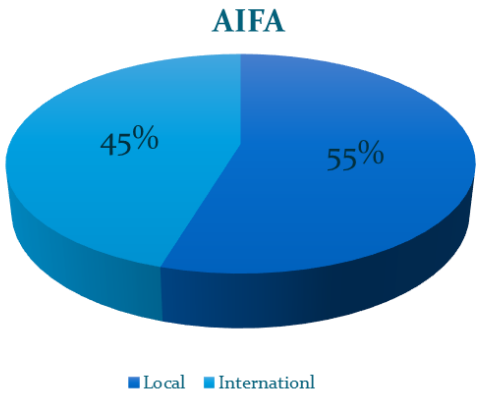
By the AICRO "data and communication" working group, February 2020.

AICRO Survey 2019 - The status of associated CROs

Introduction

According to some analyses, the global market for Contract Research Organisations (CROs) has a value of approximately $29 billion (2016) and is expected to grow at a rate of 7% to $40 billion by 2020, as Pharmaceutical sponsors continue to invest in research and development and outsource to independent service providers.
According to these estimates 41% of clinical development is outsourced, a metric that is expected to increase to 50% by 2020, as the costs and complexity of development increase in a reimbursement environment, and increasingly onerous regulation, and as sponsors seek more efficient solutions through their CRO partner.
In this context the CRO market in Italy is not officially quantified. There are no studies or reliable estimates about the economic value, the expected growth rates or the degree of market penetration.
CROs with a presence on Italian territory can be represented by two macro-categories: Italian companies and foreign ones, but with offices in Italy. According to recent information provided by AIFA (December 2019) 194 CROs are registered with the Observatory (OsSC) operating on Italian territory, of which 106 "Italian" and 88 “foreign”.
AICRO certainly represents the largest and most known and active CROs in Italy, but the lack of data and analysis hat could best characterise the category significantly limits the ability of CROs to be incisive in its relationship with the institutions, regulatory bodies and all interested parties. The limited ability of the category to effectively communicate its "weight" and the added value it generates is also a decisive factor in the full affirmation of the CRO "industry".
In November 2019 AICRO conducted a survey among member companies to quantify at least in part, the number of actors operating and really active on the national territory, the employment dimension, the economic dimension, market penetration. A snapshot that expresses the overall dimension and which can be a stimulus for more in-depth market analysis, underline the importance of CROs in the production chain of new compounds and medical devices and the weight they represent also in "cultural" and educational sense, collaborating with universities and other training institutions.



Results

At the time of the survey, 23 companies were AICRO members (apparently 12 % of the CROs surveyed in OsSC, but probably by far the most representative ones). The survey was shared with all members. The response rate was 95%. Practically all members contributed to this first analysis.

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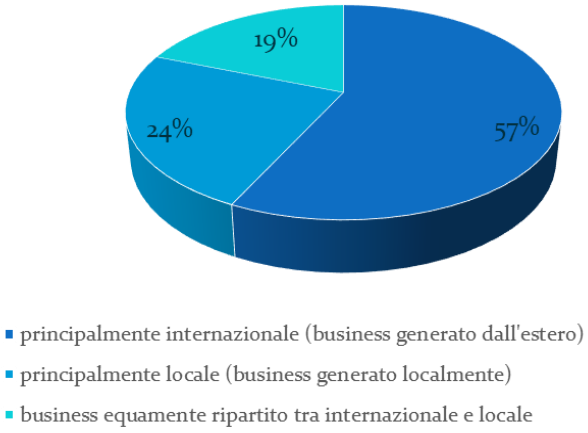
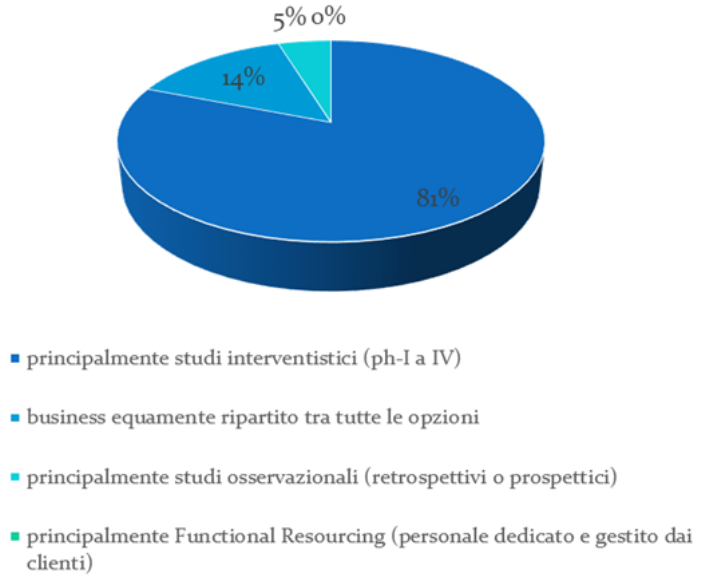
1. <u>Characterization:</u> a first series of questions was aimed at characterizing CROs with respect to the Italian context and the type of activity.
61% of CROs represent international companies with a presence in Italy. 39% are Italian companies, some of which are associated or "federated" with other companies abroad.
74% of CROs are headquartered in Lombardy (82% in Milan), 17% in Lazio, and the remainder in other regions.
The characterization of the associates with respect to the type of activity, reveals that the majority (57%) "mainly" deals with international business (i.e. generated abroad). 24% "mainly" of local business (i.e. generated in Italy) and 19% of business equally divided between international and local. A better quantification of the weight of locally generated business would allow to know more precisely the investments destined to Italy and consequently understand the attractiveness of the Italian market for clinical trials.



The majority (81%) of associates are mainly involved in Interventional Clinical Trials (Phase I - IV). The 5% are almost exclusively concerned with observational/epidemiological and generally non-interventional studies. 14% have a "mixed" characterization in this sense.



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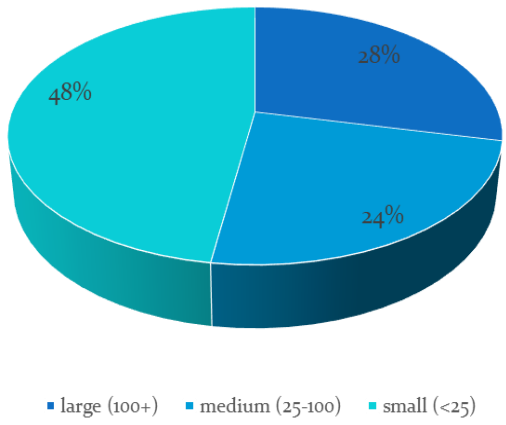
It would be interesting to understand how the "specialization" of CROs in the Italian context evolves with respect to all types of studies and clinical investigations. The possibility for CROs to provide specialized teams and services for the so-called Real World but also for medical devices and other "futuristic" models would seem attractive considering the global context.

Associated companies use a very large part of employed professional resources and apparently the use of freelance staff and consultants is used with a tactical approach. Only 5% of respondents declare the use of external collaborators "to a consistent extent".

2. Human Resources

The associated CROs employ more than 2200 employees (all contractual forms). A plausible estimate of the aggregate investment of the member companies is in the range of 120 -130 MioEur/year for labour costs alone. It is interesting to note that according to a recent report by Farmindustria, research and development employees in Italy amount to about 6000. However, it is not clear how much the CRO world is related to these numbers.

The majority of members are characterized as small CROs. The average number of employees per company is 105 but the median is only 25. In particular, 28% have more than 100 employees, 24% between 25 and 100 employees and 48% have less than 25 employees.



Further research in this area is not known at the moment, but it is plausible that the other CROs permanently present in the territory, not associated with AICRO, are mostly medium or small in size.

The size of the companies seems to correlate with the type of business: in small companies the locally generated business appears to prevail while in medium or large companies the business generated at an international (global) level prevails.

As far as the professional types are concerned, it should be noted that the profession of Clinical Research Associate (CRA) largely prevails with about 1000 employees. There are around 400 people in charge of regulatory affairs and start-up. Project Managers/Team Leaders are around 390 employees. Statisticians/data management staff in the aggregate are around 90 employees. All other professions are covered by about 400 employees.

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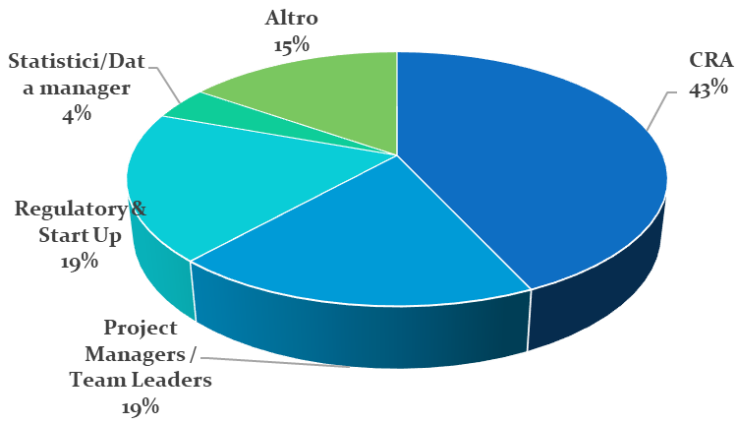

The CRA is still (and historically) the entry-level profession to the world of clinical research. Being a very demanding profession, the average duration of employment in this profession is generally "short" (4 - 5 years) and usually finds its development in other professions (e.g. PM/Team Lead).
It is the typical profession in great and constant demand and very scarce availability on the market. Constant and conspicuous investments are necessary to find this type of resources and to ensure an adequate turnover. The "academic" training does not cover (completely) the constant demand for these professions and the CROs contribute largely to the investments needed for training.
Both the Project Managers and the Specialists in Regulatory Affairs and Start Up, are more specialized professions and to some extent still "niche". Both technical and "soft" experience and skills are required to fill these roles in clinical research.
Generally, the duration of employment is much longer than for CRAs. Given the great added value they bring, however, there is great demand and relatively little availability and, at least for Project Managers, there is great competition between countries to ensure representation in the so-called CoE (Centre of Excellence).
Also, in these cases the investment in training is essential and very demanding.
Specialists in Statistics (biometrics) and Data Management can count at least in part on the availability of academic training. They are relatively more represented in medium/small size CROs and more related to locally generated business.
These are also highly sought-after professions and although the theoretical foundations may derive from (academic) studies, experience in the field is a differentiating factor.
Since these are activities that can be covered virtually anywhere, competition with similarly qualified resources from low labour cost countries (e.g. India) is very relevant.
All other professions are represented by about 400 employees. Among them (by way of example only): - Management - Quality professionals (Quality Assurance/ Quality management) - Pharmacovigilance, Contract negotiation specialists, other "Subject Matter Experts".
Some of these professions or roles are of paramount importance and are often only accessed after considerable experience and only with appropriate attitudes/skills. Only in some cases is training available, which often has to be disseminated/transferred in a controlled manner.

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3. Investments and payments

The member companies contributed financially to the revenues of the "system" with approximately 73 -75 million euro in 2018 through payments made to the trial sites and the regulatory authority.
The payments made to the Ethics Committees and to the Regulatory Authority for the activation of the new studies (including amendments to the protocols) amount to approximately € 22 -23 million (30% of the total).
The payments made to the trial sites were around 51 -52 million euro to cover the costs incurred by the SSN (NHS) for the execution of the studies and the contribution of the centres to enrolment (70% of the total).
Although these payments ultimately reflect the investments of industry and sponsors in general, the CROs have considerable influence in directing these investments to the most suitable and prepared facilities to manage the execution of the studies and are therefore important partners of industry in managing the return on investment.
In this respect, efforts are evident in the increasing cooperation between clinical research institutions and CROs. However, it would be interesting to deepen the level of general awareness of the economic value of trials at the sites and the value that a collaboration with the CROs can bring to all parties involved.
Although the data relating to the number of studies "launched" in 2018 are less robust, due to objective difficulties in defining and often documenting this data precisely, it is possible to draw some conclusions about the market penetration of CROs in Italy for the year examined.
According to the AIFA report, during 2018, 666 clinical (interventional) studies were authorized.
The data provided by the survey of about 330 studies on 2500 sites (including the observational studies - in any case in a clear minority) launched by 18/21 associates, would seem to indicate a high or very high market penetration by the associated CROs (>50%?).
It is desirable that further analyses, more detailed and precise, are carried out in this sense. In general, a common sharing of certain and shared indicators would be important. The number of studies activated in the time unit is in fact only a partial indicator of market trends. More precise indicators in the industry should include the type of studies, the type of sponsor and above all the number of sites and patients involved.

Conclusion:

CROs have long been established partners of sponsoring companies, trial sites and institutions in the field of clinical research. The CRO market is constantly expanding and it is expected that in the near future the volume of studies and sites managed by the CROs will become the majority vs those managed directly by companies and sponsors of different kinds.
There are no overly precise indicators in Italy regarding the size and types of activities of the CROs. This analysis provides some data of CROs associated with AICROs, among the most representative in the Italian market.
Overall, the associated CROs employ more than 2200 people specialized in leading roles in the design, supervision and execution of clinical trials. Many professions are considered of high added value and are in low availability and high demand.
The CROs contribute to the entry into the job market of young graduates, collaborate in improving awareness of the importance of research and integrate academic training programs in the pharmaceutical and health care fields in general.
CROs ensure independence and impartiality in the conduct of clinical trials and ensure compliance with the highest methodological and ethical standards.

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The CROs manage, in collaboration with the sponsoring companies, very substantial investments by acting in close collaboration with the research sites.
Starting from basic data, it is desirable that greater attention be paid to the potential and opportunities that the CROs offer to the research environment, expanding and refining quantitative analysis and including the CROs themselves among the major stakeholders to define the future of clinical research in Italy.