic environment, health and primary education, higher education and training, goods market efficiency, labor market efficiency, financial market development, technological readiness, market size, business sophistication, and innovation, which are in turn organized into three subindexes: basic requirements, efficiency enhancers, and innovation and sophistication factors.

According to the *Global Competitiveness Report 2016-2017*, China retains its 28th rank among 138 economies for the third year in row. Its overall score improves, thanks to progress in some of the areas of competitiveness that contribute to shaping the country's innovation ecosystem. These include: higher education (54th, up 14), innovation (30th, up one), and business sophistication (34th, up four). Yet, China still lags behind in technological readiness (74th, unchanged) despite a significant improvement in all components of this category since last year. The gains posted in these categories are partially offset by a worsening fiscal situation—the budget deficit more than doubled between 2014 and 2015, to reach 2.7 percent of GDP—but China still ranks a strong 8th in the macroeconomic pillar. In addition, little progress has been made over the past year in two areas that are critical for accelerating the transition to a new growth model in which growth will need to be increasingly driven by innovation. First, goods market efficiency (56th, up two) is undermined by various distortions, including the lack of competition caused by high barriers to entry for foreign firms (113th) and new businesses—it takes over a month to start up a business. Second, inefficiencies and instability characterize the financial sector (56th, down two)—the result of inefficiencies, non-performing loans, lack of competition, and suboptimal allocation of capital.[385]

[385] World Economic Forum (2016). The Global Competitiveness Report 2016-2017, p.28 http://www3.weforum.org/docs/GCR2016-2017/05FullReport/TheGlobalCompetitivenessReport2016-2017_FINAL.pdf

Fig. 4.7 China Indicators of Global Competitiveness Index



Source: World Economic Forum (2016)

Notwithstanding the inefficiencies in the financial and market regulatory environment, China is the first country in the world for market size. In a phase of slow, if not stagnant, economic growth worldwide, China, with its booming pharmaceutical market, is the place to be in order to gain long-term competitiveness and profitability.

3. Pharmaceutical industry segmentation and competitive environment

In his seminal book Competitive Strategy (1980), professor Michael Porter proposed that there are 5 forces that determine the long-term profitability potential of an industry, and are therefore relevant for strategic decision-making in international markets, namely the intensity of rivalry, the threat of entry, the threat of substitutes, and the bargaining power of buyers and suppliers. With its industry-based approach, Porter's Five Forces model allows to scan the competitive arena influencing profitability in a specific industry.

Taking a research based family firm as key player in the role of drug manufacturing, the competitive forces that shape the Chinese pharmaceutical industry will be outlined. The aim is to understand whether or not such firms may be at a disadvantage in accessing the market, compared to larger MNCs.

First of all, it is important to assess which are the forces and the involved parties that shape competition in the pharmaceutical industry:

- Threat of entry. It depends on the height of entry barriers, all those elements that make it costly, difficult or even impossible to enter an industry. The pharmaceutical industry is characterized by high barriers to entry mainly due to the high costs associated with R&D activities and compliance with regulatory standards. Further barriers affecting entry costs include: economies of scale, capital requirements, access to distribution channels, incumbent competitive position, cost disadvantages independent of scale, such as patents, access to know-how, access to limited resources, favorable locations, government subsidies or policies and learning or experience curves, product differentiation.
- Threat of substitutes. Substitution happens when competitors develop new business models, products or services that become a substitute for existing competitors, thus depriving demand-incumbent products of end-users. Generic brands are the main substitutes for patented drugs. Also, pharmacological treatments may be subsituted by a new developed medical device or surgery, while the main substitutes for non-prescription drugs are alternative methods like homeopaty, as well as traditional Chinese medicine.
- Suppliers' bargaining power. Powerful suppliers, including suppliers of labour, can affect the business by threatening to raise prices or to reduce the quality of their goods and services. The higher suppliers'concentration, the stronger their power. In the pharmaceutical industry, they could be the providers of raw materials (i.e. APIs) and

intermediates, the manufacturing and production plants, the overseas head offices who supply finished product, the local co-marketing partners who supply product and/or third party suppliers anywhere along the supply chain.[386] Each company will have different suppliers depending on whether they are OTC, ethical, or generic businesses.

- Buyers'bargaining power. It refers to the negotiating power of buyers to deny any price increase and to shift easily from one supplier to another. The pharmaceutical industry is unique because patients usually lack the power of bargaining drugs' price. The choice of which drug is consumed by a patient to treat a particular condition is largely made by the treating physician.[387] It is Government, hospitals, pharmacies and health insurance providers those having negotiating power and may seek price reductions as well as higher quality and better services. Government and health authorities can significantly influence the market through mandatory price reductions and price or reimbursement caps, while among hospitals and pharmacies, only those who buy in bulk quantities are able to excercise a certain buyer power.
- Intensity of rivalry. Rivalry among existing competitors takes the forms of price discounting, new product introductions, advertising campaigns, and service improvements. It increases when market growth starts to slow down due to overcapacity and limits the profitability of an industry when it is too high.[388]In the pharmaceutical industry, there is a high degree of rivalry among industry leaders. Examples are the rivalry in the erectile dysfunction space where Bayer and GlaxoSmithKline claim that Levitra works faster than Pfizer's viagra, or Eli Lilly and Icos claim that Cialis works longer than Pfizer's Viagra.[389]

Once the main forces at play in the pharmaceutical industry have been assessed, the focus can be shifted on how these forces shape the Chinese market in its main segments, OTC and prescription.

[386] Competitive strategy in the Pharmaceutical Industry. http://thought-leadership.top-consultant.com/UK/Competitive-Strategy-in-the-Pharmaceutical-Industry--978.html
[387] https://www.cornerstone.com/Publications/Articles/Analyzing-Competition-in-the-Pharmaceutical-Indust
[388] Porter, M. E. (2008). The Five Competitive Forces that Shape Strategy. Harvard Business Review, p. 32. http://s3.amazonaws.com/academia.edu.documents/32580687/HBR_on_Strategy.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1495878953&Signature=c7hx9NCKuxVHMip6wkURkPXZgkM%3D&response-content-disposition=inline%3B%20filename%3DHBR_on_Strategy.pdf
[389] The Guardian (2003). GSK and Bayer's orange pill challenges Viagra. https://www.theguardian.com/business/2003/aug/21/glaxosmithklinebusiness

3.1. OTC drug market

The Over-the-Counter (OTC) drug market consists of medicines sold directly to a consumer without a prescription from a healthcare professional, including:

-Traditional Chinese Medicine

-Cough and cold preparations (tablets, mixtures, lozenges, topical remedies, inhalers)

-Vitamins and minerals (multi-vitamins, single minerals, single vitamins, tonics, cod liver oil)

-Indigestion preparations (tablets, powders, mixtures)

-Analgesics (Paracetamol, Ibuprofen, Aspirin and other analgesics)

-Medicates skin products (anti-bacterials, acne treatments, anti-fungal, disinfectants and other)

-Topical OTC medicines (anesthetic products, anti-itch products, antibiotic creams/gels)

-Plasters & bandages (adhesive bandages/plasters, first aid tape, gauze pads/rolled gauze, liquid bandages and other tape or bandage)

-First aid kits and other (anti-smoking aids, rectal medications, eye/ear drops, sleeping aids, and motion sickness).

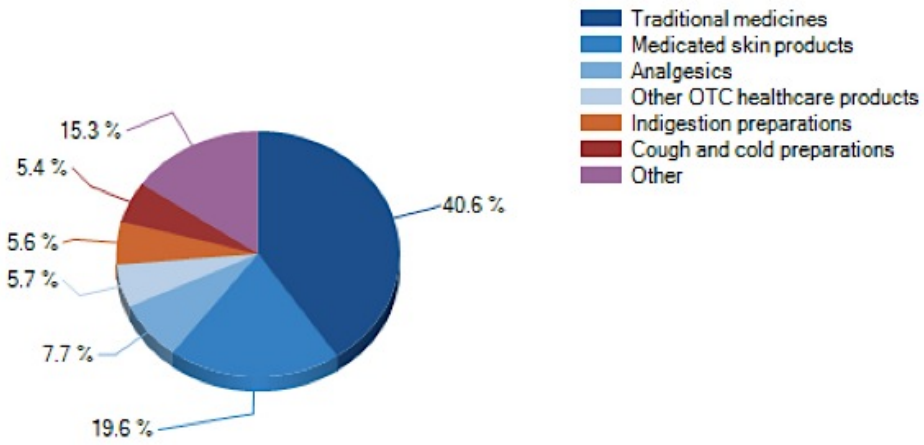
According to MarketLine (2016), The Chinese OTC pharmaceuticals market generated total revenues of $19,005.3m in 2015, with a compound annual growth rate (CAGR) of 6.2% between 2011 and 2015. As a share of the OTC market, traditional Chinese medicines registered total sales of $7,717.8m, equivalent to 40.6% of the market's overall value.[390]

The market is forecast to continue to grow with an anticipated CAGR of 6.1% for the five-year period 2015 - 2020, which is expected to drive the market to a value of $25,516.5m by the end of 2020. Comparatively, the Singaporean and Indian markets will grow with CAGRs of 3.4% and 9.5% respectively, over the same period, to reach respective values of $636.9m and $3,252.5m in 2020.[391]

OTC pharmaceuticals are mainly sold through drug stores/pharmacies and convenience stores/gas stations, which account for 66.7% and 18.1%, respectively. Other distribution channels are specialist retailers (9.2%), and hypermarkets/supermarkets (5.9%).[392]

[390] MarketLine (2016). OTC Pharmaceuticals in China, p. 7. www.marketline.com
[391] Ibidem
[392] Ibidem, p. 12

Fig. 4.8 China OTC pharmaceuticals market distribution (% by value 2015)



Source: Marketline (2016)

Five Forces Analysis

The degree of rivalry in the OTC segment is moderate. The Chinese OTC market is fragmented, with the top four players accounting for 20.5% in 2015.[393] Most of the leading firms are large multinationals, such as Johnson & Johnson and GlaxoSmithKline, which account for 5.3% and 3.6% market share respectively.[394] However, major gains of local players such as Huangshan Tianmu and Nin Jiom, which both have a market share of 5.8%,[395]suggests that rivalry might become more intense due to the presence of local firms. Also, as most OTC manufacturers are similar to one another, companies struggle to demonstrate that a drug has a greater clinical benefit than another and also through a strong brand image.

The threat of new entrants is moderate. Manufacturing OTC drugs involves a high level of specialization and expertise with high upfront investment costs, making the market difficult to enter. Also, the need to conform to safety standards imposed by the CFDA, and to other regulations such as the need for advertising pre-approval, serve as further entry barriers. Also, customers'preference for well established brands like Johnson & Johnson may deter SMEs from entering the market, as building brand awareness can be expensive and time-consuming. Because family firms are usually smaller than large MNCs and have scarce financial resources, they may find it difficult to invest in new product development, as it requires high development costs from extensive clinical trials. Therefore, a way for them to achieve efficiency is through collaboration with larger firms.

[393] MarketLine (2016). OTC Pharmaceuticals in China, p. 19. www.marketline.com
[394] Ibidem p. 11.
[395] Ibidem

However, fostered by an ageing population, a global trend toward self-medication, and a sustained market growth, opportunities for new companies in over-the-counter pharmaceuticals still exist.[396]

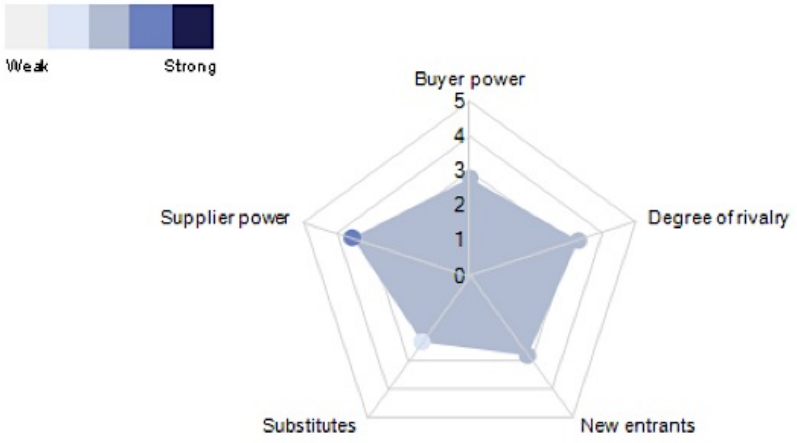
The threat of substitutes is weak. Prescription drugs are an obvious substitute, but these are normally used to treat more serious ailments, also due to the fact that, for minor ailments, consumers prefer self treatment to a prescription from a doctor which requires an appointment to be made. The fact that many pharmaceutical companies produce both OTC and prescription pharmaceuticals, further diminishes any threat from this particular substitute. Alternative medicines such as homeopathy are more complementary, rather than substitutive.[397]Brand loyalty further decreases the threat of substitutes.

Overall buyer power is moderate. Because the principal distributors of OTC drugs - pharmacies, drugstores and covenience stores - have small operational size, thus lacking scale, they generally have less buyer power than large supermarkets and larger chains. As larger chains may have a stronger negotiating power over smaller firms, these should focus on smaller distributors.

Supplier power is strong. OTC drug makers require a wide range of specialized ingredients. As smaller pharmaceutical companies do not have sufficient infrastructure to manufacture chemical ingredients themselves, they are often heavily reliant upon API manufacturers. Being APIs most often supplied to pharmaceutical companies under contractual arrangements, switching costs increase, thus enhancing the power of suppliers. The high levels of regulation surrounding pharmaceutical ingredients can further strengthen the bargainging position of reliable suppliers that fulfill regulatory criteria, or weaken the bargaining position of those who do not have a proven track record.[398]

[396] Ibidem, p. 17.
[397] Ibidem, p. 18.
[398] Ibidem, p. 16.

Fig. 4.9 Forces driving competition in the OTC pharmaceuticals market in China, 2015



Source: MarketLine (2016)

3.2. Prescription drug market

The prescription drug market consists of ethical drugs, for which a prescription from a healthcare professional is required. The Chinese pharmaceuticals market grew at a CARG of 18.7% between 2010 and 2014, to reach a value of $94.4 billion in 2014. Unpatented branded drugs have always continued to perform well after patent expiry due to the low quality of generics; moreover, the expansion of basic healthcare program and list of accepted drugs is helping to produce very good growth for the Chinese pharmaceuticals industry, which is also the biggest market in the Asia-Pacific region. However, the performance of the market is forecast to decelerate, with an anticipated CAGR of 15.2% for the period 2014 - 2019, which is expected to drive the market to a value of $191.3bn by the end of 2019. Comparatively, the Singaporean and Indian markets will grow with CAGRs of 9% and 8.5% respectively, over the same period, to reach respective values of $1.0bn and $19.3bn in 2019.[399]

Five forces analysis

The overall level of rivalry is moderate. The Chinese research-based pharmaceutical industry is dominated by several multinational corporations, alongside smaller firms such as biotech players focused on a small number of new products and generics companies. Although there is some evidence of consolidation and a trend for big pharma companies to swap key asset portfolios rather than buy each up, overall market concentration is low, with the three leading players (Yangtze River, AstraZeneca and Pfizer), generating almost 4% share of the market's value altogether.[400]It is relatively easy for research-based companies to expand output, for

[399] MarketLine (2015). Pharmaceuticals in China, p. 7. www.marketline.com
[400] Ibidem, p. 10.

example through licensing agreements with other companies, without the need to scale up their own production facilities. Rivalry is boosted by the increasing linkages between regulatory authorities and the greater likelihood of a drug being approved in multiple locations. It is moderately easy to exit the market, because many of the assets are 'weightless' – patents, trademarks, synthetic methods, and so on – and can be sold relatively easily, while many of the R&D and production facilities and equipment will have uses outside pharmaceutical research or manufacture.[401]

The threat of substitutes is strong. Patients may choose traditional medicine, which constitutes a significant market in China (28.55% of the total generated by the country's pharmaceutical industry in 2015).[402] Cheaper generics of off-patent drugs, which generate roughly 60% of the value of the pharmaceutical market[403], and biosimilars, are the main substitutes to branded drugs, as there are few switching costs involved in using them for patients. However, it should be noticed that not all drugs have an effective generic replacement and, in some instances, it is even the original company that produces the generic in order to try to prevent generic makers from muscling into the market.[404]

The threat of new entrants is moderate. Regulatory barriers to new entries are relatively high and mainly linked to the satisfaction of quality and safety standards imposed by the national regulator, weak intellectual IP protection, as well as the use of restrictive formularies that list only certain drugs as 'preferred' for a specific therapeutic area, thus reducing the market size of non-formulary drugs. A start-up company that intends to develop an entirely new biotech drug will need significant up-front investment and many years to bring a drug that meets regulatory requirements to market. However, it is easier to enter the country with an existing drug through licensing.[405] Overall, considering the strong market growth, and recent development in the regulatory environment aimed at speeding up the drug approval process and strengthen IP law enforcement to boost innovation within the country, the threat of new entrants is assessed as moderate.

Supplier power is moderate. APIs are supplied on a contractual basis and so pharmaceutical companies are likely to risk high switching costs if they consider taking their business elsewhere. To reduce their reliance on any particular company, drug manufacturers tend to purchase their raw materials from numerous suppliers, thus reducing supplier power for those

[401] Ibidem, pp. 19-20.
[402] State Council (2016). China issues first white paper on Traditional Chinese Medicine. http://english.gov.cn/news/top_news/2016/12/06/content_281475509319677.htm
[403] MarketLine (2015). Pharmaceuticals in China, p. 18. www.marketline.com
[404] Ibidem, p. 12.
[405] Ibidem, pp. 16-17.

chemicals that show little differentiation between suppliers. However, when specialized facilities or raw materials are required, supplier power is much stronger. Large pharmaceutical companies have turned to producing their own chemicals to reduce costs, while smaller companies remain reliant on API manuacturers.[406]

Buyer power is strong. Buyer power is strengthened by buyers'oligopsony status (few buyers, many sellers) and price control policies adopted by public or private-sector drug purchasers, such as health insurers, hospitals, pharmacies and similar institutions. The Chinese Government uses several strategies, including profit controls (via government guiding price), price cuts and/or freezes, and negotiated prices to discourage pricing overstatement. Movereover, due to the aging population in China, there is increasing pressure to control public levels of health expenditure and further reviews by the NDRC are expected.[407]

Fig. 4.10 Forces driving competition in the pharmaceuticals market in China, 2014

Source: Marketline (2015)

[406] Ibidem, p. 15.
[407] Ibidem, pp. 13-14.

3.3. Implications for family firms

The pharmaceutical industry is characterized by high profitability. In the US, the first pharmaceutical market in the world, it lists among the industries that have recorded the highest average return on invested capital (ROIC) between 1992 and 2006.[408]However, faced with market stagnation and higher operational costs in Western countries, pharmaceutical firms look at the Chinese market in search of new growth opportunities. According to market forecast, the Chinese pharmaceutical market will continue to record double-digit growth in almost all segments and therapeutic areas. Big pharma have already taken their steps in the country and many more players may consider entering the market. Yet, competitive forces may potentially affect firms' profitability differently according to a firm's size, financial resources, business area, etc.

Being family firms the focus of this paper, to which next chapter is dedicated, it is useful to determine the implications for this kind of firms.

The Chinese pharmaceutical market is highly fragmented. While there are many domestic companies, they are often too small to compete with foreign companies, whose medicines are often considered more effective and are higher demanded. Therefore, the majority of the Chinese pharmaceutical companies are focused on manufacturing generic drugs, while many foreign companies, including the world's biggest pharma companies, have developed their own manufacturing and distribution networks.[409]

Compared to their larger, often public-listed non-family competitors, market competitive forces can penalize privately-held family firms.

With regard to firm's size, SMEs may encounter higher entry barriers. As supported by Acs et al. (1997), *"financial market imperfections, differences in legal systems, cultures, and languages can make international business ventures risky for small and medium size firms. Barriers to entry that limit international expansion are systematically higher for smaller firms than for larger firms."*[410]

Among the main barriers, financing problems and poor information about labor, raw materials or output market conditions can lead new entrants to make costly mistakes. New market entrants also may find it difficult to attract good workers and support firms because of

[408] Porter, M. E. (2008). The Five Competitive Forces that Shape Strategy. Harvard Business Review, p. 28. http://s3.amazonaws.com/academia.edu.documents/32580687/HBR_on_Strategy.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1495878953&Signature=c7hx9NCKuxVHMip6wkURkPXZgkM%3D&response-content-disposition=inline%3B%20filename%3DHBR_on_Strategy.pdf

[409] Pacific Bridge Medical (2014). China Regulatory and Market Access Pharmaceutical Report 2014. p. 8.

[410] Acs, J. Z. et al. (1997). The Internationalization of Small and Medium-Sized Enterprises: A Policy Perspective. Small Business Economics, Vol. 9, p. 8.

employment and contracts with established firms. Furthermore, large firms may find it easier to overcome government's entry barriers than do small firms, as they have more resources and contacts and can afford delays, lawyers, bribes and campaign contributions.[411]

In addition, it could be more difficult for these firms to retain the best workers. If it is true that China is improving in the formation of skilled labor, it is also true that pharmaceutical multinationals have engaged in a wage battle in order to retain the best workers.[412]

Scholars generally agree that family firms "*are not simply a unique phenomenological setting but are significantly different from nonfamily firms*",[413] therefore, the main issue might not be the competitive environment itself, but the resources available to family firms that can be deployed in order to face it.

Internationalization is based on the opportunity of exploiting abroad the competitive advantages that a firm has in the domestic market. Such advantages can be in the form of *resources* – intangibles, technology, brands, culture, managerial capabilities – or *knowledge,* in the sense of information on both international markets and international expansion management.[414] Being family firms usually at a disadvantage when accessing resources and capabilities mainly due to limited capital to fund both family and business growth; the inflexibility and resistance to change of entrepreneurial leadership; disparate family goals, values, and needs; conflicts among sibling successors; and lack of managerial capabilities and foreign market knowledge, internationalization may be perceived as too risky, especially for small and medium-sized family firms. Notwithstanding the risk aversion stemming from the fact that almost all family's wealth is invested in the business, family firms have unique attributes that constitute potential advantages over non-family businesses in terms of efficiency and improved performance, such as greater organizational commitment and an orientation toward the longer term. Zahra et al. (2008), for instance, found that "*family firms benefit from having a culture valuing the involvement of their family members in its decision-making process and adopting a stewardship perspective in managing their operations.*"[415]When coupled with a stewardship culture that fosters employee empowerment, organizational commitment augments strategic flexibility, that is the ability to respond

[411] Ibidem, pp. 10-11.
[412] HR (2017). Winning the War for Talent in China. http://www.hrmagazine.co.uk/article-details/winning-the-war-for-talent-in-china
[413] Berrone et al. (2012). Socioemotional Wealth in Family Firms: Theoretical Dimensions, Assessment Approaches, and Agenda for Future Research. Family Business Review, Vol. 25, No. 3, p. 259.
[414] Fernández Z., Nieto M. J. (2005). Internationalization Strategy of Small and Medium-Sized Family Business: Some Influential Factors. Family Business Review, Vol. XVIII, No. 1, pp. 77-78.
[415] Zahra et al. (2008). Culture of Family Commitment and Strategic Flexibility: The Moderating Effect of Stewardship. Entrepreneurship Theory and Practice, p. 1051.

quickly to changing circumstances by addressing new demands of existing customers, adopting emerging technologies, or developing and defining new markets (Volberda, 1996), thus reducing the tendency to be passive, stagnant, and risk-adverse. As a matter of fact, a strong relationship was found between a firm's strategic flexibility and competitive orientation, which is fundamental as compe- tition increases globally and these firms have to adapt quickly to market, economic and technological shifts. Internationalization and the allocation of resources abroad, of course, requires a high degree of flexibility and quick response to market shifts. The pharmaceutical industry is no exception, as increased safety regulations and high R&D expenses have placed significant pressures on firms' profitability, which makes it a competitive market. Thus, quick response to changes in the regulatory environment as well as the flexibility to adapt to different regulations in foreign countries is fundamental.

Also, both the role of the family and the degree of family involvement in the business can affect the approach to foreign markets. The family business literature suggests that the family's influence is highest when the firm is owned and managed by the founding family and that it tends to weaken as the firm transitions into subsequent generations, thus affecting the firm's performance and strategic position. Three stages of family firms have been highlighted: in the first stage, the family is owned and controlled by the founding family, in the second stage the business is owned and managed by the extended family (new generations enter the business), in the last stage the firm is owned by the extended family but managed by external professionals.[416][417]

Gómez-Mejía et al. (2014) argue that the main difference between family and non-family firms lies in the different criteria they adopt to judge risk in strategic decisions, that is whether the socioemotional endowment will be preserved for the former and whether there will be financial gains for the latter. However, as the firm moves into the last stage, financial concerns become more important and could even outweigh concerns about SEW.

Having analyzed the nonlinear effects of both family ownership and family involvement in the top management on the performance of SMEs, De Massis et al. (2015) concluded that being a family firm can be both beneficial and destructive to an organization's performance, depending on the degree of family involvement as well as on firms' size.

[416] Gómez-Mejía et al. (2007). Socioemotional Wealth and Business Risks in Family-controlled Firms: Evidence from Spanish Olive Oil Mills. Administrative Science Quarterly, Vol. 52, p. 109.

[417] De Massis et al. (2015). The Impact of Family Involvement on SMEs' Performance: Theory and Evidence. Journal of Small Business Management, Vol. 53, No. 4, p. 928.

The benefits of family management derive primarily from the alignment of interests between owners and managers, plus the positive effects of kinship relationships within the group of managers, while the drawbacks are associated with an excessively redundant human capital of family members.[418]However, high levels of family involvement in the management translates into limited availability of knowledge, skills, and perspectives. Such constraints are particularly evident in small firms in a growing phase: a firm's growth implies that the family has to take more and more complex decision, but the firm usually lacks the necessary number of family members who are willing and able to make them.

Likewise, ownership dispersion negatively affects performance, because when an excessive number of family members gets involved in ownership, they will bring into play their presumably more heterogeneous, and potentially conflicting, interests.

In chapter one, the impact of governance on the internationalization process of family firms has been discussed. It has been often argued that complementing family managers with external professionals from outside the familial network may reduce any potential deficiencies in a family firm's human capital and is thus positive related to internationalization. External managers compensate for the lack of information about foreign markets; also, Fernández and Nieto (2005) found empirical evidence on the positive relationship between generational changeovers and stable relationships with other firms through shareholding or agreements and international expansion.

In conclusion, family firms are unique in that the family private sphere and the business overlap. Being a family firm has both positive – long-term commitment, low agency cost, tendency to limit debt load – and negative –difficulties in raising capital and attracting top talents, nepotism, risk aversion – implications that impact on the firm's performance, including the internationalization pattern and outcome. Yet, 19% of the companies in the Fortune Global 500, which tracks the world's largest firms by sales, are family-controlled.[419]While larger family firms may behave more similarly to non-family firms, small and medium-sized family firms can overcome the barriers to entry foreign markets by building stable relationships with other companies. For instance, having another company as a large shareholder can provide financial, technological, and human resources including managerial capabilities, marketing expertise, or distribution channels, which could be essential resources to enter foreign markets, while alliances allow family SMEs to share some

[418] Ibidem, p. 940.
[419] The Economist (2014). Business in the Blood.
http://www.economist.com/news/business/21629385-companies-controlled-founding-families-remain-surprisingly-important-and-look-set-stay

of the fixed costs involving foreign markets, which would otherwise be too high for them to face on their own. Similarly, joint ventures with local partners provide capital, technology, or distribution networks. Finally, collaborative agreements could also be a way to improve the international performance of family businesses, as they are useful for gathering information or covering the uncertainty of the internationalization process.[420]

Although socioemotional wealth theory seems to explain almost all differences between family and non-family firms, industry-specific considerations that take into account the characteristics of the pharmaceutical industry should be contemplated, as they may affect pharmaceutical family firms'strategic decision making.

In next chapter, I will attempt to verify this hypothesis by examining the internationalization pattern of four Italian leading pharmaceutical firms and to develop some proposals for family firms in order to approach the Chinese pharmaceutical market.

[420] Fernández Z., Nieto M. J. (2005). Internationalization Strategy of Small and Medium-Sized Family Business: Some Influential Factors. Family Business Review, Vol. XVIII, No. 1, pp. 80 - 81.

Chapter 5 – How do family firms internationalize? A multi-case study of Italian pharmaceutical firms

1. Italian players

With an overall turnover of 30 billion euro and exports accounting for 73% of manufacturing of the 200 companies located in Italy, the pharmaceutical industry in Italy plays a leading role in the international scenario; within the EU, Italy ranked second after Germany for number of companies and production value in 2015, and is expected to become the first in the medium-term. Furthermore, it accounts for 26% of total pharmaceutical production and 19% of total sales in Europe. [421]

Data from Istat and the Bank of Italy show that pharmaceutical industry ranks first in Italy for competitiveness, productivity, R&D intensity, export and Human Resources quality compared to other manufacturing sectors. These features make the pharmaceutical industry a fundamental asset for economic growth. The industry employs 63,500 highly qualified employees in 184 manufacturing plants, 6,100 researchers, and invests 2.6 billion euro each year, of which 1.4 in R&D. Italy's commitment to R&D is demonstrated by the contribution of Italian research: more than 7,000 medicines are being developed globally, of which 324 Italian biotechnological products, but also vaccines, advanced therapies, rare diseases and sex-difference medicines.[422]

40% of pharmaceutical companies in Italy are family-owned companies, wholly funded with Italian capital (the remaining 60% is foreign owned).[423] These companies are characterized by added value and investments in production and R&D per employee higher than the average of the manufacturing industry. Coupled with economic recession and the slow rate of growth in Italy, the aforementioned structural features should drive these companies to expand to foreign markets.

This is particularly true for the top ten Italian pharmaceutical companies, Menarini, Chiesi, Bracco, Recordati, Alfasigma, Angelini, Zambon, Italfarmaco, Kedrion, and Dompé.[424]

While all of them are engaged in foreign markets in various ways through exports, distribution agreements, or have established subsidiaries abroad, some of them (ie. Recordati,

[421] Farmindustria (2016). Facts & Figures of Pharmaceutical Industry in Italy. https://www.farmindustria.it/index.php?option=com_jdownloads&Itemid=0&view=finish&cid=103969&catid=78

[422] Ibidem

[423] Ibidem

[424] About Pharma (2016). Ecco la top 10 2016 delle industrie farmaceutiche a fatturato italiano. http://www.aboutpharma.com/blog/2017/02/22/458650/

Italfarmaco, Kedrion, and Dompé) do not operate in the Chinese market. On the contrary, some others, i.e. Menarini, Chiesi, Alfasigma, and Zambon have grasped the opportunities and managed the difficulties of this unique market and are being very successful in China.

Here below, the profile of four leading Italian pharmaceutical companies will be outlined and their strategies in the Chinese context will be discussed.[425] These companies have been chosen because they are among the largest in Italy (in terms of turnover), for which sufficient online information was available.

[425] All the informations regarding those companies are retrieved from their official websites.

1.1. The MENARINI Group

Founded in Naples in 1886 and headquartered in Florence, the Group is composed of three divisions: Menarini Ricerche, which deals with all R&D activities, Menarini Biotech, which follows the creation of a biotechnological drug from the early stages of research, through the pilot scale and up to industrial production, and Menarini Diagnostics, focused on Diabetes, Haematology, Clinical Chemistry, Urinalysis, and Immunology.

The group is present in over 100 countries, including 70 with direct presence thanks to a network of agents, and in more than 30 countries with distributors and local partners. Menarini is an undisputed leader in Italy, among the major pharmaceutical players in Eastern and Central Europe, the Baltics, Ukraine and Belarus, and it ranks second in Russia and Kazakhstan. The group is also present in Central and Latin America, Asia, as well as North, Central, and South Africa markets.

80% of its 16,365 employees works abroad, while the remaining 20% works in Italy; also, 72% of its turnover of 3.326 billion euros in 2015 derived from foreign operations.

Research centers are located in Italy, in the four sites of Lomagna, Florence, Pisa, and Rome, but also in Berlin and Barcelona. Fourteen production plants are located around the globe: in Florence (2 sites), Pisa, L'Aquila, Lomagna, Berlin (2 centers), Dresden, Kaluga, Istanbul, Shannon, Jakarta, and Guatemala which in 2014 produced 530 million packs altogether. Worldwide, Menarini employs about 2,200 individuals for manufacturing its medicinal products. Of these, more than 500 experts are engaged in quality control and quality assurance activities. Furthermore, Menarini has 345 Quality Control employees and 85 Quality Assurance employees. On average, more than one million controls are carried out each year: 1.088.000 in 2012. Each Menarini lab technician attends 35 hours of training and refresher courses every year.

According to IMS World Review, in 2015 the Group was the 19th company out of 5,541 in Europe and the 39th out of 21,317 in the world.

The therapeutic fields covered by Menarini's research programs focus especially on Cardiovascular, Gastroenterology, Antibiotics and Respiratory drugs, products for the treatment of Diabetes, Anti-inflammatories, and Analgesics. Since its foundation, the group has more than 25.000 patients enrolled in pivotal clinical trials, 3.200 patent applications (of which 273 priority) and 6 innovative drugs registered internationally (in the cardiovascular, anti-infective, analgesia areas) available in over 70 European and non-European countries.

For thirty years Menarini has also been a leader in the biotech sector in Italy. Its biotechnology center of excellence in Pomezia complies with the highest manufacturing standards (cGMPs) and has been authorized by the Italian Medicines Agency (Agenzia Italiana del Farmaco - AIFA) to produce pharmaceutical products for clinical use.

In the field of Diagnostics, Menarini is present with more than 1,000 employees and a network of 13 affiliates throughout Europe. Specialized in the two business areas of Self-Testing and Laboratory, Menarini Diagnostics currently provides approximately 500 million sensors for self- testing per year and has close to 10,000 laboratory instruments installed all over Europe. Its laboratory division operates in the Analysis of hemoglobins, Urinalysis, Autoimmunity and Cell pathology.

Asia represents one of the Group's most successful markets: ever since its first joint venture in India in 1995, Menarini has been increasing its presence in the Asian market. In 2011 it acquired the Invida Group, a strategic partnership between Quintiles Inc., Temasek Holdings and the Zuellig Group originally formed in 2005. The strategic acquisition of the Invida Group, soon rebranded Menarini Asia-Pacific, allowed Menarini to distribute its products throughout India, China, Singapore, Australia, Hong Kong, Indonesia, Malaysia, New Zealand, South Korea, Taiwan, Thailand, the Philippines, Vietnam, Pakistan, and Macao.

With its regional headquarter in Singapore, the company employs 3,000 employees across the Asia-Pacific region, whose market has been growing at about 20% per year, contributing to about 12% of Menarini’s global revenue.

Menarini Asia-Pacific operates across the entire commercial value chain, from clinical development, regulatory approval and product launch to lifecycle management.

Being a wholly-owned subsidiary of the Menarini Group, it has access to a global network of R&D infrastructure. The region also presents vast opportunities for Menarini Group to capitalize on Asia’s rapidly expanding patient population, quality data, skilled talents and competitive costs.

Menarini Asia-Pacific manages a diverse portfolio of proprietary healthcare brands as well as licensed brands from global biotech and multinational companies that cover several therapeutic fields, such as dermatology, select specialty care, consumer health, men's health, cardiovascular and allergy / respiratory.

Partnering is a critical component of Menarini Asia-Pacific's business model, which is basically based on attracting partners globally and working with them to commercialize products across the region. As multinational healthcare companies re-prioritize portfolios and

seek experienced and trusted partners to enter large and emerging markets, Menarini Asia-Pacific provides the one-stop advice and tailor-made solutions for partners desiring to enter single or multiple markets across the region. Working closely with its partners through dedicated Alliance Management teams, the company partners products at various stages in their development lifecycle, from clinical research and local regulatory approval through to launch and on-going commercialization, as well as products undergoing lifecycle management. Menarini Asia-Pacific leverages its significant regional experience with Asian patient and physician insights, as well as world-class resources, to provide three main partner solutions: regional in-licensing, brand acquisition and co-promotion/marketing opportunities.[426] The deep regional experience and depth of Menarini sales and marketing teams offers partners the flexibility of various models of collaboration.

In China, the Asia- Pacific Division has local offices in Beijing, Shanghai and Hong Kong. In 2013, a manufacturing plant, Menarini (China) Investment Co. Ltd., and Menarini's Chinese headquarters at the Wuhan National Bioindustry Base ("Wuhan Biolake") in Hubei Province were officially inaugurated. Being the first foreign enterprise to enter Wuhan's Biolake as a wholly owned foreign pharmaceutical holding company demonstrates the faith and long-term commitment to the Chinese pharmaceutical market and is expected to be a competitive advantage for Menarini, whose objective is to build Menarini as a trusted brand in China. Selecting Biolake as the preferred partner to grow its business aspiration in China was a deliberate and strategic choice aimed at bringing innovative products into the country by working hand in hand with local people.

Dr. Pietro Giovanni Corsa, General Manager of Menarini Group, asserted the Group unwavering confidence in the future of China, the world's fastest growing healthcare market, which they believe would continue to grow as a leading global economic powerhouse across a broad spectrum of industries, including the biomedical sciences sector.

There is a strong presence of the descending family in the current governance of the company, represented by the siblings Lucia and Alberto Aleotti, who, following the death of their father Alberto Aleotti in 2013, have recently admitted Domenico Simone and Juerg Witmer to join the board, the former thanks to the experience gained at Menarini, where he has been working for more than 48 years, making a career from scientific informant to general manager; the

[426] There are two major forms of joint marketing which are used to promote a pharmaceutical product, namely co-promotion and co-marketing. Co-marketing involves two companies selling the same drug under two different trademarks in direct competition, whereas co-promotion allows two companies to combine their resources and promote the product under one name. Overall, co-promotion is playing an ever greater financial role in pharmaceutical collaborations, especially when marketing drugs with large sales potentials.

latter thanks to his international experience, especially in the Far Eastern markets. Also, the Aleotti siblings have attempted to renew the R&D functions of the Group by employing an external business development manager formed abroad, Stefano Pieri, who had previously gained experience at Ely Lilly in Italy. The Group is also looking for young talented graduates for attracting new ideas in the area of R&D.[427]

It is not possible not to mention the recent scandal involving the Menarini siblings, who have been accused of tax fraud, with serious legal consequences. Since 2010, the Aleottis have been dealing with the tax evasion case filed by the Italian authorities. In September 2016, Lucia and Alberto Aleotti were convicted for corruption, money laundering and tax evasion, receiving respective sentences of 10 years, 6 months and 7 years, 6 months, while over one billion euros in foreign accounts have been confiscated.[428] It was discovered that the Aleotti family had been committed a fraud to the detriment of the Italian healthcare system for almost 30 years - from 1984 to 2010 - by setting up fictitious offshore companies which, through a system of fake billing, inflated the prices of the company's pharmaceutical products, which were ultimately acquired by the National Italian health care system with the exaggerated costs passed on to the taxpayer. However, the court of Florence acquitted Lucia and Alberto Aleotti of the allegation of fraud against the Italian healthcare system, while the conviction for money laundering refers only to the personal capital of the deceased Alberto Sergio Aleotti, which the court has found to come from tax fraud. The family also had a secret bank account in Liechtenstein and it came to light that they exercised pressure on politicians to dissuade them from supporting the purchase of generic drugs by the health care system. The legal advisors of the Aleotti family are working in order to let the siblings escape all the allegations at the Court of Appeal.

Being ethics and transparency one of the main values of the Group, the allegations of tax fraud and corruption are likely to impact on the image of the Group and on that of the Aleotti family itself. For the moment being, the thousands of jobs at Menarini are safe, but if the Court of Appeal upholds the decision of the lower court, Menarini could cease to exist as a family-owned multinational.

[427] Il Sole 24 Ore (2017). Da Roche a Janssen: più di 2mila Posti dai Big del Pharma. http://www.ilsole24ore.com/art/impresa-e-territori/2017-01-16/da-roche-janssen-piu-2mila-posti-big-pharma--101311.shtml?uuid=ADTyiAVC

[428] Repubblica (2016). Firenze, maxi condanna per frode ai vertici dell'azienda Menarini. http://firenze.repubblica.it/cronaca/2016/09/09/news/menarini_la_sentenza-147460034/#gallery-slider=147464551

Tab. 5.1 Strengths, Weaknesses, Opportunities and Threats of Menarini

Strengths	**Weaknesses**
Strong international presence with 80% of the employees working abroad and 72% of the turnover generating abroad Strict quality control, from raw materials to the finished product Strong presence in the diagnostics field Strong commercial infrastructures Diverse portfolio of marketed products, including both proprietary brand products - OTC, prescription drugs and medical devices – and in-licensed products from both Big Pharma and small pharmaceutical companies (aggressive pursuing of in-licensing opportunities especially in the Asia-Pacifi region)	Reliance on in-licensed products and proprietary patented drugs Current weak proprietary R&D pipeline – weak late stage pipeline Potential patent expiration exposing the company to generics'competition
Opportunities	**Threats**
High growth in the Asia-Pacific region Expansion in China with the establishment of headquarters in Wuhan Biolake. The partnership with the East Lake New Technology Development Zone of Wuhan (Cina) could open new R&D opportunities that would drive pipeline portfolio growth, while strengthening brand recognition	Healthcare cost containment measures Delays in drug approvals in China due to a backlog in the approval procedures Weak enforcement of IP protection in developing countries including China

1.2. CHIESI Pharmaceutical S.p.A.

Established in 1935 in Parma, Chiesi is a family-owned pharmaceutical company with a strong focus on research, development, production and the commercialization of innovative medicines in the Respiratory, Neonatology, Rare Disease and Special Care therapeutic areas.
With a turnover of more than €1.467 billion sales in 2015, more than 80% of which originates outside the domestic market, Chiesi is among the top 50 pharmaceutical companies in the world. The Chiesi Group employs approximately 4,500 people, 560 of whom are dedicated to R&D activities, and 720 of whom work at production sites in Italy, France, and Brazil. Reaching a total of €302,000,000, investments in R&D went up by nearly 30%, exceeding 20% of total sales, which makes the Chiesi Group the first Italian company for R&D investments in the pharmaceutical sector and the 6th most innovative Italian company among all industries.
Headquartered in the purpose-built and fully integrated new Research and Development Centre in Parma, the R&D team also has important activities in Paris, Chippenham (UK), Cary (US) and now in Lidingo (Sweden) and Hillerod (Denmark): the latter two sites comprise the new colleagues from the recently acquired Zymenex. The goals of this experienced cross-functional team are highly focused on the delivery of the pipeline on a global basis and increased productivity to support the growth goals.
Most of Chiesi's medicinal products originate from in-house research whilst others involve cooperation and partnerships with other pharmaceutical companies, such as Pharmaxis, Veloxis, Holostem, Uniqure, and Zymenex. 75% of the turnover comes from the products developed by the Chiesi R&D division.
The number of R&D programs is constantly increasing and diversifying, therefore enriching the company's therapeutic range. In fact, the traditional therapeutic areas of the Chiesi Group (respiratory, neonatology and special care) are now complemented by new research areas and know-how in several sectors: rare diseases, biotechnology, gene therapy and transplantation. Chiesi is now widening its range of products with different types of drugs which now accompany traditional small molecules, including biotechnological products (proteins) and advanced therapeutics (gene and cell therapies), innovative ways to approach these new disease areas.
This strategy enables the company to keep developing and enriching its pipeline. During the past 6 years the Group, due in part to the investment in R&D, has achieved sustainable growth: a 75% increase in income, the launch of a new product on average every two years, the opening of seven new subsidiaries and the creation of over 750 new jobs.

At the end of the 1970s, the first subsidiary in Brazil was opened. Since then, the company has continued to expand abroad: starting from 1987, Chiesi has opened affiliates in Pakistan, France, Spain, Greece, the United Kingdom, Austria and the Eastern European countries, the United States, Germany, the Maghreb countries, Turkey, Bulgaria, China, and Scandinavia. Nowadays it operates in 5 continents with 26 branches and distributes pharmaceutical products to more than 70 countries.

In 2008, Chiesi entered as a pioneer in the world of regenerative medicine by founding Holostem Advanced Therapies Ltd, and in 2013, with the acquisition of the Danish biopharmaceutical company Zymenex, moved into biotechnology, positioning itself today at the height of innovation in the biopharmaceuticals sector.

In 2008 Chiesi Pharmaceuticals (Shanghai) Co. Ltd. started up in China with the commercialization of *Curosurf*, a product already distributed in the country by a former partner, indicated for the prevention and treatment of neonatal respiratory distress syndrome (amongst the most common causes of neonatal death). Thanks to its presence in all the major neonatology congresses and the expansion in the central and western provinces, Chiesi soon became the leading company in China for surfactants. In 2013 the company strengthened its presence in China: the CFDA granted market authorization for *Peyona* (orphan drug for hospital use for treatment of primary apnoea of premature newborns), *Foster* and *Clenil UVD* for the treatment of asthma; regional headquarters were established in Beijing, Shanghai and Guangzhou for commercial activities and relations with local authorities.

In 2015 Group revenues from China exceeded 60 million euro with 35% growth compared to 2014. Notwithstanding the significant market downturn affecting the surfactant area, which only recorded 1% growth, the whole respiratory market grew by 11%, also thanks to the expansion of the field force from 66 to 112 sales representatives in order to cover the faster-developing lower tier cities. Investments have also been made to strengthen training and other supporting functions. The field force, composed of 131 reps out of a total headcount of 173 employees, has been reorganized into 5 regions controlled at the central level. Investments were also made to strengthen the training department and other supporting functions at the central level.

As a result, Chiesi has become the reference company in neonatology in China: *Curosurf* achieved 75.8% market share and *Peyona* is listed in 250 new hospitals (its sales grew by 70% on 2014). Thanks to Chiesi's JV with Eddingpharm, whose team negotiated provincial biddings, *Foster* and *Clenil* obtained listings in 274 hospitals. The target is to reinforce

leadership in neonatology and continue the expansion in the respiratory market. Currently, plans have also been made to launch *Budiair* with the support of another partner.

The CEO Ugo di Francesco acknowledges that, with a pool of patients of almost 1.5 billion people, China offers great growth opportunities in every therapeutic area. Therefore, the company is betting big on both the USA and the so-called 'Pharmerging' markets, including China, even though India is not a priority for the moment.

The firm is characterized by a strong family presence and active participation at all levels. R&D, for instance, a critical component of pharmaceutical firms, is entirely headed and managed by members of the Chiesi family.

The Head of the R&D Department, Andrea Chiesi, is responsible for the definition of the R&D strategic plan and yearly budget, tracking of costs, activities and timelines of projects, as well as the coordination of the planning activities of the projects from the Chiesi R&D, the search and management of public grants to R&D projects, R&D site and the scientific information/intelligence gathering and diffusion.[429] And it is Andrea Chiesi the one who supports the firm's constantly increasing commitment to innovation, suggesting that family involvement can be beneficial to the business.

[429] http://www.cgteurope.com/speakers/andrea-chiesi

Tab. 5.2 Strengths, Weaknesses, Opportunities and Threats of Chiesi

Strengths	**Weaknesses**
Strong internal R&D pipeline – 75% of total revenues are generated by products developed by internal R&D (42 new projects in 2015, of which 7 in preliminary phase, 15 in early development phase, 15 in pivotal trial or regulatory authority presentation phase) R&D partering projects enhanced the company's therapeutic range, enriched its pipeline and shortened new product launch period (18 patent filings in 2015) Strong international presence with a robust product portfolio and distribution in over 70 countries Strong position in China in neonatology as a result of strategic partnerships and increased presence on the territory	Divestiture and out-licensing of products to sustain high R&D investments and manufacturing scaling up Higher complexity due to the recent centralization of of the direct management of all the production plants Potential patent expiration exposing the company to generics'competition
Opportunities	**Threats**
Leadership reinforcement in the special care area and neonatology in particular, developing as a reference supplier for hospitals Expansion in new therapeutica areas (rare diseases, biotechnology, gene therapy and transplantation) Consolidation of its presence in neonatology and development in the respiratory therapeutic area in the Chinese market Registration of new drugs in the Chinese market Intensification of international expansion to grasp new market opportunities	Healthcare cost containment measures and price cuts of key products in the European market Delays in drug approvals in China due to a backlog in the approval procedures In a huge country like China, retaining and training the teamwork remains a challenge Weak enforcement of IP protection in developing countries including China Fluctuating exchange rates affecting the Russian and Brazilian markets, where devaluation eroded turnover growth in 2015

1.3. ALFASIGMA Group

Alfasigma is a major pharmaceutical group created in 2015 by the aggregation of two historic Italian companies, Alfa Wassermann and Sigma-Tau. Alfasigma's majority shareholder – with 75% share - is the Golinelli family from Alfa Wassermann. Some members of the Cavazza family from Sigma-Tau own 20% share, while Intesa Sanpaolo, previously shareholder of Sigma-Tau and sole bank financing the acquisition process, has taken the remaining 5% participation.

Alfa Wassermann

Alfa Wassermann is one of the principal Italian Pharmaceutical Groups with a strong international vocation. Alfa Wassermann was founded in 1948 by Marino Golinelli in Bologna. The Group operates directly with 12 wholly owned affiliates, employing 1370 employees worldwide (of whom 670 are based in Italy), while indirectly its products are sold in over 60 countries via qualified local distributors. In the EU Alfa Wassermann has consolidated its presence in France, Spain, Portugal, where it acquired important local companies. In Eastern Europe, where the Group had already conquered important market segments since the Eighties thanks to agreements with distributors and licensees, Alfasigma has created new structures since 2004 (Rumania, Poland, Czech Republic and the Slovak Republic). As a result of a very effective international growth strategy, Alfa Wassermann has managed to gain significant market share also in Russia, where it operates directly since 2008; China, where the group directly promotes its products through a structure that manages both the registration and the scientific communication of Neoton®, Vessel®, and Xifaxan® (a brand under which Rifaximina will be launched); Tunisia and Mexico, where branches were opened in 2004 and 2011, respectively. Furthermore, the group also operates in the United States through Alfa Wassermann, Inc.: the company supplies analytical, hospital and private laboratories with a line of highly automated and reliable clinical chemistry analyzers, based on cutting-edge technologies. Alfa Wassermann, Inc. is also one of the international leaders in separation technology and markets a line of ultracentrifuges used by the leading producers of influenza vaccines. Its operative headquarters is located in New Jersey, while international sales are co-ordinated by the sister company, Alfa Wassermann B.V., based in Holland.
In 2015 the total group turnover was €429.3 million, of which over 60% was generated by products developed in its research laboratories. International sales generated 53% of the turnover, of which subsidiaries account for 35% and the remaining 18% was generated through exports and licensees.

Ever since its inception in 1948, Alfa Wassermann has constantly been investing in research and innovation, developing breakthrough New Chemical Entities (NCE's) such as Rifaximin-α (Normix®), a pharmaceutical product with diverse gastroenterological indications, now on the market in 39 countries. In the USA, branded as Xifaxan®, the product is ranked among the top 50 pharmaceutical products in revenues.

Other group key Brands include Vessel®, Fluxum®, and Dicloreum®. In Italy Alfa Wassermann is also very active in the Over The Counter sector with well-known household brands, including NeoBorocillina®, Ketodol®, and Dicloreum®.

The historical location of Alfa Wassermann in Bologna is the "Italian heart" of the research activities together with the Company Headquarter and the research laboratories, where new products are developed. Alfa Wassermann's products are manufactured, packaged and released by its plant in Alanno (Pescara, Italy), recently restructured and enlarged to a total area of 17.600 square meters. Apart from company's drugs, the plant also packs thousands of pieces a year for other domestic and international pharmaceutical companies. Alfa Wassermann is committed to the development of new technologies, with the goal to guarantee the highest standards of quality as well as efficiency in its manufacturing processes.

Alfa Wassermann's international activities are managed out of its Milan-based International Division.

Sigma-Tau

Sigma-Tau is one of the most important Italian pharmaceutical groups, with a leading role at international level.

Sigma-Tau was founded in 1957 by Claudio Cavazza: he was at the head of the company until 2011, year of his death. Since the very beginning, Claudio Cavazza carried out pioneristic chemical and pharmacological studies on *carnitine*: this was an extraordinary intuition that, thanks to a life committed to research with passion and determination, opened new horizons to knowledge. The idea that a therapy, and with it the vision of Medicine, could not disregard pharmacology based on biology and metabolism became the approach to health culture that made the Sigma-Tau Group one of the benchmark companies in the Italian pharmaceutical sector.

Sigma-Tau develops, manufactures and sells synthetic drugs, as well as drugs of natural and biotechnological origin. It invests on average 16% of its turnover in R&D and employs approximately 400 researchers currently working on a significant discovery pipeline. As a result, 300 patents applications have been filed since 1998. The company's strong degree of

internationalization is also evident to the maximum degree in the constant development of research ventures in collaboration with numerous Italian, European and North American scientific institutes, including public and private research centers, test laboratories, clinics, and hospitals. The research center in Pomezia (Italy), is dedicated to pre-clinical discovery and development, as well as the coordination of clinical development and registration activities.

Currently, different activities are ongoing in order to expand proprietary platforms and provide opportunities for partnering. In biotech, discovery activity is currently focused on the identification of new monoclonal antibodies to address various types of cancers, alongside with the development of innovative biotech products acting on already validated targets (bio betters).

In January 2010, the Sigma-Tau Group acquired the pharmaceutical business of the American company Enzon, and specifically 4 products for the treatment of rare cancers and the manufacturing plant of Indianapolis, Indiana, taken over directly by the company's American subsidiary, Sigma-Tau Pharmaceuticals Inc. based in Gaithersburg, Maryland, which markets the acquired products in the United States. The transaction was completed as part of a commitment that Sigma-Tau first demonstrated back in 1984, when it was the fourth company in the world to be assigned an Orphan Drug Designation,[430] and received seven more during the following years. Applications for five additional Designations have been filed with the European authorities.

Sigma-Tau is also engaged in the fight against Malaria, a disease that threatens more than 40% of the world's population, for which the company has developed Eurartesim®, a highly effective Artemisinin-based Combination Therapy (ACT) that has been approved by the European Medicine Agency (EMA) in 2011.

The Group owns a rich product portfolio, marketed in Italy and abroad, in the following therapeutic areas: Cardiometabolic, Orthopedics and Rheumatology, Bronchopneumology, Infectious Diseases, Oncology, Neurology, Gastroenterology, Dermatology, Urology, and

[430] The Orphan Drug Act (ODA) of January 1983, passed in the United States, with lobbying from the National Organization for Rare Disorders and many other organizations, is meant to encourage pharmaceutical companies to develop drugs for diseases that have a small market. Under the ODA drugs, vaccines, and diagnostic agents would qualify for orphan status if they were intended to treat a disease affecting less than 200,000 American citizens. Under the ODA, orphan drug sponsors qualify for seven-year FDA-administered market Orphan Drug Exclusivity (ODE), tax credits of up to 50% of R&D costs, R&D grants, waived FDA fees, protocol assistance and may get clinical trial tax incentives. Orphan drug designation means that the sponsor qualifies for certain benefits but it does not mean the drug is safe and effective and legal to manufacture and market in the United States.

Gynecology. The Group is a leader in nutraceuticals and produces food supplements of high scientific interest. Its product range also includes high-end dermo cosmetics lines, as well as oral and personal care products.

The Sigma-Tau Group has headquarters in Pomezia (Rome, Italy) and subsidiaries in France, Switzerland, Belgium, the Netherlands, Germany, UK, India, with production plants in Italy as well as in Spain and US. Concerning the Pharmaceutical Business, Sigma-Tau has 1,410 employees and closed 2015 with a turnover of €478.2 million, of which 25% generated from international sales (11% through distributors and the remaining 14% through subsidiaries).

Alfasigma

In order to face competition and invest the necessary resources in research, development, and innovation, the two companies decided to pool their assets in terms of workforce, products and skills, and thereby lay the foundations for further growth.

With a turnover of over 900 million Euros, the new group is among the top five players in the pharmaceutical industry in Italy, both in terms of Prescription and OTC products.

Since the two companies are complementary at the international level, overlapping only in France and Spain (where, however, they can achieve a more competitive size by adding together the turnovers), Alfasigma started operations with a significant direct presence in as many as 18 countries, including the USA, China, Russia and various European countries, with about 2,800 total employees of whom about 1,840 working in Italy and 960 in the subsidiaries abroad. The Italian operational sites are: Bologna, Milan, Pomezia, Alanno, and Sermoneta. While Milan and Bologna house the International Division and the Group's headquarters, respectively, the last three locations are production sites equipped with the very latest cutting-edge technologies.

As stated by Stefano Golinelli, chairman of Alfasigma, for the future, the group is putting great emphasis on China, where Alfa Wassermann was already present, and where, between the two companies, they have 4- 5 proprietary products already registered, but also the United States and eastern Europe. In fact, at the beginning of this year, the group announced the acquisition of Pamlab, a U.S. based company with a leading position in the manufacturing and distribution of medical foods for brain and metabolic health, from Nestlé Health Science. For many years now, Alfasigma's rifaximin product has been marketed in the U.S. under the tradename Xifaxan® by license to Salix / Valeant. Alfasigma has further strengthened its presence in the world's largest market by creating Sigma-Tau Healthscience USA, Inc., which

markets VSL#3, a potent probiotic medical food bought, in June 2016 and now by acquiring Pamlab.

Thanks to its extensive portfolio of products, Alfasigma has a leading position in the Italian market in the fields of Orthopaedics-Rheumatology, the Cardiometabolic area, Diabetology, and Gastroenterology.

The business plan foresees further growth for both the Italian and the International activities. Also, the Group invests a significant share of its turnover in R&D in order to identify therapies that can offer new treatment opportunities for those who have to cope with illnesses with high clinical and social impact. In this respect, the international success of Rifaximin- α (Normix) reflects the group's commitment.

The R&D center in Pomezia concentrates mainly on immuno-oncology, specifically through the study and development of proprietary biotechnology platforms aimed at innovative, targeted therapies.

Tab. 5.3 Strengths, Weaknesses, Opportunities and Threats of Alfasigma

Strenghts	**Weaknesses**
More resources in R&D and manufacturing Wide portfolio of products based on a series of patents which have led the company become an important player in various therapeutic areas Strong position in the domestic market Significant direct presence in 18 countries, thanks to a network of both directly controlled companies and distribution agreements. Strong commitment to R&D and alliances with research organizations Production of extensive and diversified products for other pharmaceutical companies Competitive position in the field of nutraceuticals and medical food	Potential patent expiration exposing the company to generics'competition Increasing complexity due to recent partnership between Alfa Wasserman and Sigma-Tau Weak presence in the fast growing Asian market
Opportunities	**Threats**
Further expansion in international markets, e.g. in the high-growth market of the medical food segment in the USA Good development prospects in developing markets, characterized by growing economies and good receptiveness to pharmaceuticals Registration of new drugs in the Chinese market Development of research collaborations with Chinese science institutions Growth in the field of diseases with high unmet medical need thanks to financial incentives, extended exclusivity and ease of gaining marketing approval for orphan drugs in the EU and USA, which offset the risks of low profitability in a market with a limited number of patients	Healthcare cost containment measures Delays in drug approvals in China Weak enforcement of IP protection in developing countries including China Absence of a nationwide legislation for orphan drugs in emerging countries, including China, which puts profitability at a stake in this field.

1.4. DOMPÉ Pharmaceutical S.p.A.

Dompé Farmaceutici S.p.A. is one of the leading biopharmaceutical companies in Italy, dedicated to the development of innovative therapeutic solutions for rare and orphan diseases. Founded in Milan in 1940, the company has its major industrial and biotechnological research facilities in L'Aquila, which guarantees national and international supplies of proprietary products and produces recombinant proteins to treat rare diseases, and an R&D unit in Naples. As part of its international development strategy, in 2014 Dompé opened its offices in New York, to coordinate the R&D activities in North America, while in 2015 it opened its first two branch offices within Europe: Tirana, where Dompé will market an expanding range of OTC and ethical primary care products and is planning to launch new products in the near future, and Barcelona, where the company extended its previous collaboration with Spanish R&D centers and where commercial operations will be carried out.

In 2016 Dompé took over the Pharma division of the pharmaceutical Group Bracco and has recently formed the Dompé Primary, the Company's division involved in the development and distribution of ethical drugs and OTC products, dietary supplements, medical devices and cosmetics, in a number of therapeutic fields (cardiovascular, gastrointestinal, paediatric, neurological, endocrinological, urological, ophthalmic, stomatological and respiratory diseases) and in the areas of integration of vitamins and minerals and of personal hygiene.

A recent agreement with Omega Pharma for the distribution of its OTC products in over 50 countries starting from 2017 is an important step in the pursuing of its strategy for the internationalization of its portfolio, from the OTC drugs to those for the treatment of Rare Diseases.

Research and development operations are aimed at finding innovative therapeutic solutions for rare and orphan diseases primarily in areas with unmet treatment needs, such as of Diabetology, Ophthalmology, Oncology, Ophthalmology, and Organ Transplantation. In 2014 the Company invested 19% of its sales revenues in R&D. During the year, 14 clinical trials were initiated worldwide and are being conducted with the support of an international network consisting of 70 excellence research institutes. In 2015 Dompé expected to invest € 42.5 million in R&D, i.e. 25% of its revenue. 21 clinical studies are in progress at present, involving a total of 1,200 patients and 200 research centers worldwide. In 2017 Dompé expects a 250 million euro turnover, of which 15% will be invested in R&D.

Since 2007, the CEO Eugenio Aringhieri has promoted the company's reorganization and, with the aim of making the Group an internationally recognised science-based company, he

has supported high-tech startups, particularly active in biotechnologies: in 2008 he consolidated its partnership with Amgen by creating Amgen Dompé, an equal joint venture of which he was President, and established the strategic programme and priority objectives of Biogen Dompé, an equal joint venture - of which he was CEO - between Biogen Idec, the world's leading biotech company, and Dompé, thus consolidating their initial marketing agreement into a partnership by creating a new company in Italy and Switzerland.

With a focus on the value of innovation in research into biotechnological therapeutic solutions to global health problems, Aringhieri promotes an international approach based on the network, which consists in the development of collaborations with an extensive network of centres, including companies, universities and research institutes, accurately selected for their scientific, diagnostic and therapeutic expertise and their approach focused on constant innovation in the study of new treatment solutions.

He was Vice-President of the Board of Directors of Philogen, an outstanding Italo-Swiss biotech company dedicated to developing products for the treatment of cancer, rheumatoid arthritis and certain eye diseases, of which Dompé is the majority shareholder.

He also joined the Board of Directors of AAA (Advanced Accelerator Applications), a leading company in the field of molecular medicine. In the same year, he became President and Managing Director of Anabasis, an Italian biotech company that develops innovative drugs based on rhNGF (the discovery of which led to Prof. Rita Levi Montalcini being awarded the Nobel Prize) for the treatment of serious eye diseases for which no effective therapy is currently available, whose acquisition was completed in February 2012.

Aringhieri has also actively supported high-tech startups and since 2016 he has been a Member of the e-Novia Board of Directors, a company focused on fostering business innovation through international research projects and partnerships.

Apart from conducting basic research or clinical studies in collaboration with a number of facilities in the USA, Europe, and Russia, in order to accelerate the process of new drug discovery Dompé unites the expertise of its drug discovery team with that of universities and other research centers, which further extend its scientific network. Therefore, the company has engaged in a number of collaborative projects, research agreements and material transfer agreements (MTAs)[431] with external partners (companies, universities, and research institutes) in Canada, Brazil, USA, France, Switzerland, Spain. The company is partnering, among

[431] Contract that governs the transfer of tangible research materials, including reagents, cell lines, plasmids, but also chemical compounds, between two organizations. It defines the rights of both the provider and the recipient with respect to the materials and any derivatives. MTAs are most common for transfers between academic or research institutions, transfer from academia to industry and vice-versa.

others, with the Italian pharmaceutical company Angelini in its drug discovery activities and has a research agreement with the Institute of Infectious Diseases of Beijing Ditan Hospital, Capital Medical University, in China for the inflammation area.

Dompé's unique approach to drug discovery is based on a proprietary technological platform (GPCRbase™, Ligen™ and LigandBase™, and MolecularAssemblies) designed to accelerate the selection of drug candidates for development.

In 2015, the Committee for Orphan Medicinal Products of the EMA (European Medicines Agency) has designated rhNGF, the experimental biotech molecule developed by Dompé's R&D division drawing from the studies of the Nobel Prize in Medicine Rita Levi Montalcini, as the orphan drug for the treatment of neurotrophic keratitis. One year later, the EMA also approved the request for authorisation to market cenegermin eye drops (Oxervate®), developed for the treatment of moderate and severe neurotrophic keratitis in adults.

The next three years will be crucial for Dompé, as it is in the late stage of several different projects in different therapeutic areas with a high unmet medical need, for which Dompé could become the first company in the world to deliver a treatment.

Company's product portfolio is currently sold in 40 countries. The therapeutic areas covered by Dompé include:

- Diseases of the respiratory apparatus, such as asthma, rhinitis, cough and chronic obstructive pulmonary disease (COPD);
- Osteoarticular or rheumatic disease like arthrosis, arthritis, and related musculoskeletal disorders, of which osteoarthrosis (OA) is the most frequent;
- Rare diseases, such as pulmonary arterial hypertension, which is often associated with other disorders like connective tissue diseases (scleroderma, lupus), liver diseases (portal hypertension), viral infections (HIV), congenital heart diseases, and recurrent pulmonary thromboembolism;
- OTC products for the treatment of headache, dry and wet cough, sore throat, inflammation, and menstrual pain. This is a new line available since 2012 distributed by pharmacies, parapharmacies, and supermarkets.

Tab. 5.4 Strengths, Weaknesses, Opportunities and Threats of Dompé

Strenghts	**Weaknesses**
Increasing R&D investments Strong network in each branch of pharmaceutical industry that accelerates the selection of drug candidates for development. Expanded portfolio of products in the primary care and self-medication field through recent acquisition of the Pharma Division of the Bracco Group in order to spread risk.	Potential patent expiration exposing the company to generics'competition. Weak commercial infrastructure Poor direct presence in international markets
Opportunities	**Threats**
Biotechnology has the potential to find solution for still untreated illnesses, opening up new research horizons Further expansion of the R&D network in 'pharmerging countries', thanks to governmental incentives, lower R&D costs and a wide pool of potential patients. Commercial expansion in international markets to increase sales Financial incentives, extended exclusivity and ease of gaining marketing approval for orphan drugs in the EU and USA which offset the risks of low profitability in a market with a limited number of patients	Healthcare cost containment measures. Delays in drug approvals in China. Absence of a nationwide legislation for orphan drugs in emerging countries, including China, which puts profitability at a stake in this field. Weak enforcement of IP protection in developing countries including China

1.5. Same industry, same international approach?

Looking at the history of these four companies, some similarities, as well as some differences in both their governance structures and international approach emerge.

First of all, these firms are owned by one family, with the only exception of the newly created Alfasigma, in which ownership is divided among the Golinelli family from Alfa Wassermann -Alfasigma's majority shareholder with 75% share - , some members of the Cavazza family from Sigma-Tau, who own 20% share, and Intesa Sanpaolo, previously shareholder of Sigma-Tau and sole bank financing the acquisition process, which has taken the remaining 5% share.

Secondly, all the firms have an external CEO, who is also involved in the Board of Directors. Family members usually hold the charge of President or Chairman, which means that, although they own the company, they are not directly involved in the actual management. Chiesi is the only exception, as family members are involved in the business at various levels both in the Board, where they are complemented by an external CEO, and in the management team, where they collaborate with external professionals. Also, the number of external board members is usually one, two only in the case of Menarini, which means that the minimum percentage of family board members is 50%, as for Menarini (2 out of 4) and Dompé (1 out of 2), while it increases to 75% in the case of Alfasigma (3 out of 4) and reaches 85% at Chiesi (6 out of 7).

Thirdly, all these firms are characterized by the involvement of second or subsequent generations. Menarini and Alfasigma are run by second generation (the founder of Alfa Wassermann, Marino Golinelli has only an honorary charge), while both second and third generations collaborate at Chiesi. Dompé is the only company in its fourth generation.

As it will be discussed in the following section, the involvement of new generations coincides with either the beginning or the intensification of the firms'international expansion. The same positive correlation is observed between the presence of external CEOs and firms'internationalization.

With regard to the internationalization patterns, these firms seem to follow a similar gradual pattern that usually starts with exports, licence or distribution agreements and then move to more capital-intense forms of investments, such as greenfields and acquisitions. Also, a general tendency to expand in either culturally or geographically close country, ie. Spain and European countries at large can be observed, while investments in emerging markets like

China and India are always preceded by investments in countries that are perceived as 'closer' and usually start with local partnerships before committing to the market, as in the cases of Menarini and Chiesi.

Regarding investments' distribution, all these firms have established R&D centers and manufacturing plants in Italy and abroad. However, while R&D functions are mainly located in Europe (excluding Eastern Europe) and the USA, manufacturing plants are located around the globe, suggesting that these firms tend to concentrate value-added activities either in the domestic country or in countries where pharmaceutical R&D is cutting-edge.

Ultimately, these firms share an increasing commitment towards both R&D and internationalization. They all reinvest a consistent percentage of turnover to finance R&D projects (between 15-20%), including Menarini, though it currently seems to be more focused on commercialization and owns a weak late-stage pipeline. Also, these firms show an interest in pursuing internationalization. The two bigger Menarini and Chiesi are confident in the growth of the Chinese market, while Alfasigma and Dompé currently seem more focused on the USA, where the legal environment for orphan drugs (which constitutes an important part of their business) is favorable, though Alfasigma is planning to add new drugs to the few proprietary products already registered in China.

This summary highlights that some similarities among these four firms do exist; however, taken alone, it tells much neither on the family nature of these firms nor on their international approach. Therefore, in the following sections these results (summarized in Tab 5.5 and Tab. 5.6) will be compared to existing theories of internationalization and family firms, in an attempt to understand how the 'familiness' of these firms affects their internationalization process and what theory better serves the purpose of explaining the relationship between family firms and internationalization. Industry-related considerations will also be included in the analysis.

2. Italian family firms in the pharmaceutical industry: evidences from existing theories

In chapter one of this paper various theories regarding the themes of *internationalization* and *family firms* were presented, in an attempt to understand the reasons why companies decide to go abroad, if common patterns of internationalization do exist, what kind of organization can be defined as 'family firm', and in what aspects these firms differ, if they differ, from non-family businesses, with a special focus on how the 'familiness' of these firms affects their internationalization process.

Although family firms represent the dominant form of economic organization throughout the world, they have received scarce attention; only recently there has been an increase in empirical studies on the subject, that have examined the impact of family ownership on internationalization, although with sometimes antipodal empirical finding (see Zahra 2003; Fernàndez & Nieto 2006).

The cases of four leading Italian family firms operating in the pharmaceutical industry give us the chance to make a critical comparison with the existing theories and findings, and could shed a new light on the subject, basically because these firms are (a) family-owned, with various degree of family involvement in the governance, (b) highly involved in international markets.

Being based on four firms, this paper cannot give an exhaustive view of the family-firms' panorama in Italy; however, some preliminary assumptions can be developed, which could pave the way for further empirical testing on wider firms' samples.

Operating in the highly globalized pharmaceutical industry, Menarini, Chiesi, Alfasigma, and Dompè betray traditional literature that depicts family firms as risk-averse and less prone to internationalize. Furthermore, the internationalization patterns of these firms partially follow the *incremental* process suggested by Johanson and Vahlne (1977), according to which *psychic distance* affects the establishment chain of firms abroad, which will, therefore, start with irregular exports, followed by exports via an independent representative (agent), the establishment of a sales subsidiary and finally that of a foreign manufacturing subsidiary. Looking at the internationalization process of Menarini, Chiesi, Dompé, and Alfa Wassermann and Sigma-Tau instead of the recently formed Alfasigma, as summarized in Tab. 5.5., it emerges that, except for Menarini, which started foreign operations by acquiring the Spanish laboratory Puig Sala in 1965, and Sigma-Tau, which created an affiliate in Spain in 1973, all other firms began with exports through a network of either distributors or licensees; however, when it comes to the psychic distance, the results are controversial.

Chiesi started foreign operations by exporting to Eritrea and Austria in the 1940s, when Giacomo Chiesi run a laboratory that would turn into a real pharmaceutical factory later in 1955. Exports continued, and in 1979 the first office abroad was opened in Brazil. Ten years later the company launched the anti-inflammatory *Brexin* that was soon marketed in over 60 countries, which marked the beginning of a stronger international expansion in both European and non-European countries through affiliates.

A similar pattern was followed by Alfa Wassermann: with the establishment of the International Division in 1989, a network of distributors and licensees was created in over 60 countries, paving the way for subsequent acquisitions and FDI.

Slightly different is the pattern of Dompé: started as a chain of Pharmacies, whose production of galenic formulations on the basis of British standards transformed the typical work of a pharmacy into a business developed activity, with branches in England, Switzerland and Italy, the activity was converted by Franco Dompé into an industrial business by founding Dompé Farmaceutici. Then, thanks to Sergio Dompè, the company developed a dense network of alliances and partnerships with global biopharmaceutical companies, while the first subsidiary abroad was opened in 2014 in New York.

With regard to the *psychic distance,* Johanson and Vahlne (1977) postulate that differences in culture, language, education, business practices, and industrial development also affect both the time order of entry and the target country. Therefore, companies are more likely to invest in geographically and/or culturally closer countries, before embarking on internationalization projects that involve more distant countries. This seems to explain why Spain, which together with Italy, France, Portugal, and Switzerland (French-speaking areas), belongs to the Latin Europe cluster that was influenced by Roman culture, was the first country targeted by Menarini and Sigma-Tau. Furthermore, the experience accumulated in Spain could have helped Menarini to enter Central and Latin America, thanks to the historical ties that these countries have with Spain, as a consequence of which they share a common language and similar practices. Likewise, all these firms have generally expanded in more 'distant' countries such as India and China only after previously establishing affiliates throughout Europe and America. Such evidence corroborates the idea that family enterprises are more likely to choose psychically close countries when expanding globally (Harris, Martinez, & Ward, 1994) and locate their operations in close proximity to the residence of family members (Kahn & Henderson, 1992; Shaw & Young, 2001), and may also explain why Zahra

(2003) found that family influence was positively associated with international sales, but negatively associated with the number of countries that the firm sold to.[432]

However, the concept of *psychic distance* does not hold when trying to explain why, for instance, Chiesi opened an affiliate in Pakistan in 1987 and only years later in France and Spain. Obviously, there are other key factors influencing the selection of the target country, as well as the method of entry. Because these firms often opt for forms of direct investment abroad, especially mergers &acquisitions and greenfields, Dunning's OLI framework may suits their analysis better, for at least two reasons. Firstly, these firms are characterized by the ownership of patents, which are income-generating assets that only one firm possesses; secondly, being R&D costs particularly high in this specific industry, market expansion abroad is vital for pharmaceutical firms in order to recoup R&D expenses, be profitable and survive over the long period. However, due to the interconnection between the pharmaceutical industry and people's health, governments all over the world regulate this sector with policies that may consistently affect the extent to which firms perceive it to be convenient to locate value-adding activities abroad. Therefore, government policies, especially those related to IP protection and tax incentives, as well as labor costs, the presence of skilled personnel and pool of patients all constitute *location-specific advantages* that play a key role in the selection of both the target country and the entry mode. This could explain why, for instance, Chiesi choose Pakistan to open its first affiliate abroad in 1987, as the country might have offered some advantages that were not available in other'psychic closer countries at that time (ie. France or Spain), in terms of labour costs, IP protection law, government incentives and so on.

Likewise, the OLI model could also explain why FDI are common among pharmaceutical firms. Being a high capital and technology intensive industry characterized by quite high barriers to entry and high competition, the pharmaceutical sector is highly dependent upon FDI.[433]Because contracting out is risky, as it implies revealing the proprietary information (e.g. how to use the technology or the patent) to another party that could steal it and become a competitor, pharmaceutical firms tend to prefer FDIs.

If the proprietorship of innovative technologies, as well as the outcome of highly expensive R&D operations (resulting in exclusive patents) constitutes a potential ownership advantage

[432] Graves C., Thomas J. (2008). Determinants of the Internationalization Pathways of Family Firms: An Examination of Family Influence. Family Business Review, Vol. XXI, No. 2, p. 154.

[433] Mercurio B., Kim, D. (2016). Foreign Direct Investment in the Pharmaceutial Industry: Why Singapore and not Hong Kong. Asian Journal of Comparative Law, No. 10, p. 237. doi:10.1017/asjcl.2015.12

for pharma firms, which are therefore willing to replicate it in different countries internally, thus without incurring in high transaction costs, the motives behind the selection of a particular country can be disparate. The most cited taxonomy of FDI motives is the one based on the OLI model developed by Dunning (1993) that distinguishes four kinds of FDI: *resource- seeking* (to seek critical natural and human resources), *market- seeking* (exploit new markets for the firm's finished products), *efficiency-seeking* (to optimize the international allocation of the firm's international activity through international specialization and global sourcing) and *strategic asset-seeking* (to purchase existing firms and/or assets in order to sustain or advance a firm's competitive position). In the light of such classification, the acquisitions of the Invida Group by Menarini and that of Torrex by Chiesi can be defined as market-seeking, as such acquisitions allowed the two companies to gain access to the Asia-Pacific region and the Eastern European countries, respectively. Chiesi's acquisition of the biopharmaceutical firm Zymenex and the acquisition of the 'specialty care' branch of Enzon Pharmaceuticals by Sigma-Tau were instead aimed at acquiring strategic assets to augment research in the biopharma in the case of Chiesi; to expand its portfolio of products in the case of Sigma-Tau. It can also be speculated that Menarini placed manufacturing plants in Guatemala and more recently in China to advantage lower labor costs, thus making a resource-seeking investment.

As FDIs promote the economic growth of the recipient country in various ways, not only in terms of transfer of capital but also in terms of diffusion of knowledge and importation of advanced technology (so-called "technology transfer"), know-how, technological and managerial skills, as well as increased levels of employment and tax revenue, expansion of local production and exports, and enhanced local innovation capacity, countries seek to attract FDI in the pharmaceutical industry.[434]Attractive policies that strengthen patent protection and/or provide tax breaks and financial incentives play an important role in the selection of the target country.

My idea is that, although most of these firms have followed a 'traditional' pathway to internationalization, in line with the findings of Graves & Thomas (2008), being FDI common among pharmaceutical firms for their typically strong O advantages, some choices may be better explained by recurring to Dunning's OLI model: these four companies have decided to expand in countries where location-specific advantages were stronger, rather than in countries that they perceived as 'closer', while the intensity of the investment abroad, that is, the mode of entry, has been determined by a combination of both *internalization-advantages* and

[434] Ibidem

strategic motivation. The choice of culturally distant countries may also be explained by what Johanson and Vahlne (2009) defined *experiential knowledge*: companies leverage previous experience in international markets to properly manage more distant and unfamiliar external environments.

Comparing the internationalization processes of these firms with the main internationalization theories confirms that, although some observable patterns exist, it is not possible to formulate a univocal theory of internationalization, as such process is strictly related to each company's *inward growth,* which, as stated by Welch and Luostarinen (1988), comprises the internal situation of a company in terms of organizational capacity, personnel and organizational structure, all aspects that affect the method, sales objects and target markets, in other words, their *outward movement*.

Therefore, it is perhaps more useful to analyze a firm's internationalization process in relation with its governance structure in order to understand how these two factors interact.

As stated in chapter one, internationalization is a strategic decision depending on resource commitment and, as such, is influenced by the ownership type, in charge of dictating the amount of resources that are to be committed to the firm's internationalization strategy. Therefore, an efficient governance structure that is able to manage the complexities of investing abroad may actually help firms to become international (Sanders and Carpenter, 1998). In this respect, family ownership have proved to negative affect internationalization (Fernandez & Nieto, 2006), while CEO ownership has proved to lead to an even more risk-adverse behaviour (Calabrò et al., 2013), which could be explained by what Gòmez – Mejìa et al. (2011) define as *socioemotional wealth*, nonfinancial benefits that family-owners derive from the family firm, which affects managerial decisions, leading to decisions that may seem financially unprofessional, among which, the decision to appoint an unskilled or inexperienced family member as CEO. Apart from the CEO lack of skills and/or abilities, the pursuance of the firm's continuity beyond generations may prevent the CEO from taking on the risk of pursuing internationalization. Also, internationalization can be affected by family firms' difficulty to obtain the necessary financial resources and accumulate intangible resources (Fernandez & Nieto, 2005).

The results of the aforementioned studies clearly clash with evidence from the four family-owned pharmaceutical firms examined in this paper, which operate both directly and indirectly in many foreign markets worldwide. By observing the structure of their boards of directors and management team (summarized in Tab. 5.6), it emerges a constant among all

these firms: the presence of an external CEO and external managers, while the charges of Chairman and Vice-Chairman are always held by members of the founder family. Such evidence seems to confirm the new theoretical framework recently proposed by D'Angelo et al. (2016) under which a positive correlation exists between the presence of external managers and internationalization. External managers possess the critical knowledge and capabilities that family members usually lack but that are essential for developing and coordinate operations in foreign markets. To rephrase D'Angelo et al. (2016), the family possesses strong internal or *bonding* relationships with other members of the firm, but lacks external, or *bridging*, social capital which is indeed provided by external managers.

It is no coincidence that, for example, Chiesi appointed Ugo Di Francesco as CEO. His international experience gained at Novartis, Amgen, and Sigma-Tau, for which he had charges of growing responsibility, is what Chiesi needed to face the challenges of growth that the Group has set itself.

The same is true for Dompé, whose CEO Eugenio Aringhieri has been promoting the company's functional reorganization and given impetus to its industrial strategy with the aim of making the Group an internationally recognized science-based company. At the same time, he has been promoting an international approach based on the network. To this end, he joined the Board of Directors of AAA (Advanced Accelerator Applications), a leading company in the field of molecular medicine and has been a Member of the e-Novia Board of Directors, a company focused on fostering business innovation through international research projects and partnerships.

Likewise, the addition of Juerg Witmer to the Board of Directors of Menarini in 2013 (it was the first time an independent non-executive director joined the board), underlines the Menarini Group's projection towards Asia Pacific, where just over one year before it had acquired the Invida Group operating in 13 countries. As a matter of fact, during his career at Roche, Dr. Witmer had acquired valuable knowledge of the Far East markets, spending six years in Hong Kong, first as Marketing Manager and then as General Manager of China. Also, thanks to his significant international standing and vast experience in multinational companies in various sectors, including the pharmaceutical industry, he has brought a significant added value of knowledge to the company.

Another interesting aspect that these firms have in common is that their internationalization process usually starts or becomes more intense with the involvement of second or subsequent generations, in accordance with the idea that the involvement of new generation in the

ownership and/or management often stimulates and fosters internationalization (Fernández & Nieto, 2005).

An entrepreneur in the Pharmaceutical and Biotechnology industries, Sergio Dompé, representative of Dompé's fourth generation joined the company in 1976 and re-defines the strategies of the Group by investing in research and concentrating on three therapeutic areas: anti-inflammatory, osteo-articular and respiratory.

When Giacomo Chiesi handed over the management of the company to his two sons Alberto and Paolo in 1966, Chiesi Farmaceutici was a small company. Then, Alberto and Paolo started a continuous expansion and internationalization process by opening the first office abroad, in Brazil in the late seventies.

Lucia Aleotti joined Menarini as a graduate in 1991 to assist her father first and as managing director of Menarini South soon after. The early years of her work coincide with the international expansion of the Group that, after creating the French branch, acquired the Berlin-Chemie from the reunited Germany by participating in a public auction.[435]

The presence of later generations or non-family members can, therefore, reduce the risk aversion traditionally shown by many family enterprises.

However, it cannot be neglected that a number of studies found instead that later generations often take part into the family business even though they lack the skills required for a certain job. 'Nepotism', that is, the practice of favoring relatives in the business, is the main cause of the low levels of qualified staff in family firms and, although beneficial for family members, it is counterproductive for the firm (Fernández & Nieto, 2006). Graves and Thomas (2006) note that the founders' reluctance to relinquish control and the subsequent preference towards family members, make family firms less likely to hire nonfamily 'professional' managers and less likely to use formal control systems as they internationalize, thus affecting the internationalization outcome negatively. The issue of nepotism is further complicated by the *socioemotional* involvement of the family in the business, which makes it difficult for the owning family to dismiss a family member in the case of unsatisfactory performance (Gómez-Mejía et al., 2011). Apart from the fact that employing family members can lead to hiring suboptimal employees, family firms may find it difficult to attract highly qualified managers,

[435] Repubblica (2012). Lucia Aleotti dai farmaci a Mps. Menarini va in Banca ma non in Borsa. http://www.repubblica.it/economia/finanza/2012/04/02/news/lucia_aleotti_dai_farmaci_a_mps_menarini_va_in_banca_ma_non_in_borsa-32643258/

as they tend to avoid these firms due to exclusive succession, limited prospects of professional growth and lack of perceived professionalism.[436]

Yet, the idea that the managerial capabilities of family businesses lag behind that of non-family businesses, thus affecting performance and internationalization, does not suit the cases of the firms analyzed in this paper. The involvement of new generations has boosted the internationalization of these firms. One reason is that later generations are expected to be more qualified, better prepared and thus able to bring new strategic ideas that build on the underlying competencies developed for earlier strategies.[437] Another reason is that the potential for the early involvement of children in the family firm can produce deeper levels of firm-specific tacit knowledge.[438] Through direct exposure and experience, later generations acquire important notions and may decide to specialize in performing a particular job within the firm.

This consideration also supports the idea that when family members possess the necessary skills, the business benefits of their involvement in the management. Taking Chiesi as an example, it can be noted that the appointment of Andrea Chiesi as R&D manager have had a positive impact on innovation. As a matter of fact, the company is reinvesting an increasing amount of its turnover in research and development of new products.

To summarize, the involvement of family members in the business can be both positive and negative. Family members can be an asset as employees, as they are more loyal and willing to work for nothing if necessary, and later generations can be a new engine for firm's growth, but when relatives lack the necessary skills, blind nepotism can lead to disastrous consequences for firm's performance. However, families that are able to acquire the necessary resources externally are more likely to succeed and undertake sound business practices.

In conclusion, studies focused on the internationalization process of family firms have led to conflicting results: some have demonstrated that family ownership negatively impacts on internationalization (Fernandez & Nieto), while others have instead proved the opposite (Zahra, 2003). Others have shifted the focus on the *degree* of family involvement (Sciascia et al., 2010; D'Angelo et al., 2016), concluding that it is not family ownership itself to affect

[436] Sirmon D. G., Hitt M. A. (2003). Managing Resources: Linking Unique Resources, Management, and Wealth Creation in Family Firms. Entrepreneurship Theory and Practice, Vol. 27, No. 4, p. 342.
[437] Fernàndez Z., Nieto M. J. (2005). Internationalization Strategy of Small and Medium-Sized Family Business: Some Influential Factors. Family Business Review, Vol. XVIII, No. 1, p. 79.
[438] Sirmon D. G., Hitt M. A. (2003). Managing Resources: Linking Unique Resources, Management, and Wealth Creation in Family Firms. Entrepreneurship Theory and Practice, Vol. 27, No. 4, p. 342.

internationalization, but an excessive family ownership concentration that interfere with internationalization and mitigates the positive effect of external managers.

D'Angelo et al. (2016), in particular, argue that the preservation of *socioeconomic wealth* may become the primary goal and interferes negatively with the scope of internationalization. However, my opinion is that socioemotional wealth theory is also able to explain why the four pharmaceutical enterprises considered in this paper show high levels of internationalization. An empirical study on 1,237 family-owned olive oil mills in Southern Spain by Gómez-Mejía et al. (2007) challenged the prevalent notion that family-owned firms are more risk averse than non-family firms, concluding that family firms can be both risk willing and risk averse at the same time, and that risk willingness or aversion is motivated by the preservation of the so-called *socioemotional wealth*, which involves all those affect-related values that an owning family derives from its family business. Internationalization is an important aspect of the pharmaceutical industry, which allows pharmaceutical companies to obviate the limited size of national markets, as well as recover the huge investments in R&D operations. Additionally, being health problems and needs basically the same all over the world, an innovative product could be possibly sold in every market. Motivated by the willingness to guarantee long-term survival of the firm in order to pass it down to subsequent generations, family-owned pharmaceutical firms may be willing to accept the risks of internationalizing. In this light, although hazardous, internationalization enables to preserve, or even enhance, a firm's socioemotional wealth. Therefore, as part of a firm's SEW, the firm's long-term commitment translates into a stronger commitment to development and differentiation, contributing to international success (Gallo and Sven, 1991). Yet, Gómez-Mejía et al. (2007) distinguish between two types of risk: *performance hazard,* which concerns the potential for negative consequences associated with a strategic choice, in terms of either the probability of failure or the possibility of below-target performance (where the target for comparison may be the firm's past performance or other firms' performance), and *venturing risk*, that is the search for alternative opportunities when the firm is unhappy with its status quo, which causes variance in the performance. Supported by empirical findings, they conclude that family firms may be more reluctant to incur venturing risks, as they increase performance variability, and therefore further increase the firm's probability of failure, but may be willing to incur the risk of greater performance hazard in order to preserve their socioemotional wealth.[439]

[439] Gómez-Mejía L. R. et al. (2007). Socioemotional Wealth and Business Risks in Family-controlled Firms: Evidence from Spanish Olive Oil Mills. Administrative Science Quarterly, No. 52, pp. 106-107.

There is empirical evidence of such dual attitude towards risk in the analysis of the four Italian pharmaceutical family firms. On one hand, these firms show high levels of internationalization, thus betraying traditional literature that depicts family firms as risk adverse and less prone to internationalize; on the other hand, they try to limit the risks related to international expansion by excluding or limiting operations in those countries that are perceived as *too* risky, though they offer tremendous growth opportunities. Emerging countries like China and India are an example: by looking at the internationalization patterns of the four pharmaceutical firms, it emerges that they all started operations in China much later than in other countries, showing that expansion in this market is considered only once the firm has reached a certain size and international reach, thus becoming able to spread the risks. This last hypothesis could then explain why firms like Dompé are still ignoring the sustained double-digit growth of the Chinese pharmaceutical market and why the first approach to this market for Chiesi, Alfasigma and Menarini was via exports. Likewise, for both Chiesi and Menarini the shift to a more capital-intense form of investment was preceded by a phase of accumulation of market knowledge.

Based on previous considerations, it is possible to conclude that family firms do internationalize and take on risks, especially if they operate in a highly globalized industry which requires international presence in order to build and sustain competitive advantage, but, because of the limited resources available and their emotional attachment to the business (in the name of which they take a long-term perspective), these firms try to limit the risks of investing abroad by selecting countries in which investments are perceived to be safer first, while approaching riskier markets like the Chinese one later on.

Tab. 5.5 The internationalization process of Menarini, Chiesi, Alfa Wasserman, Sigma-Tau and Dompé

Year	Menarini	Year	Chiesi	Year	Alfa Wasserman	Year	Sigma-Tau	Year	Dompé
1965	Laboratorios Menarini in Barcelon	1940s	Exports to Eritrea and Austria	1989	The International Division was established and a network of distributors and licensees was created in over 60 countries in the world.	1973	Affiliate in Spain	1858-1940	Gian Antonio Dompé and from 1898 his son Onorato establish a chain of Italo-English Pharmacies in Italy, England and Switzerland, on the basis of British standards
1977	First co-operations with major multinationals	Late 1970s	First office abroad in Brazil			1974	Affiliate in France, Sigma-Tau S.a.r.l.		
1982	First affiliate in Central America	1987	Affiliate in Pakistan	1998	Alfa Wassermann Inc. in the USA	1984	Sigma-Tau Pharma AG in Swutzerland	1988	Dompé Biotec, reference centre for innovation in Italy and Europe is founded to market drugs developed in the USA. Dompé starts building parterships andinternational alliances
1992	Acquisition of Berlin-Chemie starts expansion into Centre and Eastern Europe	1992	First European affiliate in France	2003	Acquisition of two companies in the Iberian peninsula: Bama-Geve S.L. in Barcelon (Spain) and Biosaúde-Produtos Farmacêuticos Lda in Lisbon (Portugal)	1986	Sigma-Tau BV in the Netherlands to commercializes OTC and ethical products in Belgium and The Netherlands		
1992	Menarini France	1995	Affiliate in Spain						
1994	Partnership agreement with Raunaq Industries to enter India	1998	Affiliate in Greece	2004	Affiliate in Tunisia and Polska	1994	Sigma-Tau GmBG in Germany to supply the German and Austrian markets	2005	Jv with Biogen Idec gives birth to Biogen Dompé in Italy and Switzerland
2001	Affiliate in Argentina	1999	Acquisition of Trinity Pharmaceuticals in the UK	2007	Affiliate in Romania	1998	Incorporation of Sigma-Tau Health Science Srl	2008	Creation of the Jv Amgen Dompé (concluded in 2014)
2001	Acquisition of IE Ulagay to access Turkey	2001	Acquisition of Torrex in Austria gaining access also to Eastern Europe countries. (Slovenia, , Hungary, Czech Republic and the CEE region)	2008	Affiliate in Russia	2005	Incorporation of Sigma-Tau Ltd. In the UK	2014	Subsidiary in New York to strengthen presence in the USA and coordinate R&D of new drugs.
2005	Partnership with Invida Group for accessing Asia-Pacific markets			2010	Acquisition of Laboratoires Iprad in France				
				2011	Affiliate in Mexico	2007	Incorporation of Sigma-Tau Research Switzerland SA located in Mendrisio (CH).	2015	First two branch offices within Europe, in Tirana and Barcelona

-continue-

Year	Menarini	Year	Chiesi	Year	Sigma-Tau
2008	Menarini Mexico	2002	Took over of the Asche AG in Germany.	2007	The Group lands in the Chinese market and becomes a majority shareholder (29.9%) of Lee's Pharmaceutical Holdings Ltd based in Hong Kong.
2010	Distribution in Australia starts	2007	Chiesi Turkey and Torrex Chiesi Bulgaria Ltd. Are registered	2008	Incorporation of Sigma-Tau India Private Ltd.
2010	Agreement for building a production site in Russia	2008	Chiesi Pharmaceuticals (Shanghai) Co. Ltd. started up	2009	Incorporation of Sigma-Tau Pharma Belgium SPRL based in Brussels.
2011	Acquisition of the Invida Group in Asia	2009	Asche Chiesi GmbH in Germany is renamed Chiesi GmbH	2010	Acquisition of the "specialty care" business of Enzon Pharmaceuticals, whose manufacturing plant in Indianapolis (currently Sigma-Tau Pharma Source Inc.) is taken over by Sigma-Tau Pharmaceuticals Inc., its distributor for the US.
2013	Manufacturing plant and a headquarter in China		Strategic alliance with Cornerstone Therapeutics in the USA		
		2010	Chiesi Belgium		
		2013	Acquisition of the Danish biopharmaceutical company Zymenex		
		2015	Chiesi Nordics is born, aggregating Denmark, Finland, Norway and Sweden. New organizational model of the Regions (Europe, Emerging, USA)		

Tab. 5.6 Governance composition of Menarini, Chiesi, Alfasigma and Dompé as of 2017

	Menarini	**Chiesi**	**Alfasigma**	**Dompé**
Board of Directors	Lucia Aleotti Chairman	Alberto Chiesi President	Marino Golinelli (founder of Alfa Wassermann) Honorary President	Sergio Dompé Chairman
	Alberto Giovanni Aleotti Vice Chairman	Paolo Chiesi Vice- President	Andrea Golinelli Vice President with special assignment on Innovation	Eugenio Aringhieri CEO
	Domenico Simone Board Member	Alessandro Chiesi	Stefano Golinelli Chairman	
	Juerg Witmer Board Member	Andrea Chiesi	Giampaolo Girotti CEO	
		Maria Paola Chiesi		
		Giacomo Chiesi		
		Ugo di Francesco CEO		
Management	Pietro Giovanni Corsa General Manager	Paolo Chiesi Vice-President and Head of R&D	n/a	Marcello Allegretti Chief Scientific Officer
	Pio Mei General Manager	Alessandro Chiesi Head of Region Europe		Giuseppe Andreano Chief Financial Officer
	Thierry Poiraud New Product Portfolio Development Strategy Department Director	Andrea Chiesi Head of R&D Portfolio Management		Valentino Confalone Head of Europe Biotech
	Stefano Pieri Corporate Director Licensing and Business Development	Maria Paola Chiesi Head of CSR		Carmen Di Marino Chief Legal Officer
		Giacomo Chiesi Head of Global Business Development		Davide Polimeni Head of Primary Care
		Giacomo Chiesi Business Development Executive, Region US		Alessandro Protti Chief Human Resources Officer

- continue-

		Ugo Bettini Head of Group Human Resources and Organization		
		Andrea Bizzi Head of Corporate Marketing		
		Thomas Gauch Head of Strategic Planning		
		Antonio Magnelli Head of Global Manufacturing Division		
		Ken McBean General Manager Chiesi USA, Inc.		
		Mark Parry-Billings Head of Corporate Drug Development		
		Danilo Piroli Head of Corporate Finance		
		Cosimo Pulli Head of Region Emerging Countries and IMDD		
		Marco Vecchia Head of Legal and Corporate Affairs		

3. Investment prospects for family firms in the Chinese market

Although progressive market liberalization and improvements in both the business and the regulatory environment are encouraging for foreign investors, mainly attracted by China's market size, starting operations in China is still challenging. As a matter of fact, being China the second pharmaceutical market in the world, on the surface, its pharmaceutical industry may appear very attractive, and China may seem to be a vast market with a strong central government and strong growth opportunities. However, as shown in previous chapters, China is a conglomerate of disparate markets that vary in their levels of economic and social development—from modern municipalities like Shanghai and Beijing, where officials are used to dealing with foreign investors, to the less-developed western provinces. Though the central government has been taking steps to improve overall business operating conditions by instituting a stronger rule of law, building a more modern financial system, and creating a more transparent business environment—especially since China joined the World Trade Organization (WTO) in 2001—development and implementation remain uneven across the country.[440] A high degree of fragmentation at both policy and industrial level brings inefficiencies, delays in drug registration approvals, quality-related issues, as well as the risks related to corruption and low enforcement of the recently amended IP protection law, thus providing foreign firms with enormous business opportunities but also with enormous risks.

Operating in a highly globalized industry and faced with economic stagnation in the domestic market and high competition, Italian pharmaceutical firms have seized the opportunities offered by international markets. Some of them, including Menarini, Chiesi, and Alfasigma, have already committed to the Chinese market. However, some intrinsic characteristics of the family firm – long-term commitment, scarce financial resources, unwillingness to lose control over operations, closeness to external investors etc. – may hinder the internationalization process in a unique and complicated country like China. In this section, the way in which a company's 'familiness' may either facilitate or restrain expansion in the Chinese pharmaceutical market will be discussed.

Dealing with the complex regulatory environment is one of the main issues to deal with in China. Although many sectors of China's economy have become more market oriented, numerous restrictions and a massive bureaucracy still hinder full implementation of regulations and make the approval process unpredictable. Moreover, the interpretation of PRC regulations tends to vary from place to place, and, in some cases, several authorities or departments are responsible for implementing the same regulations.

[440] China Business Review (2006). Managing Business Risks.
https://www.chinabusinessreview.com/managing-business-risks/

From the analysis of the Chinese pharmaceutical market and regulatory environment developed in chapter 2 and 3, a number of complexities emerge. Above all, the involvement of a high number of ministries in charge of healthcare and drug-related administrative activities as well as regulatory fragmentation at both central level and between the central and provincial governments are responsible for uncertainty and delays in drug approvals, quality standards, pricing and reimbursement, creating a climate that can be difficult for foreign firms to deal with. Two typical examples are drug registration, for which lengthy clinical trials might be required, causing additional costs for the company; and tendering, the primary mechanism by which companies sell a drug within a province, which is carried out separately and with different criteria by each of China's provinces. Dealing with all the relevant authorities takes time and often translates into additional costs that make the cost of doing business in China higher than expected.

Perri et al. (2013) argue that cultural distance between a firm's home and host country affects the occurrence of the so-called *hidden costs*, i.e. "*unanticipated costs of implementation*" that arise from inappropriate estimates of challenges and opportunities as a consequence of an information asymmetry that influences the performance of foreign market entry.[441] Given their limited size, and the scarcity of resources due to their reluctance to access capital from external sources, family firms may find it difficult to develop the necessary overseas networks that facilitate the identification of opportunities (Kontinen and Ojala, 2011). Fascinated by prospects of large, growing markets and high revenue opportunities the risk is to underestimate the real costs of accessing the Chinese pharmaceutical market. Nevertheless, the leverage of experience knowledge accumulated on international markets and the building of relationships with local partners such as suppliers, distributors, and institutions, can speed up the process of local market knowledge accumulation,[442]thus allowing them to deal with such a complex environment.

Chiesi, for instance, started distributing Curosurf with the help of a local partner. Also, thanks to a JV with a local partner, whose team negotiated provincial biddings, two of its drugs were listed in 274 hospitals. Furthermore, by participating in all major congresses and by strengthening its presence on the territory, the Group maintains relations with local authorities.

However, finding the right partner may not be easy for at least two reasons. Firstly, the concept of business ethics is still fairly new in China, therefore fraud, corruption, nepotism, and other unethical behavior should be avoided by performing due diligence on partners, vendors and investment targets. [443] Secondly, many financial, human resources, procurement, and subcontracting

[441] Perri et al. (2013). The hidden costs of going global: insights from firm's entry into foreign markets. Università Ca' Foscari, Venezia, Department of Management, Working Paper Series, No. 26, p. 2.
[442] Ibidem
[443] China Business Review (2006). Managing Business Risks.
https://www.chinabusinessreview.com/managing-business-risks/

transactions in China lack transparency and documentation, which makes it difficult to determine what information is accurate and what is exaggerated or even false.[444]

In addition, a single partner is not sufficient in a country that not only is huge but also characterized by a highly fragmented pharmaceutical market with a low concentration that counts thousands of manufacturers as well as pharmaceutical distributors.

As pharmaceutical products heavy rely on the protection of intellectual property rights, this is another critical aspect that these firms have to face. The Chinese environment for IP protection is complicated, especially for SMEs, which may lack the ability to regularly monitor suppliers, distribution networks and the marketplace. Despite recent improvements of the Patent Law, concerns still exist regarding the proliferation of counterfeit drugs and the unauthorized disclosure of undisclosed test or other data generated to obtain marketing approval for pharmaceutical products.[445]

According to the PwC's bi-annual global survey of 2,800 family businesses in 50 countries titled "*The 'Missing Middle': Bridging the strategy gap in family firms (2016)",* family businesses' growth outlook could be curtailed by the organisation's own lack of long-term strategic planning rather than economic factors or other external concerns, meaning that basically, family firms are having to navigate the same challenges of megatrends and intense competition in the marketplace that non-family businesses are having to navigate in order to ensure their competitiveness, relevance, and sustainability,[446]thus confirming that the main obstacles for these firms are related to their internal resources and capabilities rather than to the outside business environment (Kontinen and Ojala, 2010).

Although family firms may be at a disadvantage, when compared to non-family MNCs in terms of knowledge of international markets, assets and financial resources, international networks, professional management team with international experience, entry barriers in foreign countries (due to the inability to reach economies of scale in production and purchasing economies), however, they can advantage of a number of strengths. First of all, family firms have a general long-term orientation and are characterized by quick decision making, which stems from the stable exchanges of knowledge and experiences among family members involved in the business. Long-term commitment translates into a 'patient capital' that favors the creation of value over years rather than quarters, which means that these firms are more likely to internationalize in the long term, notwithstanding poor short term results. Indeed, 72% of the family firms surveyed by PwC, listed

[444] Ibidem

[445] Regulatory Affairs Professional Society (2016). USTR: 97% of Counterfeit Drugs in US Shipped from Four Countries. http://www.raps.org/regulatoryDetail.aspx?id=24854

[446] PWC (2016). 2016 Family Business Survey – The 'missing middle': Bridging the strategy gap in family firms. http://www.pwc.com/fambizsurvey2016

the different ways of measuring success beyond profit and growth among their main differentiating factors. Likewise, 55% say they take a longer-term perspective on decision-making, and 71% say they make those decisions faster than their peers.[447] Furthermore, family firms that are likely to be more successful in the international expansion are those capable of innovating and using information technology (Kontinen and Ojala, 2010).

De Chiara &Minguzzi (2002) sustain that a firm's international competitiveness is not related to its size, even if it admits that small firms have to struggle more because of their structural handicaps, but it depends on the capabilities of the management team and on the competitive and comparative advantages that the company has.

The four cases of Italian family-owned pharmaceutical firms analyzed in this chapter clearly demonstrate that family firms can be highly innovative, highly internationalized and even successful in a complex, culturally different, emerging economies like China.

Considering previous considerations regarding the Chinese pharmaceutical market and the features attributed to family firms, the following investment proposals can be formulated for family firms that are willing to approach the booming yet risky Chinese pharmaceutical market:

- Make the sufficient financial resources available. gain experience from 'closer' international markets first
- Ensure the appropriate management capabilities are developed, otherwise 'professionalize' the management team: have at least one person from the staff entirely dedicated to the internationalization process to China. Hiring an external manager with previous experience in the country is fundamental for dealing with the complex regulatory environment and for building relationships with local partners and local authorities to access information about the market and accelerate the learning process.
- Identify trustworthy partners in different regions by performing due diligence or having someone who can help dealing with local contacts, i.e. a consulting group with experience in the country.
- Invest in 'patient capital': good relationships (guanxi 关系) with Chinese partners and the local authorities is a key to success in China. However, developing such relationships can be time-consuming and resource intensive and requires frequent contacts with the Chinese counterparts and long-term commitment.
- China is transforming into a more innovation-friendly and innovation-driven country. Therefore, the export of an innovative drug to China or investments in joint R&D projects with local partners can facilitate market entry and market penetration.

[447] Ibidem

Being the factors that restrain the internationalization of family firms mainly internal, the owners of family businesses have to provide stewardship for the business, by becoming more open to global trends and outside advisors, by adapting to innovations and best practices and by diversifying the business. It should be used to identify skills gaps and where outside professional talent might be needed to grow the business.

With sustained double-digit growth, the Chinese pharmaceutical market, first in the world for market size and second for pharmaceutical sales, offers a wide range of opportunities to foreign companies. Although family firms may be at a disadvantage compared to their non-family counterparts, as investments in China might be more expensive and riskier for these firms due to their limited financial resources and international networks, an accurate strategic planning and the involvement of experienced managers can help the firm to develop the business in China.

It is not possible to formulate a univocal strategy to access the Chinese pharmaceutical market, as investment opportunities vary according to the therapy areas, as well as the resources available and the strategic objective that firms want to pursue abroad. However, by looking at the internationalization path of Menarini, Chiesi, Alfasigma, and Dompé, family firms operating in the pharmaceutical industry can learn an important lesson: in the name of the long-term preservation of the *socioemotional wealth*, the 'familiness' embedded within the business can foster innovation and international expansion, but it is only when 'familiness'meets managerial expertise that success can be achieved. Additionally, from the discussions presented in previous section, it emerged that, of the aforementioned firms, those that have expanded in China (Menarini, Chiesi, and Alfasigma) have done so gradually, and only after having established themselves in both the domestic and in what they perceived as 'safer' foreign countries, suggesting that the challenges posed by particularly complex and risky markets like China should be taken on once the firm has secured its position in other markets and is, therefore, able to spread the risks and face the potential 'hidden costs' of doing business in China.

Conclusions

This paper has been developed around two main themes: the Chinese pharmaceutical industry and the internationalization of family firms. The aim was to understand the internationalization behavior of family firms and to make some investment proposals for their expansion into the Chinese pharmaceutical market. To do so, the internationalization patterns of four Italian leading pharmaceutical firms were analyzed and compared with existing theories of family firms.

From such comparison the following conclusions can be drawn: on one hand, these firms seem to follow the incremental pattern proposed in the Uppsala Model: they internationalize sequentially and usually starting from a geographically or culturally close country, unless they can leverage specific advantages (as those proposed in Dunning's OLI model) that justify early investments in more distant countries; on the other hand, they betray traditional literature that depicts family firms as risk adverse and thus less inclined to internationalize than non-family firms. In fact, all the firms analyzed in this paper are characterized by high levels of innovation and presence in foreign markets. Yet, the fact that the firms that have expanded in China (Menarini, Chiesi, and Alfasigma) have done so gradually, and only after having established themselves in both the domestic and in what they perceived as 'safer' foreign countries, suggests that, although family firms do internationalize and are therefore willing to take on risks, they try to limit such risks by excluding operations in those countries that are perceived as too risky, notwithstanding the growth opportunities these countries could offer. Also, the results achieved by these firms abroad can be associated with the presence of external CEOs and skilled managers, and in all cases the internationalization process was started or intensified with the entry on the scene of new generations, proving that when family members are skilled and committed to the firm, family involvement can be beneficial for the business.

In addition, there is an industry-related consideration to be made. The pharmaceutical industry is a complex and unique industry, characterized by massive State intervention, huge R&D expenditure and a high degree of internationalization. Market expansion is vital for pharmaceutical companies to recoup the huge investments in R&D operation and obviate to the limited size of the domestic market. Therefore, the industry in which these firms operate plays an important role because it pushes for the development of innovative drugs which, being health problems basically the same worldwide, could potentially be sold everywhere.

China became the world's second pharmaceutical market in 2015. With its enormous population and the lack of safe, efficient and high-quality domestic treatments, the country offers tremendous growth opportunities to foreign companies, especially now that it is experiencing an epidemiologic

transition due to an aging population, rapid urbanization, changes in lifestyles and environmental issues. Faced with patent expiration, pipeline drought, slow growth and reduced revenues in developed countries, pharmaceutical companies consider the so-called 'pharmerging countries' a new engine for growth.

Though promising, the pharmaceutical market in China is fraught with risks that can be disastrous for firms that usually have limited financial resources and lack market knowledge necessary to operate in such a complex environment. Nevertheless, it is still possible for these firms to access the market. The key to success is the right combination of 'familiness' - in terms of long-term commitment, patient capital, low information asymmetry and quick decision making – and managerial expertise.

China offers a wide range of opportunities in the pharmaceutical field, from exports to contract manufacturing and contract research, from JVs with local partners to wholly owned subsidiaries. Furthermore, under Government incentives, the country is preparing for a radical shift from a low-end manufacturing, export- oriented, to an innovation-driven, consumption-oriented country. However, lack of transparency, high territorial and industrial fragmentation, low IP enforcement could put profitability at a stake. The development of a precise strategic plan, that involves partnering with local players and appointing a professionalized management team have made the difference for firms like Menarini, Chiesi, Alfasigma, and Dompé and can still make the difference for family firms.

In the light of such conclusions, *socioemotional wealth theory* appears to be the theory that best suits the interpretation of the relationship between family firms and internationalization. The emotional attachment of family members to the business is the very distinctive feature of these firms, in which the business and the private sphere often overlap. Being rooted in and empirically tested on family firms, it accounts for all those non-financial aspects that permeate and affect the business both positively and negatively, ie. the willingness to pass on the business to future generations and involve family members even though unskilled, the ambivalence towards risk, the willingness to retain control even when it means closeness to external finance and external expertise and so on.

Theories borrowed to explain family firms such as the Agency Theory and the Resource Based View Theory can only partially explain the phenomenon and are often limited to defining what are the characteristics that make family firms differ from non-family firms. Also, when tested on family firms, such theories have led to conflicting results. The socioemotional wealth perspective, instead,

is a new theory generated by using unique family business findings. It accounts for the *nonlinear* effects of family ownership and considers the evolution of the firm across family stages.

The fact that family- owners seek utility in the form of preserving socioemotional wealth generated by the noneconomic aspects of family businesses is at the roots of the dissimilarities between family and non-family firms. As a matter of fact, while executives in non-family firms are mainly concerned with financial factors, family firms are less driven by prospects that are financially lucrative but threaten socioemotional wealth. Conversely, they are likely to incur performance hazard, thus taking on large financial risks if it protects, enhances or prevents extensive losses of the firm's socioemotional wealth. As a consequence, the desire to preserve SEW affects both strategic decision-making and organization governance.

Depending on how outcomes are perceived to affect socioemotional wealth, family firms can be risk willing or risk adverse, but are generally less likely to diversify, as diversification often means seeking to finance via debt financing or equity participation, which either reduces family control over the firm and diminishes family's socioemotional wealth.[448]

Likewise, the preservation of socioemotional wealth affects the composition of boards of directors of family firms, in the sense that family firms might, for instance, prefer projects that are financially less optimal or hire family members irrespective of their abilities because these decisions might provide other benefits to the family firm, such as improving its reputation or retaining more devoted employees.[449]

This does not exclude that, as the firm grows and new generations and/or external managers/investors enter the business, the firm may behave more similarly to a non-family firm. Indeed, SEW perspective purports that:

> "personal attachment to the firm, self-identification with the firm, the "utility generated by the ability to exercise authority" (Schulze, Lubatkin, and Dino, 2003a: 182), social capital and such—socioemotional wealth—should be stronger in the founding-family-controlled and managed firms (stage one) and that it should be relatively lower as the firm moves into later stages, namely, ownership and management by non-founding extended family (stage two) and ownership by extended family members who are not involved in the firm's management (stage three). Hence, independent of financial considerations, losses in socioemotional wealth should weigh less heavily on a family firm's willingness to give up control as it moves from stage one through stage three."[450]

[448] Kalm M., Gómez-Mejía L. R. (2016). Socioemotional Wealth Preservation in Family Firms. Revista de Aministração, Vol. 51, p. 410.
[449] Ibidem, p. 411.
[450] Gómez-Mejía L. R. et al. (2007). Socioemotional Wealth and Business Risks in Family-controlled Firms: Evidence from Spanish Olive Oil Mills. Administrative Science Quarterly, No. 52, p. 109.

Putting SEW theory and industry-related considerations together, it is, therefore, possible to explain the choices of the four family firms operating in the pharmaceutical industry on which this paper is based. Also, the positive relationship between external managers and/or external investors and internationalization is confirmed and explained as a consequence of the attenuation of the importance to preserve SEW.

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