MENA Machine

Maha Al-Farhan at ClinArt International examines legal and regulatory authorities and research ethics committees in the Middle East and North Africa (MENA)

Although clinical trials have been conducted in the MENA region since the 1990s, recently there has been rapid development in the infrastructure of clinical trials. New international players are establishing offices throughout the region, indicating its increasing international profile, and at the same time there are more enquires from physicians for training, or to be considered as investigators in ongoing clinical trials. There are also frequent questions about conducting clinical trials in the region from major pharmaceutical companies and global CROs.

THE QUESTIONS ASKED

We conducted a survey across the region to gain precise, accurate and up-to-date information about active clinical research ethics committees (REC), regional regulatory authorities (RA), the most sought after therapeutic area, and the recommended investigators. Two surveys were constructed, one aimed at RECs and the other at RAs.

The RECs questionnaire was composed of 10 sections:

- General information – this section was aimed at updating our REC contact list, as well as obtaining official information about the history of the REC, recently approved clinical research protocols, the composition of the committee, and hospitals covered by the REC.
- Standard operating procedures – this examined which phases of clinical trials are accepted for review, published SOPs, regulations, guidelines and membership status, such as Office for Human research Protections (OHRP) registration.
- Study protocol submission procedure – this considered the application form, documents to be submitted, any applicable fees, meeting frequencies, interim reporting, safety reporting and the final report.
- Clinical trials agreements (CTAs) – this section investigated the role of RECs in reviewing CTAs, as well as any recommended fee structure and cost of tests and procedure that should be taken into consideration when reviewing a CTA.

Figure 1: Map of the Middle East and North Africa region

- Vulnerable subjects – here we asked who the REC considers to be vulnerable subjects, such as paediatrics, women, the handicapped and prisoners.

- Patient recruitment policy – we asked the REC about their procedure with regards to different patient recruitment methodologies, such as mass media advertising, online advertisement, posters and so on.

- Experienced investigators – we inquired about the most experienced investigators and most active applicants of research proposals. This section helped us differentiate between key opinion leaders who are usually recommended by the sponsor's sales department and good investigators who are eager to contribute to science.

- Electronic case report forms – although the internet is largely available throughout the region, in some hospitals there may be limits to internet access and use of the hospital's IT infrastructure. This question provided a good starting point to recommend sites and to list potential limitations at the study site selection stage.

- Storage of investigational products – this helped us decide the suitability of study sites for any given study protocol. We asked about dedicated clinical trials storage areas and available fridges and freezers. We also asked about access control and the name of the pharmacist responsible for clinical trials.

- Research centres – this section examined which research centres are available in some hospitals, taking into account that more hospitals are seriously considering the establishment of suitably dedicated research centres. We wanted to find out the maximum amount of information regarding these research centres.

The RA questionnaire is very similar to the regulatory questionnaire, but there were additional sections examining:

- Applicable laws

- Networks of REC

- Investigational products importation

THE RESULTS ANALYSED

Twelve RAs responded to our questionnaire: Jordan, Lebanon, Kuwait, Qatar, Bahrain, the UAE, Oman, Saudi Arabia, Egypt, Tunisia, Morocco and Algeria, as well as over 90 RECs. It is worth noting that, initially, few respondents answered all questions in our questionnaire; however, having presented this data at meetings and conferences, we started receiving more spontaneous information. We treat the database as a live document, whereby we apply ongoing updates as new information becomes available to us. We plan to conduct at least one major annual review of all data included in order to ensure its validity.

Table 1: The acceptance of different phases of clinical trials according to country

Country	Phase I	Phase II	Phase III	Phase IV
UAE			✔	✔
Qatar			✔	✔
Oman			✔	✔
Bahrain			✔	✔
Kuwait			✔	✔
Saudi Arabia		✔	✔	✔
Egypt		✔	✔	✔
Jordan	✔	✔	✔	✔
Lebanon	✔	✔	✔	✔
Tunisia			✔	✔
Morocco			✔	✔
Algeria			✔	✔

Ninety-three committees responded to the questionnaire; we checked their OHRP status and we were pleasantly surprised to learn that almost half are registered. We questioned some of those that were not registered with the OHRP for the reason why, and the most common answer was that it was not mandatory. We also asked about their written SOPs, regulations and guidelines: while almost all of the committees stated that they have their own guidelines, only 37 supplied us with their written documents. All except three confirmed that they follow GCP guidelines, with the number of members ranging from 5 to 24. The largest National Ethics Committee is the Jordan Ministry of Health.

As for the submission procedure, all RAs and RECs accept submissions made by principal investigators, 23 would also accept submissions made by study sponsors and CROs, and two RAs and 14 RECs confirmed that they charge a fee that ranges from $500 to $3,000. It is a general requirement that clinical trial agreements and financial compensation are presented in the submission dossier of clinical trials. Often the REC questions the cost implication to the hospital overheads, 13 committees had actually decided a fee structure that includes the institute as well as the investigator. Fee per patients is also scrutinised in order to ensure that the clinical trial in consideration will not abuse hospital resources or implicate additional costs to the patient.

As for accepted practices of advertising for study subjects' recruitment, nine committees have some sort of policy with regard to patient advertisement. The remaining committees do not have such a policy, but they generally agreed that it should be reviewed in order to avoid coercion.

We identified over 520 experienced clinical research investigators working in over 100 hospitals, with the most common approved clinical trials being in the

Table 2: Highly rated clinical research centres in the MENA region

Country	Clinical Research Centre 1	Clinical Research Centre 2	Clinical Research Centre 3
Jordan	King Hussein Cancer Centre	Jordan Hospital	Jordan University Hospital
Lebanon	AUB Medical Centre Foundation	Hotel Deiu	Saint George Hospital
Kuwait	Mubarak AlKabeer Hospital	AlAmiri Hospital	Dasman Center
Qatar	Hamad Medical Hospital	AlAmal Hospital	Weill Cornell Medical Collage – and SIDRA
Bahrain	Salmaniya Complex	Bahrain Defense Force Hospital	
UAE	Sheikh Khalifa Medical City	Tawam Hospital	Rashid Hospital
Oman	Sultan Qaboos University Hospital	Royal Hospital	Nizwa Hospital
Saudi Arabia	King Faisal Specialist Hospital	National Guard Hospital	King Saud/King Abdul Aziz University Hospital
Egypt	Kiser El-Aini	AinShams University	Alexandria University
Tunisia	Farahat Hatched University	Pasteur Institute	Institute of Salah Azaiez
Morocco	Faculty of Medicine and Pharma at the University of Casablanca	Institute Pasteur du Maroc	Centre d'Oncologie Clinique le Littoral
Algeria	Marie Curie Center	MOH Hospitals	

areas of oncology, neurology, endocrinology, haematology, cardiovascular, respiratory, infectious diseases, gastrointestinal, and orthopaedic/rheumatology.

We analysed about 100 hospitals that had participated in the survey to identify the most suitable clinical research sites. Our rating procedure was based on:

- Research infrastructure
- Number of experienced investigators
- History of clinical trials
- Size of the hospital

Table 2 summarises our findings, which are far from exhaustive. Some good sites were excluded from this list due to a lack of response from the hospital research offices.

Eleven committees stated that they routinely accept applications involving eCRFs, with appropriate restricted-access computer areas available. This is not to assume that the remaining hospitals do not accept eCRFs, rather it is an indication for further attention to be given to IT infrastructure when validating sites selected for eCRFs studies – for example, the provision of mobile internet connections and computers. Twenty-four committees stated that they were aware of a dedicated research department in their institute, and a similar number stated that all study medication was stored in specialised compartments in the main hospital pharmacy department under the supervision of a dedicated pharmacist.

Questions directed at RAs were similar to those asked of committees with the addition of a further section related to the importation of investigational product. In order to import study medication/investigational product, regional RAs were in unison in their requirements, stating that they need clinical trial approval and product details, such as name, LOT and batch number, expiry data, certificate of analysis, GMP certificate, certificate of origin, and a copy of the IP label in English and in Arabic. Since most countries in the MENA region do not accept applications for early-phase clinical trials (see Table 1); these regulatory authorities also requested marketing authorisation documents in the country of origin.

CONCLUSION

Our survey has established a road map for conducting clinical trials in the MENA region. We do recommend updating this information twice yearly as laws and regulations are being clarified continuously. It is very important for those planning their studies to have a full understanding of specific capabilities and challenges before considering the region.

Acknowledgment

The author would like to thank the ClinArt team for their contributions and suggestions, and Dr Antoinne Estephan, who inspired the idea of building a database of centres of clinical research excellence.

About the author

Maha Al-Farhan is the chair of the Gulf Countries Chapter of the Association of Clinical Research Professionals (ACRP) – a US-based Association that aims to provide global leadership to promote integrity and excellence for the clinical research profession. Through the ACRP, Maha has coordinated and conducted numerous ACRP-certified training courses in the Gulf and Saudi Arabia, and is actively coordinating networking meetings and conferences. Maha is also a founding member of the first regional clinical research organisation in the MENA region, ClinArt International, where she works as the CEO. **Email:** maha.alfarhan@clinart.net