

L.Fratocchi, A. Onetti, A. Pisoni, M. Talaia

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Università degli Studi dell'Insubria

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LOCATION OF VALUE ADDED ACTIVITIES IN HI-TECH INDUSTRIES. THE CASE OF PHARMA-BIOTECH FIRMS IN ITALY*

Luciano Fratocchi, Alberto Onetti, Alessia Pisoni, Marco Talaia

This paper aims at analysing the main features of the activities carried out by the Italian biotech industry. This topic is so wide and various that particularly we decided to focus on the value added activities of the so-called “pharma-biotech”, i.e. pharmaceutical firms that have diversified in the biotech business or pharmaceutical spin-offs. First of all we try to identify the main activities carried out by the studied companies. Particularly, we focus on R&D carried out on biotech, trying to measure its extent both in terms of employees involved and of percentage of total investments. Moreover, we provide a picture of the range of R&D activities performed and the contribution arising from the cooperation with actors in and out of the industry. It is worth pointing out the exploratory scope of this paper that at the present is not yet able to provide through managerial guidelines for decision makers. With this respect, the sample is composed of companies operating in Italy in specific business within the biotech industry. More specifically, in order to reach earlier presented goals, attention was paid on the so called red biotech segment, that is biotech companies which develop drugs and diagnostics. This segment - which is predominant at worldwide level - was further divided accordingly to the adopted business model: born-biotech companies (more focused on R&D activities) and pharma-biotech companies (generally operating also manufacturing and sales activities). The research interest was finally focused on the latter segment, which was divided among pharma-oriented and biotech-oriented companies.

The paper is structured in four main sections. In the first one, the most relevant features of biotech firms are discussed on the base of a literature review. In the second paragraph, adopted methodology is presented and sample main characteristics are discussed. In the third section, the main results regarding the localization of R&D activities study carried out on the biotech activities in Italy are presented. The conclusions complete the paper.

Keywords: Biotech, Localization, R&D, MNCs, Value added activities.

Alberto Onetti, Associate Professor, Department of Economics – University of Insubria, Via Monte Generoso, 71 - 21100 Varese VA, Italy, e-mail: aconetti@eco.uninsubria.it

Luciano Fratocchi, Associate Professor, Department of Mechanical Thermal and Managerial Engineering – University of L’Aquila-Località Monteluco di Roio 67040 L’Aquila AQ, Italy, e-mail: Luciano.fratocchi@ing.univaq.it

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Alessia Pisoni, PhD Candidate, Department of Economics – University of Insubria, Via Monte Generoso, 71 - 21100 Varese VA, Italy, e-mail: apisoni@eco.uninsubria.it

Marco Talaia, Research Fellow, Department of Economics – University of Insubria, Via Monte Generoso, 71 - 21100 Varese VA, Italy, e-mail: mtalaia@eco.uninsubria.it

1. INTRODUCTION

The proposed contribution can be ascribed to the huge stream of research related to the reconfiguration of the value chain activities at the international level. Such a topic has become more and more actual because of both the markets globalisation and diffusion of networked architectures within internationalised companies (see, among others, Bartlett 1983, 1984, 1986; Bartlett & Goshal 1986, 1987, 1989, 1990; Bartlett, Doz & Hedlund 1990; Forsgren 1989, 1990, 1993; Forsgren & Holm 1993; Forsgren, Holm & Johanson 1990, 1991, 1992, 1994; Forsgren & Johanson 1992; Forsgren & Pedersen 1996, 1998; Forsgren, Holm & Thilenius 1993; Hedlund 1979, 1980, 1981, 1984, 1986, 1994; Hedlund & Aman 1984; Hedlund & Ridderstrale 1994a, 1994b; Hedlund & Rolander 1990; Lipparini & Fratocchi 1999).

Within such a stream of research, we decided to focus the attention on the biotech industry, due to its specific features, that deeply influence both the strategic behaviour of firms and the economic environment of the countries where they operate.

First of all, the investigated sector is characterized by a high content of technological innovation (being R&D expenditure generally more than 30% of total sales). With this respect, the recent study of Hopkins & al. (2007), according to which the biotech revolution would be simply a “myth”, seems to be a little exaggerated in its conclusions, since it does not consider the huge amount of research projects actually still in their development earlier stages. The high-tech nature of the investigated industry, in turn, leads to a competition essentially based on “intensive knowledge” (Pavitt 1984). Consequently, enterprises definitively benefit of particularly qualified human resources that strictly depend on a high level university system. With this respect, JunKunc (2007) had recently demonstrated that the radical increase of the importance of specialized knowledge in such an industry dramatically impacts on the possibility to include secondary shares in biotech-related IPOs.

Moreover, (public and private) research centres and health care providers represent strategic partners as well. As a consequence, co-localization and agglomeration in geographical clusters (such as the Cambridge area, Bio-Vallée, and Medicon Valley) typically characterize the biotech industry (see, among others, Mytelka & Farinelli 2000). With this respect, Chiaroni & Chiesa (2006) recently proposed a taxonomy of biotech clusters based on how they have emerged. More specifically, they describe three main typologies:

- a) spontaneous clusters, which emerge from the concentration of specific conditions (e.g., the presence of an excellent scientific base and/or of an entrepreneurial culture), such as in the case of Cambridge area;
- b) policy-driven clusters, which directly originate from policy makers action: with this respect, authors make a distinction among policies related to an industry/firm restructuring (such as in the case of Uppsala, in Sweden) and those specifically devoted to the biotech development (such as in the case of France or Germany).

With this respect, it is worth noting that the relevance of “national systems” for the integration of technological progress with public interest is largely recognized, since, at least, Bartolomew (1997);

c) hybrid clusters, such as in the case of Milan (Italy) and San Diego (USA).

Furthermore, the huge level of technological innovation implies substantial investments, which, in turn, call for enormous financial resources. A recent work (Pisano 2006) shows that nowadays in the biotechnology industry very few companies are able to make a profit. Therefore, the access to capital (mainly equity) represents a basic factor, especially for start up companies. The presence in loco of seed and venture capitalists such as private equity firms can boost the development of the biotech sector.

Another characterizing element of biotech firms is the “metasectorial” nature of such business, emerging from the convergence of differentiated industries, such as pharmaceuticals, chemicals (and more specifically the combinatory one), information and communication technology (as clearly showed by the so-called bioinformatics firms), human and veterinary medicine, food processing. This convergent nature implies the simultaneous presence in the sector of very differentiated economic players, coming from different competitive fields. At the same time, biotechnology platforms can be applied in different market contexts; with this respect, it is generally accepted the idea to classify biotech firms along the following segments: “red” (pharmaceutical and diagnostic business), “green” (agriculture, zootechnics and veterinary medicine), “white” (industrial and environmental field) and “bioinformatics”.

Due to dispersion of such various sources of knowledge and application fields all over the world, biotech firms are diffused in several territorial contexts. This because the knowledge necessary for the construction of a sustainable competitive advantage are scattered in a plethora of geographic areas (Cookson 2005), which need to be contemporarily garrisoned (the so called “meta-national” business approach quoted by Doz, Santos & Williamson (2002)). Those evidences explicitly induce to adopt new theoretical frameworks to investigate such a business. With this respect, Madhok & Osegowitsch (2000), proposed the adoption of a dynamic capabilities and technology accumulation perspective for investigating the biotech industry. More recently Mathews & Zander (2007) advanced the idea of linking the internationalisation and entrepreneurial perspectives.

An additional relevant element characterizing biotech companies is their “born global” nature (Melén, Rovira & Sharma 2004; Gurău & Ranchhod 2005). With this term we refer to the fact that the competition patterns in biotech field are necessarily global, being multi-domestic strategies (Porter 1986) absolutely impracticable. As a consequence, heterogeneous players populate the biotech sector. On the one hand, there are born biotech firms facing the global competition since the beginning of their own existence; on the other hand, there are MNCs that entered in biotech industry carrying out diversification processes from their main field of activity (for instance, those coming from the pharmaceutical industry). Even if the latter are generally global player, they have to face a change in their internationalisation strategies. With this respect, we totally agree with Knight & Cavusgil (2004) when they state that born-global firms lever up a distinctive (with respect to multinational companies) mix of strategies that permit them to succeed at the world level.

On the basis of what previously discussed, it appears worth to thoroughly investigate the biotech sector in Italy. In order to do that, we decided to focus our attention on the

value added activities. In order to define them, it is necessary to take into debt account the specificities of new drug creation process. This process may be divided in two main phases: the candidate compound discovery and the medicine development. The latter is further articulated in non-clinical – that is, animal and cell base studies - and clinical development phases – that is, studies on healthy (Phase I) or sick people (Phase IIa, IIb and III) and trials with registered products (Phase IV). Non-clinical and clinical developments permit, among others, to test the candidate compound safety and efficacy that is mutagenicity, single and repeat dose toxicity, safety pharmacology, pharmacokinetics, toxico-kinetics.

The paper is structured in other three main sections. In the second paragraph, adopted methodology is discussed and sample main features are presented. In the third section, the main results regarding the localization study carried out on the biotech activities in Italy are presented. The conclusions complete the paper.

2. UNIT OF ANALYSIS DEFINITION AND RESEARCH METHODOLOGY

Keeping in mind the different types of biotech firms operating at global level, we have decided to focus our attention to a less heterogeneous population. In so doing, we initially narrowed the analysis to the red biotech segment, because of its absolute predominance both in Italy (73% of enterprises, 94% of total revenue and 86% of investments) and at worldwide level (51% of EU firms and 60% of USA ones¹). In order to specifically investigate the localization of high value activities, companies performing exclusively sales activities were excluded. They were further divided accordingly to the adopted business model: born-biotech companies and pharma-biotech companies. The former have a predominant focus on R&D (more than 70% of total investments), while the second are represented by pharmaceutical or biotech companies managing also manufacturing and sales activities. Finally, companies belonging to the pharma-biotech segment were divided in:

- pharma-oriented companies, that is pharmaceutical firms that have diversified in the biotech business even if it does not yet represent the main activity field;
- biotech-oriented companies, that is firms born as spin off of pharmaceutical firms or companies whose business model presents strong ties to traditional pharmaceutical firms.

We refer to Blossom Associati-Assobiotec 2007 Report for the data and the segmentation criteria of Italian biotech sector. The focus on the pharma-biotech segment arises from the following evidences:

- firstly, our country has traditionally attracted direct investments from the foreign pharmaceutical companies, as both green-field investments and mergers&acquisitions;
- secondly, in Italy there is a considerable number of subsidiaries of pharmaceutical firms acting as centres of excellence, that are obtaining specific charters at a continental and even at worldwide level with respect to the development, production and sales of specific therapeutic solutions (see for instance the case of Glaxo Wellcome or Bristol Myers Squibb). Consequently it might be assumed that Italy has been considered - in the recent past - an interesting location to develop high value added activities, such as R&D in the drug industry;

- the pharma-biotech companies generate the 59% of the revenue of the Italian biotech sector and realize the 61% of total investments;
- among the pharma-biotech companies, there is an huge presence of MNCs. For a multinational corporation, differently than for a SME, the localization is a matter of choice because, typically, a wider range of investing options in different countries are available: therefore, investigating these companies and the changes they make in their localization choices can provide valuable insights about the potential of Italy as venue able to intercept (and maintain) FDIs.

As a consequence, we found a sample of 39 pharma-biotech companies, 23 of which are classified as biotech-oriented and 16 as pharma-oriented. For each of them we carried out a desk analysis mainly focused on annual reports – to evaluate dimension and amount of investments - and data from Chamber of Commerce – to investigate shareholders and financial presence in other companies. After that, we have sent them a questionnaire in order to collect both qualitative and quantitative data. The questionnaire is made up of the following sections:

- General information: location(s) in Italy, eventual listing at stock markets, country of origin (only for subsidiaries);
- Managed activities: research and development, clinic development, production, and sales;
- Collaborations with selected actors: university and other research centres, multinational firms, incubators and scientific parks, hospitals and clinics;
- Economic and financial data: total number of employees (at world level and in Italy for multinationals), total amount of revenue (at world level and in Italy for multinationals), percentage of people devoted to R&D; percentage of revenue arising from biotech technologies/processes; amount of investments in research and development (at world level and in Italy for multinational), percentage of such investments in biotech technologies/processes;
- Therapeutic areas of specialization;
- Number of products/projects in the different stage of the pipeline;
- Number of processes developed in Italy: attention was mainly focused on fermentation, purification, M-Ab, cells/tissues c., rec DNA, rec protein, fluorescence, new platform, lab on a chip, assay set up, others.

As shown in Table 1, we obtained a quite huge redemption rate for each segment of the investigated population (biotech- vs. pharma-oriented, Italian vs. multinationals, Italian MNCs vs. subsidiaries), as a consequence we are quite confident on the possibility to give a specific characterization of each of them.

Table 1. Redemption rates.

Pharma biotech	Italian Independent Firms	Multinational Companies (MNCs)		Total
		Italian MNCs	Subs of foreign MNCs	
Biotech-oriented	81,82%	100,00%	63,64%	73,91%
Pharma-oriented	100,00%	50,00%	44,44%	56,25%
Total	85,71%	60,00%	55,00%	66,67%

It is worth noting the main features of the respondents.

First of all, they are generally concentrated in a selected number of clusters (Table 2). More specifically, the 96% of pharma-biotech companies are located only in three regions: Lombardy in the North, Tuscany and Latium in the Centre. Lombardy is the area with the higher concentration of R&D activities, with an almost equal distribution of large, medium and small companies and of biotech-oriented and pharma-oriented ones. On the contrary, Latium is featured by a stronger presence of large pharma companies, more oriented to manufacturing and sales activities than to R&D. In Rome and Latina, for instance, we found a higher percentage of pharma-oriented companies (26,07% of the total) with respect to biotech-oriented ones (18,76%). This result may be explained by the huge presence, in such two areas, of pharmaceutical companies, especially large multinationals (we refer, among others, to Pfizer, Merck Sharp & Dohme, Bristol Myers Squibb). This presence arises from the proximity to Rome and the availability of fiscal incentives and grants in those areas, which were considered less developed until the beginning of '90s. Finally, in Tuscany biotech-oriented companies show a slight dominance (the 17,64% of the total versus the 11,11% of pharma-oriented ones). In this region we find out two big multinational companies (Chiron, Grifols) that started their activities in the early nineties. In our opinion that this could have boosted in that region the trend to invest in R&D.

If we analyse data at a district level, two main clusters emerge: Milan² (where is located the 53,85% of total pharma-biotech) and Rome (19,23%). In Tuscany, there is a more fragmented situation being pharma-biotech companies almost equally distributed in three local districts: Pisa, Siena, and Florence. Being them quite close each other, it may be assumed they belong to the same cluster, often referred (Blossom Associati & Assobiotech 2007) as the “Tuscan biotech cluster”.

Table 2. Geographical distribution of the respondents.

Region	District	Biotech-oriented	Pharma-oriented	Total
Lombardy	Milan	58,82%	44,44%	53,85%
	Monza	0,00%	11,11%	3,85%
Latium	Rome	17,65%	22,22%	19,23%
	Latina	11,11%	3,85%	0,00%
Tuscany	Pisa	5,88%	11,11%	7,69%
	Siena	5,88%	0,00%	3,85%
	Florence	5,88%	0,00%	3,85%
Campania	Naples	5,88%	0,00%	3,85%
Total		100,00%	100,00%	100,00%

In order to investigate the distribution of respondents firms according to size, we referred to the EU definitions introduced by the Recommendation 361/2003:

- A small enterprise is defined as an enterprise which employs fewer than 50 persons and whose annual turnover and/or annual balance sheet total does not exceed EUR 10 million;
- A medium enterprise is made up of enterprises which employ fewer than 250 persons and which have an annual turnover not exceeding EUR 50 million,

and/or an annual balance sheet total not exceeding EUR 43 million (considering the most favourable data);

- A large enterprise is made up of enterprises which employ more than 250 persons and which have an annual turnover exceeding EUR 50 million, and/or an annual balance sheet total exceeding EUR 43 million (considering the most favourable data).

Based on such assumptions, we noted that pharma-oriented companies are all large corporations, since they are subsidiaries of multinational companies. On the contrary, biotech-oriented firms represent a more heterogeneous group, even if the most diffused are small companies (47,06%).

Table 3. Respondents by firm size.

Firm size	Biotech-oriented	Pharma-oriented	Total
Large	29,41%	100,00%	53,85%
Medium	23,53%	0,00%	15,38%
Small	47,06%	0,00%	30,77%
Total	100,00%	100,00%	100,00%

As showed in table 4, we also noted that Italian companies are prevailing among the biotech-oriented ones.

Table 4. Respondents by country of origin.

	Biotech-oriented	Pharma-oriented	Total
Italian independent	52,94%	33,33%	46,15%
Italian MNC	5,88%	22,22%	11,54%
Subsidiaries of foreign MNC	41,18%	44,44%	42,31%
Total	100,00%	100,00%	100,00%

Analysing the firms' value chain, we noted that R&D activities are largely diffused (around 65%), with no substantial difference between biotech-oriented and pharma-oriented companies (Table 5).

Table 5. Presence/absence of R&D activities.

R&D activities	Biotech-oriented	Pharma-oriented	Total
Not performed	35,29%	33,33%	34,62%
Performed	64,71%	66,67%	65,38%
Total	100,00%	100,00%	100,00%

On the contrary, manufacturing activities (even those not related to biotech products) are mainly performed by pharma-oriented companies (89% of total respondents belonging to this group) (Table 6). This is not unexpected since pharma-oriented companies manufacturing activities are typically related to pharmaceutical activities than biotech, since biotech companies focus their efforts on drug discovery, granting production to other economic actors.

Table 6. Presence/absence of manufacturing activities.

Manufacturing activities	Biotech-oriented	Pharma-oriented	Total
Not performed	64,71%	11,11%	46,15%
Performed	35,29%	88,89%	53,85%
Total	100,00%	100,00%	100,00%

A further analysis related to manufacturing activities points out that only the 14% of subsidiaries of foreign multinationals perform them. According to this result, we can argue that the presence of multinationals in Italy seems to be focused on low value added activities, such as sales. At the same time, it is interesting that all manufacturing subsidiaries manage also R&D activities.

Finally our research focused on collaborations that biotech companies set up with other actors in- and outside the industry. As earlier explained, this is a widely recognized success factor in the biotech industry (Koput, Powell & Smith-Doerr 1996), since the high- intensity of knowledge required. With this respect, a primary relation is generally realised with universities; as a consequence we expect such collaboration is a widespread phenomena, with no respect to the business model (pharma- vs. biotech-oriented, size and “origin”). Data summarized in Tables 7 and 8 completely confirm such a hypothesis. In fact, as the tables below show, most of the firms in the sample (almost 90%) are tightly connected with Universities, a lot of them with other multinational companies (50%) and few with incubators (about 20%).

Table 7. Collaboration with Universities according to business type.

	Biotech-oriented	Pharma-oriented	Total
NO	5,88%	11,11%	7,69%
YES	88,24%	88,89%	88,46%
ND	5,88%	0,00%	3,85%
Total	100,00%	100,00%	100,00%

Table 8. Collaboration with Universities according size.

	NO	YES	ND	Total
Large	7,14%	92,86%	0,00%	100,00%
Medium	25,00%	75,00%	0,00%	100,00%
Small	0,00%	87,50%	12,50%	100,00%
Total	7,69%	88,46%	3,85%	100,00%

A second type of partner is generally represented by multinational corporations: with respect to our sample, it is logically expected that such relationships will take place only for companies established in Italy, since such a type of collaboration maybe defined for foreign subsidiaries at headquarter level (Table 9).

Table 9. Collaborations with MNCs.

	Italian Independent Firms	MNCs			Total
		Italian MNCs	Subs of foreign MNCs	Total MNCs	
NO	8,33%	0,00%	72,73%	57,14%	34,62%
YES	75,00%	100,00%	9,09%	28,57%	50,00%
ND	16,67%	0,00%	18,18%	14,29%	15,38%
Total	100,00%	100,00%	100,00%	100,00%	100,00%

Incubators represent a third relevant partner. However, it is worth noting the limited presence of such institutions in our country. As a consequence, these relationships are not very diffused, especially among multinationals, both Italian and foreign ones (Table 10). At the same time, they seem to be relevant only for biotech-oriented companies (Table 11).

Table 10. Collaborations with incubators.

	Italian Independent Firms	MNCs			Total
		Italian MNCs	Subs of foreign MNCs	Total MNCs	
NO	33,33%	66,67%	81,82%	78,57%	57,69%
YES	33,33%	33,33%	0,00%	7,14%	19,23%
ND	33,33%	0,00%	18,18%	14,29%	23,08%
Total	100,00%	100,00%	100,00%	100,00%	100,00%

Table 11. Collaborations with incubators for biotech-oriented firms.

	Biotech oriented				Total
	Italian independent firms	MNCs			
		Italian MNCs	Subs of foreign MNCs	Total MNCs	
NO	22,22%	100,00%	71,43%	75,00%	47,06%
YES	44,44%	0,00%	0,00%	0,00%	23,53%
ND	33,33%	0,00%	28,57%	25,00%	29,41%
Total	100,00%	100,00%	100,00%	100,00%	100,00%

Finally, it is interesting to note that such a type of collaborations is more diffused in the Milan area (60% of respondent companies), the most advanced biotech cluster in our country.

The fourth and last partner is represented by hospitals and clinics; with respect to them, collaborations are slightly more relevant for pharma-oriented companies (88,89% instead of 76,47% for biotech-oriented ones), mainly the large ones (92,85% of large companies instead of 75% of medium and only 62,5% of small ones).

3. RESULTS DISCUSSION

In order to analyse the location of high value activities of pharma biotech firms operating in Italy, we decided to focus our attention on two main elements: R&D and clinical development³.

Considering R&D activities in relationship to the two categories of pharma- biotech firms (biotech-oriented and pharma-oriented), we expected that higher R&D investments are more diffused among the former than among the latter, since the pharma-oriented also act in “traditional” pharmaceutical industry. In Table 12 we grouped respondent firms in classes according to the declared percentage of R&D investments in biotechnology with respect to the total R&D effort. Data show that, in each of the three considered years (2004-2006), no biotech-oriented company invests less than 20% in biotech projects, while the 33,33% of pharma-oriented belongs to this class. At the same time, comparing data at the extremities of the considered period (2004 and 2006), arises that biotech-oriented firms increased their efforts in biotech R&D projects, with no company having less than 40% of such investments in 2006. On the contrary, in the same period, investments of pharma-oriented companies remained stable.

Table 12. Investments in biotech R&D as a percentage of total R&D funds.

	Biotech-oriented			Pharma-oriented			Total		
	2004	2005	2006	2004	2005	2006	2004	2005	2006
Up to 20%	0,00%	0,00%	0,00%	33,33%	33,33%	33,33%	11,54%	11,54%	11,54%
20,1%-40%	5,88%	5,88%	0,00%	33,33%	33,33%	33,33%	15,38%	15,38%	11,54%
40,1%-70%	5,88%	11,76%	11,76%	0,00%	0,00%	0,00%	3,85%	7,69%	7,69%
> 70%	58,82%	52,94%	58,82%	0,00%	0,00%	0,00%	38,46%	34,62%	38,46%
ND	29,41%	29,41%	29,41%	33,33%	33,33%	33,33%	30,77%	30,77%	30,77%
Total	100%	100%	100%	100%	100%	100%	100%	100%	100%

Such results are aligned with a recent report issued by PWC (2007) pointing out the low investment efforts of pharmaceutical companies. At the same time, considering that pharma-oriented companies are generally bigger than biotech-oriented ones, findings under discussion are consistent also with McCutchen Jr. & Swamidass (1996).

With respect to biotech-oriented companies, the results could be, at least partially explained, by the success of such companies in terms of product pipeline. Bigger the number of products that reach the final stages in the product development cycle, more relevant the required R&D investments. With this respect, it is worth noting that the increased R&D effort is all related to Italian companies.

The same evidences rise up considering the percentage of employees involved in R&D (as percentage of the total number of workers) as a proxy of the R&D investments. As showed in Table 13, more than 47% of biotech-oriented companies has more than 50% of their employees involved in R&D activities, while none has less than 5%. On the contrary none of pharma-oriented firms has more than 25% of workers involved in research projects, while 11,11% has less than 5%.

In the period 2004-2006 the percentage of employees involved in R&D activities remains stable, but the data show also an increasing percentage of them carrying out research activities in the biotech sector.

Table 13. Employees involved in R&D activities as a percentage of total employees (average level in 2004-2006).

	Biotech-oriented	Pharma-oriented	Total
Up to 5%	0,00%	11,11%	3,85%
From 5,1% to 10%	11,76%	44,44%	23,08%
From 10,1% to 15%	11,76%	22,22%	15,38%
From 15,1% to 20%	5,88%	11,11%	7,69%
From 20,1% to 25%	0,00%	11,11%	3,85%
From 25,1% to 50%	5,88%	0,00%	3,85%
From 50,1% to 75%	23,53%	0,00%	15,38%
More than 75%	23,53%	0,00%	15,38%
ND	17,65%	0,00%	11,54%
Total	100,00%	100,00%	100,00%

Therefore the data show that the huger percentages of R&D investments are performed by biotech-oriented companies rather than by pharma-oriented ones.

As shown in Table 14, while R&D activities are carried out by all Italian companies (both independent and MNCs), only 18% of subsidiaries of foreign companies perform such activity. This confirms the lower value added orientation of the latter type of companies, which seem to conceptualise our country as a market opportunity more than a knowledge base to be exploited. Further analysing these data with respect to the ones in Table 4, it is possible to argue that Italian firms performs such activity, since they mostly are biotech-oriented.

Table 14. Presence/absence of R&D activities.

Presence/Absence R&D activities	Italian Independent firms	MNCs			Total
		Italian MNCs	Subs of foreign MNCs	Total MNCs	
Not performed	0,00%	0,00%	81,82%	64,29%	34,62%
Performed	100,00%	100,00%	18,18%	35,71%	65,38%
Total	100,00%	100,00%	100,00%	100,00%	100,00%

Based on the evidences showed in the earlier cited work of McCutchen Jr. & Swamidass (1996) we then speculate that – considering the period 2004-2006 - the increase of R&D investments is mainly ascribable to the Italian independent companies, instead than to MNCs (Italians or foreign subsidiaries). Data in Table 15 totally confirm such hypothesis: in 2006 the 66,7% of Italian independent companies performed more than 70% of their R&D investments in biotech businesses, compared to the 14,3% (altogether considered) of the multinational ones. The 2004 and 2005 data show a similar pattern as well.

Moreover data also point out that in the considered period the number of independent Italian firms highly investing in R&D further grew up: while multinationals (both Italian and subs) have a steady percentage of R&D dedicated to biotech in the period 2004-2006, Italian companies show a growing trend (the 75% of the biotech-oriented

firms invests more than 40% in R&D on biotech in 2006 compared to the 66,67% in 2004).

Table 15. Investments in biotech R&D as a percentage of total R&D funds.

	Independent Italian firms			Italian MNCs			Foreign MNCs		
	2004	2005	2006	2004	2005	2006	2004	2005	2006
Up to 20%	0,00%	0,00%	0,00%	33,33%	33,33%	33,33%	18,18%	18,18%	18,18%
20,1%-40%	33,33%	33,33%	25,00%	0,00%	0,00%	0,00%	0,00%	0,00%	0,00%
40,1%-70%	0,00%	8,33%	8,33%	0,00%	0,00%	0,00%	9,09%	9,09%	9,09%
> 70%	66,67%	58,33%	66,67%	0,00%	0,00%	0,00%	18,18%	18,18%	18,18%
ND	0,00%	0,00%	0,00%	66,67%	66,67%	66,67%	54,55%	54,55%	54,55%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

As a consequence, it seems possible to state that multinational companies (even those having an Italian headquarter) seem to de-localize R&D activities out of Italy. This topic is of great relevance and deserves further future analysis, since the strong relevance of these early results and its possible implication for the decision makers, analysis that are not the object of the present work.

Similar results are obtained also considering as explaining variable the percentage of employees in R&D activities. More specifically, almost 67% of Italian independent firms have at least half of their employees involved in R&D activities, against none of multinational companies.

Table 16. Employees involved in R&D activities as a percentage of total employees (average level in 2004-2006).

	Italian Independent Firms	Multinationals	Total
Up to 5%	0,00%	7,14%	3,85%
5,1% - 10%	8,33%	35,71%	23,08%
10,1% - 15%	25,00%	7,14%	15,38%
15,1% - 20%	0,00%	14,29%	7,69%
20,1%- 25%	0,00%	7,14%	3,85%
25,1% - 50%	0,00%	7,14%	3,85%
50,1% - 75%	33,33%	0,00%	15,38%
More than 75%	33,33%	0,00%	15,38%
ND	0,00%	21,43%	11,54%
Total	100,00%	100,00%	100,00%

The poor Italian performance in attracting R&D investments from multinationals is further demonstrated by the fact that the percentage of R&D employees in Italy is a quite small percentage of total workers performing R&D activities at worldwide level (Table 17). The 42,86% of the subsidiaries shows a ratio between Italian and world employees (involved in R&D) smaller than 5% (Table 17).

Table 17. Employees involved in Italian R&D activities as a percentage of workers operating in R&D at worldwide level (average level in 2004-2006).

	MNCs		Total
	Italian MNCs	Subsidiaries of foreign MNCs	
Up to 5%	7,14%	42,86%	50,00%
10,1% - 20%	0,00%	7,14%	7,14%
More than 20%	14,29%	0,00%	14,29%
ND	0,00%	28,57%	28,57%
Total	21,43%	78,57%	100,00%

Analysing the data in Table 17, it is possible to argue that Italy seems to be considered by multinationals more as a market opportunity rather than a location for R&D investments (Table 16), since they tend not to dedicate too many employees to this activity in Italy. It is confirmed by data comparison with Table 18, where the Italian share of worldwide revenue is presented.

Table 18. Revenue in Italy as a percentage of worldwide total revenue (data 2005).

	Biotech-oriented	Pharma-oriented	Total
Up to 5%	28,57%	14,29%	42,86%
From 5,1% to 10%	14,29%	7,14%	21,43%
From 10,1% to 20%	7,14%	0,00%	7,14%
More than 20%	7,14%	7,14%	14,29%
ND	0,00%	14,29%	14,29%
Total	57,14%	42,86%	100,00%

With respect to the target of R&D activities, it is worth pointing out that such investments are generally focused on therapeutic products (Table 19), while those related to diagnostics are quite rare and are performed exclusively by Italian independent firms (Table 20). At the same time, it is further demonstrated that biotech-oriented companies are more involved in R&D activities in therapeutics (82,35%) than pharma-oriented ones (66,67%).

Table 19. Presence/absence of R&D activities in therapeutics.

Therapeutics	Biotech-oriented	Pharma-oriented	Total
NO	5,88%	11,11%	7,69%
YES	82,35%	66,67%	76,92%
ND	11,76%	22,22%	15,38%
Total	100,00%	100,00%	100,00%

Table 20. Presence/absence of R&D activities in diagnostics.

	Italian Independent Firms	MNCs			Total
		Italian MNCs	Subs of foreign MNCs	Total MNCs	
NO	83,33%	100,00%	63,64%	71,43%	76,92%
YES	16,67%	0,00%	0,00%	0,00%	7,69%
ND	0,00%	0,00%	36,36%	28,57%	15,38%
Total	100,00%	100,00%	100,00%	100,00%	100,00%

At the same time, R&D investments in therapeutics are generally focused on so called “big killers”, that are widely diffused pathologies and, as a consequence, more profitable markets (Table 21). With this respect, it is interesting to note that in the cardio field there is a predominance of pharma-oriented companies, while in the cancer and bones/muscles fields biotech-oriented invest more than pharma-oriented ones.

Table 21. Percentage of companies involved in R&D activities according the therapeutic area.

Therapeutic area	Biotech-oriented	Pharma-oriented	Total
Cardio	23,53%	33,33%	26,92%
Cancer	47,06%	44,44%	46,15%
Bones/muscles	29,41%	22,22%	26,92%

With respect to therapeutics, data show that R&D in therapeutics seems to be generally focused on very few areas. Starting by the analysis of the received questionnaires, we have extracted the percentage of the most diffused areas in which firms invest. Here are the results:

- diagnostic: the 6% of biotech-oriented, the 11% of pharma-oriented: this is a niche R&D area, scarcely garrisoned since the 82% of biotech-oriented firms declare not to be present versus the 67% of pharma-oriented firms;
- cardio-vascular: the 23% biotech, the 33% pharma;
- oncology: the 47% biotech, the 44% pharma;
- infectious diseases: the 23% biotech, the 11% pharma;
- diabetics: the 7% biotech, 0% pharma.

With respect to clinical development, we found out that such activity is more diffused among pharma-oriented firms, since it is a final step in the drug discovery process (Table 22). Biotech-oriented companies, on the contrary, are generally more focused on the earlier steps of the drug discovery process (Table 23). At the same time, it is interesting to note that only 56% of Italian biotech-oriented companies carry out clinical development, since they cannot benefit of the R&D results earlier achieved in other countries (that is, at the headquarter level or by other subsidiaries).

Table 22. Presence/absence of clinical development activities.

	Biotech-oriented	Pharma-oriented	Total
NO	35,29%	11,11%	26,92%
YES	64,71%	77,78%	69,23%
ND	0,00%	11,11%	3,85%
Total	100,00%	100,00%	100,00%

Table 23. Pipeline composition for phase of drug discovery process.

	Biotech-oriented	Pharma-oriented	Total		Biotech-oriented	Pharma-oriented	Total
Discovery phase				Preclinical phase			
0-1	5,88%	11,11%	7,69%	0-1	5,88%	22,22%	11,54%
2-3	11,76%	22,22%	15,38%	2-3	17,65%	0,00%	11,54%
4-5	17,65%	0,00%	11,54%	4-5	11,76%	11,11%	11,54%
6-10	5,88%	0,00%	3,85%	6-10	0,00%	0,00%	0,00%
> 10	5,88%	0,00%	3,85%	> 10	5,88%	0,00%	3,85%
ND	52,94%	66,67%	57,69%	ND	58,82%	66,67%	61,54%
Total	100,00%	100,00%	100,00%	Total	100,00%	100,00%	100,00%
Phase 1				Phase 2			
0-1	17,65%	11,11%	15,38%	From 0 to 1	5,88%	0,00%	3,85%
2-3	5,88%	22,22%	11,54%	From 2 to 3	23,53%	11,11%	19,23%
4-5	0,00%	0,00%	0,00%	From 4 to 5	5,88%	0,00%	3,85%
6-10	5,88%	0,00%	3,85%	From 6 to 10	5,88%	0,00%	3,85%
ND	70,59%	66,67%	69,23%	ND	58,82%	88,89%	69,23%
Total	100,00%	100,00%	100,00%	Total	100,00%	100,00%	100,00%
Phase 3							
From 0 to 1	11,76%	0,00%	7,69%				
From 2 to 3	11,76%	22,22%	15,38%				
From 4 to 5	5,88%	0,00%	3,85%				
More than 10	5,88%	0,00%	3,85%				
ND	64,71%	77,78%	69,23%				
Total	100,00%	100,00%	100,00%				

CONCLUSION

The paper deals with the localisation of value added activities of the Italian pharma-biotech industry. The analysis carried out identifies the main features of the R&D activities performed by the investigated firms. First of all, it arises that they are generally concentrated in a selected number of regional clusters, more specifically Lombardy, Tuscany and Latium. If we analyse data at a more specific level, two main clusters emerges: Milan (where is located the 53,85% of total pharma-biotech) and Rome (19,23%). As regards the former, we also find out a certain good level of collaboration with local actors, as incubators and universities. That is a widely

recognized success factor in the biotech industry (Koput, Powell & Smith-Doerr 1996), since the high-intensity of knowledge required.

Moreover, we also try to verify the capability of the Italian country-system to attract investments from abroad. With respect to such aspect, it is necessary to point out the unanimous belief - of both, researchers and policy makers - how foreign direct investments (particularly the high knowledge and innovation based) deeply impact on the economic strength and development of the country of destination (Findlay 1978, Barrel & Pain 1997; Borenszeiten, De Gregorio & Lee 1998). In doing so, we studied separately the Italian independent firms and MNCs (both Italian and foreign). We find out a different approach to R&D investments. In 2006 the 66,7% of Italian independent companies performed more than 70% of their R&D investments in biotech business, compared to the 14,3% (altogether considered) of the multinational ones. The 2004 and 2005 data show a similar pattern as well. Similar results are obtained also considering as explaining variable the percentage of employees in R&D activities. More specifically, almost 67% of Italian independent firms have at least half of their employees involved in R&D activities, against none of multinational companies. Considering both the number of employees involved in R&D and the extent of the investments carried out by foreign MNCs and by Italian companies, it is possible to argue that Italy seems to be considered by multinationals more as a market opportunity rather than a venue for R&D investments. As regards R&D activities, we also find out that huger percentages of R&D investments are carried out by biotech-oriented companies rather than by pharma-oriented ones. In fact is not unexpected that pharma-oriented companies are more focused on manufacturing activities since they are typically related to the pharmaceutical production, while biotech companies focus their efforts more on drug discovery, granting production to other economic actors.

However, it is necessary to remember the exploratory nature of this paper, as a consequence we are not yet able to provide comprehensive guidelines for decision makers. Further analysis on biotech industry will allow us to provide them in future studies.

ENDNOTES:

¹ Data source is: Critical I, *Biotechnology in Europe: 2005 Comparative study*, BioVision, Lyon, 2005. It is worth noting that such analysis includes also support and services firms to the biotech sector – which are not considered in our paper focused at the Italian level. This could partially affect the comparison.

² It is worthy to note that Monza is a new autonomous province but is geographically contiguous with Milan, so they may be considered a unique cluster.

³ see pp. 3-4

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