Poseidon Pharma CRO

Services & Activities Outline

'Poseidon Pharma services' was born out of the need to upgrade the pharmaceutical industry and provide services other than selling and manufacturing to local and regional role players.

Thanks to newly introduced concepts and to high added value, the company aims to becoming the pioneer of clinical research assistance and the leader of the pharmaceutical 'business support' industry in the region.

'Poseidon Pharma services' consists of four departments: Clinical research department (CR), Market research department (MR), Regulatory assistance department (RA), data analyses and biostatistics (TIC & Biostat) and Information technology department. Activities and functions of each department are presented herein after .

Clinical Research Department

Within the clinical research department, all efforts are invested according to the most up-to-date standardized procedures (SOP) to deliver services of feasibility of research project, protocols elaboration, submission to regulatory authorities, implementation, monitoring, validation and coordination of clinical biology services, pharmacovigilance monitoring , reporting and reconciliation of events , IMPs management , data verification and storage ; site closures and medical writing of end of study reports.

Composition

The (CR) is composed of different project managers operating according to guidelines set by training clinical researchers such as pharmacists, physicians, and biology engineers.

Clinical researchers and project managers maintain the quality of data, a good relationship with on-site research staff and the continuity of operations. All of them were trained based on clinical practices (GCP ICH), and they periodically receive training to use the most recent techniques of monitoring and management of clinical trials.

1- Clinical Trials

(According to food and drug administration (FDA) definition)

Phase I	**Definition**	**First in-trials (healthy subjects save for exception). One dose of an experimental drug (new active substance) except for vaccines, blood derived products, cell and gene therapy.**
	Objective	**Proceedby a short-term evaluation of safety of use in terms of dose and establish a BE/BA , Pharmacokinetics/ Pharmacodynamics profile.**
	Interest in	**These trials are recently permitted by the Tunisian**

	Tunisia & Morocco	regulation.
Phase II	Definition	Clinical trials administered to a healthy human being (IIa) or sick (IIb), one or more doses, in one or repetitive administrations, of an experimental drug.
	Objective	Proceed by a short-term evaluation of Pharmacokinetics and Pharmacodynamics allowing the choice of the optimal dose(s) and the search for interactions (drugs/meals).
	Interest in Tunisia & Morocco	Phase IIa is prohibited since it is applied to healthy volunteers;only studies and trials of phase IIb can be done. International manufacturers of drugs in particular, specialized incardiology, oncology, central nervous system and immunotherapy are for the investigation of scientific proofs for measurable effects of components under research among patients.Physicians participating in these studies are generally of great eminence in their countries.
Phase III	Definition	Clinical trials demonstrating the usefulness and effect of an experimental drug (new active substance before getting market authorization (MA) or a generic before getting market authorization (MA)) on patients to provide evidence of efficiency and tolerability of the drug in a greater number of patients. The drug may be compared to a placebo or a reference treatment;
	Objective	Proceed by a medium-term evaluation of the drug pharmacodynamics in therapeutic circumstances,enabling thus dose adjustment and confirmation of its safety in experimental conditions.
	Interest in Tunisia & Morocco	Participating in a trial (Phase III) during a multicentric investigation is what physician researchers look for to back up their CVs. The benefit for manufacturers is to prove their products tolerance and efficacy in the concerned indication and to be in conformity with MA. It is understood that the patients participating in such studies benefit from free treatment of their pathology, in which coverage can continue even for two years after the completion of the clinical trial, under “a compassionate use” programmes provided by law.
Phase IV (as well as for post-	Definition	Trials conducted after a drug has been placed on themarket develop new indications. These trials are performed after obtaining MA to evaluate the efficacy and tolerability of a drug in the long run and real life conditions.
	Objective	These trials are performed to investigate the Pharmacovigilance of drugs associated with other

marketing Observational studies)		**medicines in patients to compare their activity with that of other drugs within the same indication and to refine its dosage and well understand its mechanism of action.**
	Interest in Tunisia & Morocco	**These studies allow researchers to examine situations concerning the use of drugs on a large scale and will enable to** - **Enrich knowledge of scientific community and regulatory authorities about Pharmacovigilance.** - **Promote medical practitioners' knowledge of the products and to enable them from building a well-studied attitude of an experienced, analytical user that will impact positively their adoption of the product.** - **Dispose of leading patients with medical files used for statistical scientific purposes, research, decision- healthcare policy making or as a support for market planning of manufacturers that lets them be ahead of the competition.** - **Post-marketing studies also are an inexhaustible source for data concerning Pharmacovigilance and objective and subjective discretion of a new product by doctors and patients.** - **We observe the strictest ethical rules among our entire studies and specifically the post-marketing studies in which investigators are paid for the worthwhile data that they gather and not for the number of participating patients. The inclusions should imperatively correspond to the targeted medical indications and to forwarded proved statements.**

Expertise

The clinical trials, which Poseidon Pharma provides and the targeting management implementation it assures, take place in Phase II, III and IV of the drug development. Our team has a long experience in planning, and the implementation of the different research phases. Several multinationals have trusted us for more than 5 years (Novartis, Roche, MSD, Merck, Pfizer...).

Our Geographic coverage extends through our subsidiary to Morocco , and through partners to Algeria , Egypt , Turkey and Middle East countries.

We have carried out efficiently clinical trials in a variety of therapeutics areas:

Therapeutics Areas	Clinical Phase
Rheumatology	Phase III b, Phase IV
Haematology-Oncology	Phase IV
Pneumology	Phase IV
Hepatology-Virology	Phase IV
Oncology	Phase II, Phase III
Neurology	Phase IV
Rare diseases	Phase III
Cardiology	Phase IV

Our team is prone to work on all therapeutic areas especially that we have good ties with cardiologists , endocrinologists , rheumatologists , gastroenterologists , psychiatrists , etc …

NB: Further information will be provided on request.

2- Feasibility research study

There are preliminary studies whose objectives are to determine if a programme, a procedure or a protocol of a study in particular is realisable, and to collect the necessary data to determine the sample size of a final study.

- **Policy**

There are no specific guidelines for the evaluation ofclinical trials feasibility. Therefore, we designed a questionnaire to help evaluate a planned protocol by the investigator and to let him/hemake an adequate decision with regard to the trial feasibility on one hand allow the investigator to decidewhether to participate or not in this protocol and on the other hand.

- **Objective**

The objective is to provide evaluation tools for trial feasibility, in order to:

- ✓ obtain information from a local indication on the feasibility of the clinical trial;
- ✓ identify the environment where the clinical trial will be carried out;
- ✓ confirm the timetable of clinical trials processes;
- ✓ make an enlightened decision based on the distribution of sites of the clinical trial;
- ✓ identify the targeted population for the recruitment phase of the clinical trial.

3- The Donation programmes

To strengthen the brand image and the recognition of the product among the community of doctors and patients, donation programmes are addressed to patients without health insurance coverage, who need therapy and who are not given entitlement to reimbursement of healthcare costs by CNAM (the Tunisian medical insurance fund).

We take care of the programme conceptualisation, implementation and follow up, along with checking the participants' eligibility and ensuring the compatibility of drugs through paying monitoring visits and regular reporting of the participating centres.

4- Patients' Access Programs

For specific therapeutics with interlinked processes(hospitalisation for biotherapy infusion, anti-cancer chemotherapy, immunosuppressive drug bolus for patients whose mobility is impaired (MS, etc),we initiate coordination programmes with patients, prescribing doctors, social safety organisations and health facilities, so that the patients' access to their treatment and drug administration occurs in optimal conditions.

Particular knowledge of KOLs (Key Opinion Leaders) for each speciality and a control of legislations holding the administrative handling of a drug (PHCT, CNAM, DPM ...) help us be catalysts of Market Access.

For all our assistance programmes for patients, a regular update on access, patients, compatibility of drugs and the collaboration of prescribing doctors are provided.

5- Reinforcement programmes of therapeutic compliance

This program is dedicated to patients who are treated for chronic diseases (hypertension, diabetes who are not compliant with the drug regimen…).

The attending physician benefits from this program that helps him/her to better follow up these patients during consultations through accessing an available database containing historical patients monitoring using an interactive website.

A paramedical trained person accompanies the patient throughout the program to explain for them their illness, the negative effects of drugs and remind them of the time of taking the medicines and of any other particular precautions.

6- Services of Pharmacovigilance and materiovigilance

Both for medical devices than for drugs our specialized team can keep watch on adverse events and adverse effects, with reporting by standardized procedures that are well-established and by declarations to the supervisory authorities on the national and the global scale.

By using the services of expert employees, we draft and updatethe summary of product characteristics(SPCs), periodic safety reports (PSRs) and compliance with the most rigorous international standards related to drugs and medical devices (GCP international standards , GMP , FDA CFR Part 11 , 21 CFR Parts 808, 812, 820 , ISO 14155-1 & 2 , ISO 13485 , etc ....).

7- Services of implementation and monitoring of the cold chain

Our organization is the Tunisian preferred partner of the Swiss company "Berlinger AG", "specialist of temperature monitoring systems. We understand the concepts necessary to implement and monitor an efficient cold chain, by providing full traceability and documentation in compliance with regulatory requirements thanks to a wide range of products designed to meet the specific needs of the pharmaceutical industry. More information can be provided to you by our business development manager.

Regulatory Assistance (AR)

Poseidon Pharma has a pharmaceutical and regulatory expertise to provide scientific technical support, high-level compliance with regulatory requirements.

In Tunisia, there is no law governing clinical research. For clinical trial implementation, management of pharmacy and medicine (DPM) has developed a specification inspired by European and American regulations. We also follow the guidelines of the EMEA and the GCP / ICH to prepare the regulatory and technical clinical study folder.

AR department is designed to be attached to the RC department regarding the preparation of clinical trial records and their submission to the Tunisian authorities (ethics committees, Department of Pharmacy and Medicine and Department of Public Health) and any amendment made during a study.

AR department is also responsible for assisting in the preparation of a marketing authorization folder, submission and follow-up to the authorities until the MA.

This department includes other intended regulatory aspect and requested by the pharmaceutical industry.

Market Research (MR)

Market research is a successful tool to gain visibility on the positioning of a product on the market in comparison with the drugs of the same range. The comparison comprehends three aims: how it is integrated among physicians, and users; know its therapeutic intentions; verify the effectiveness of the activity of medical examination and measure the success of the product's route of communication in product marketing.

For this purpose, different techniques are used:

1 -Qualitative studies

They are based on group meetings (group focus) and address the problem with stakeholders. Then "data mining" is prepared using "evocation" software and analysis of content.

The same approach can be achieved with individual "In depth" interview using interview guides, where the response of the interviewee is recorded and then analysed.

2 -Quantitative studies

This type of studies measures with developed scales, in which the questionnaire is structured, open or closed responses of measurable events.

These questionnaires are generally administered in during an interview at the doctor's office (F2F interview); by phone (CATI); through Internet e-mailing, or on a web interface dedicated to this effect.

We have and are committed to update databases containing details of general practitioners and specialists throughout Tunisia.

The analysis is carried out with statistical analysis software such as R , Statistica and SPSS20 and further versions.

The market research report is structured as follows:

- Introduction of the problem
- Description of the settings
- Methodology employed (technique, material of investigation, timing etc ....) recommendations

- Statement of Results
- Comparison with previous studies
- Conclusion and recommendations

Our References

We have already explored the following studies:

- Study on the intentions of the new prescription of macrolides antibiotics
- Study on the intentions of prescription of the new antiepileptic prescription in neuropathic pain.
- Reputation of gastroenterologists and their communication skills
- Market research study of type II diabetes and market perception of GLP1 analogue
- Study of perception of new associations in the treatment of high blood pressure
- Market Research on the prescription of antibiotics in acute infectious pathology of upper and lower respiratory tract.

We also took part in the development of projects within the following studies:

- Image Assessment of antibiotics in the Tunisian market
- Market Analysis for the purchasing of antidiabetics
- Study of innovation for pharmacists: identify the expectations of pharmacists in terms of innovation.
- Market analysis of antiepileptic drugs and unmet needs of physicians' prescribers.

The KOL management using services of Advisory Boards

It is now accepted that becoming a drug depends closely on efforts deployed by its holder to educate prescribers on the various problems encountered in several contexts: coverage insurance by CNAM, comparability with competitors of the same class and keeping them informed along with considering their advice about current and future patterns of innovation for clinical development. The thematic advisory boards that can be tools of conflict resolution, retention, and exploratory marketing methods allow a collection and a relevant exchange with KOLs. Our team reflects on the problem with the Product Manager / Medical Manager client and ensures the organisation and logistics tracking (invitation, local, writing PV of the advisory board, translation if required).

Biostat ICT Department

Technical pool of Poseidon Pharma Company has a great number of computers; one of which is a configured server and connected via a secure wireless internet network.
Some applications for the various projects of the company are hosted in the server and are available by remote access and via secure web platform.
The server has a great capacity of back up; therefore, that minimizes the potential for loss infinitesimal data.

Development

Our contractual developers bring their technical expertise to develop tools to meet the most demanding needs of our customers in terms of fluidity, relevance, and confidentiality.

Thus, we provide services of design, development, and implementation of databases centralized data and forms of electronic compendium called e-CRF (electronic Case Report Form).The use of e-CRF accelerates and simplifies the collection, the validation, and the processing of data. Data

quality is improved through a continuous monitoring by the CRA and the data manager. Data confidentiality is optimal thanks to the allocation of customized grant accesses to the various stakeholders of the study.

Data Management Services

Our department of ICT Biostat offers the best solutions for the study: data transmission on paper, internet or mixed.

- Receipt and registration: Upon arrival, the observation sheets are listed in the database;
- identifying control: immediate detection of misidentified records and follow-up schedules' deviations;
- Input: independent double entry, systematically doubled for discordant variables;
- Coding: dynamic coding system, adaptable to any type of dictionary and evolving final database
- Control data: presence, reasonableness and consistency of data are automatically controlled; all corrections are documented and listed.

Biostatistics Service

When designing the study, our ICT Biostat department may be involved in the following choices:

- Choosing the suitable statistical method to apply
- Writing the Statistical Analysis Plan
- Calculating the number of subjects required
- Creating randomization lists

After collecting all the data in the study, our ICT Biostat department can analyse and, in collaboration with the Studies Committee, write the statistics and clinical report:

- Writing reports according to ICH E3-E9 directives or as customer procedures,
- synthesis of information,
- help plan studies.

Our statistical department can also help you better exploit your data:

- **Statistical analysis:**
  - **Univariate Analysis: description of variables, describing the relationship between variables, correlation, chi ² ...**
  - **Multivariate Analyses:**
    - **multifactorial explanatory model (linear model, logistic model ...)**
    - **Survival analysis (Cox model, survival curves ...)**
    - **Two-way data analysis (patient monitoring).**

In addition, we also provide service through professionals to mandate medical writing articles, collect and write end of trials clinical reports.

Training Service

Our expertise in the field of Clinical Research allows us to offer programmes that ensure a continuing training in the public and the private sector: colleagues from pharmaceutical companies, investigators of a clinical trials or any person seeking to acquire or enrich their knowledge in the field. These programs are constantly updated according to the regulatory issues, pertaining to the development of the drug. The following aspects are covered according to the demand: the following aspects:

- **International regulation of clinical development: Guideline ICH / GCP, the Declaration of Helsinki,**
- **Tunisian and Moroccan regulation of clinical trials,**
- **Operational aspects of a clinical study:**
  - **start-up phases of the study**
  - **Analysis of a protocol,**
  - **Elaboration of monitoring plan,**
  - **the risk-based monitoring, Audit / Source Data Verification**
  - **Management of investigational products,**
- **Aspects of Pharmacovigilance,**
- **Aspects of data management,**
- **Statistical analysis of data of a clinical trial.**

Further information is available on our website:

www.poseidoncro.com

and our subsidiary in Morocco website : www.gayaresearch.com

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