White Paper

Patient Consent: Key Challenges in the Middle East

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Introduction

`*Agreement*, *permission*, and *authorization*'; three simple words to describe the word '*consent*.' In the clinical research world, informed consent is defined as the legal procedure by which the study participant voluntarily agrees and gives his/her permission to participate in a research study after being aware of the associated risks and benefits of participation.

Countries in the Middle East have recently appeared on the wish list for many sponsors hunting for emerging markets with motivated Investigators, large pool of treatment naïve patients, low number of competing trials and good infrastructure sites, yet sponsors still don't seem confident enough when coming to the region.

Despite these tempting factors the Middle East holds, and, considering the relatively naïve clinical research culture of the region, many sponsors still come with a long list of quality questions, with informed consent being the most important question they ask. This becomes clearly evident during the adaptation or development of the country specific informed consent form (ICF).

EXAMPLE OF THESE QUESTIONS ARE:

"How illiterate patients could be enrolled to trials while they can't read or write?"

"Why a 19-year-old adult can't provide full consent?"

"Can females in the ME consent on their own or do they need their husband's consent as well?"

Addressing these questions mandates going back to have a quick look at the informed consent challenges on both the patients' and investigators' levels.

For investigators

The way ICFs are perceived don't seem to differ between the Middle East and other research-experienced regions. It still goes back to the willingness of the Investigators to comply with the ethical principles and guidelines.

There is no doubt that ICFs are perceived by investigators as a crucial proof that patients were not deceived or coerced into research participation. Yet Middle East investigators are dealing with a research naïve culture where the majority of patients were not involved in clinical studies before and a good percentage might not be even aware of clinical research concepts, and these are all really critical!

Challenges on the investigator level may include:

- Informed consent form (ICF) being relatively complicated and requiring a long time to explain.
- Slightly complex ICF wording that can be difficult for patients to comprehend.
- Longer time taken to explain the concept behind clinical research before going through the study-specific discussion.
- Age of the participating subject and finding the acceptable legal guardian.
- Spoken language in the case of different nationalities.
- Many ICFs for the same study; some studies require patient to sign up to 5 ICFs for the different study procedures.

Nevertheless, and unlike many research-experienced countries, physician investigators (principal or sub-Investigators) are mainly the ones who handle the ICF discussions and provide their signatures as well. It's not common to delegate this role to study nurses or other site staff.

For patients

The majority of the challenges on the patients' level are attributed to the fact that the Middle East is still relatively research-naïve, along with some additional cultural considerations. Yet, despite of those challenges, patients in the ME are very open to new treatment opportunities and eager to participate in similar studies. Some of those patients already are in continuous search of treatment options – especially for orphan medications or diseases for which all available treatment options are consumed – even if it takes participating in other ongoing studies overseas.

Challenges on the patients' level may include:

- ICFs being recently too long and complicated.
- Excessively complex terminologies used.
- Illiteracy.
- Different nationalities and spoken languages.
- Contraception methods used.

At the time of ICF adaptations, according to each country' local requirements, those challenges are taken into consideration and adequately addressed as follows:

ILLITERACY

At this time, the illiteracy percentage is considered high in Egypt and relatively low in other ME countries including Lebanon, KSA, Jordan, UAE, Kuwait, Oman and Qatar.

Impartial witness signature is a mandatory signature field in all Middle Eastern developed ICFs. This signature field becomes applicable for participating subjects who are unable to read/write, thus mandating the attendance of an impartial witness who attends the ICF discussion and reads the ICF to the illiterate patient and finally provides his/her signature as a confirmation that the patient understood and agreed to participate. Contrary to what many people think, it's not mandatory for illiterate patients to provide their thumb prints as a confirmation of the participation authorization.

As part of the local practice, and in order to avoid any bias or unfair influence from people involved in the study, it's always preferable that the impartial witness be independent from the patient and the site staff as well. He/she could be one of the visitors attending the hospital at the same time of patients' consenting.

Impartial witness may be also applicable for blinded patients, unless other arrangements are already taken by similar patients in signing Legal documents or if the study of course has its own instructions of handling similar cases.

AGE/MARITAL STATUS OF THE PARTICIPATING SUBJECT

As per ICH GCP, a legally acceptable representative (LAR) is an individual or body authorized under applicable law to consent on behalf of the subject. In addition, it's the first option ICH GCP goes to in case the subject is unable to read/write.

Yet, in many Middle Eastern countries, a legally acceptable representative, as per the local law, should hold a legal document to prove his/her delegation to represent the subject in legal transactions.

Unfortunately, this is not common for illiterate patients to find, which is why an impartial witness is the first option to go for in similar cases.

Legally Acceptable Representative field is applicable in the following cases

- In the case of minors: Legal age differs between Middle Eastern countries. All Middle Eastern countries consider any individual 18 years and above as an adult subject who is able to consent for himself/herself. However, for Egypt and Kuwait subjects below 21 years of age are considered minors and should be accompanied by Legally Acceptable Representatives/Guardians (Mother/Father). Both the minor and parent(s) should sign.
- Husbands as Legally Acceptable Representatives: Only in some sites in the KSA and Kuwait can husbands be added as legal representatives, especially in trials involving data collection on the female subject's newborns. Other than that, no Local laws or regulations in the Middle East mandate having the husband's signature if his partner is enrolled in a study.

DIFFERENT NATIONALITIES AND SPOKEN LANGUAGES

The different nationalities and spoken languages are common challenges faced in some of the Gulf countries, particularly the UAE, the KSA and Kuwait. As of the time of this writing, expats make up 77% of the UAE population. They also make up a high percentage of the population in Kuwait and the KSA. This makes it really difficult to expect which language a study participant will be speaking. And while the option of ICF translation to different languages is valid, not all ECs accept reviewing languages other than English and Arabic.

One of valid option provided is translations. A translator is someone who speaks the primary language of the patient and the ICF language as well. A translator will attend the ICF discussion and help the patient express themselves and elaborate effectively to the ICF. This mandates that the patient understands, to a good extent, the ICF's language, which will most probably be English.

We also need to consider the fact that Arabic is the primary and most prevalent spoken language in the Middle East, unlike other countries where more than 15 languages are spoken. While this may not be the case for Gulf countries, where expats are working, it is addressed as stated above.

USE OF CONTRACEPTION:

While each study protocol allows the usage of certain contraception methods, not all are approved by ethics committees in sites in the Middle East. Tubal ligation and vasectomy are examples of the unallowed contraception methods since both involve sterilization, which is prohibited from the religious perspective.

Alternatively, sexual abstinence is an acceptable contraceptive method, especially for single ladies.

Conclusion:

These apparent challenges should call for investigators, institutional review boards and regulatory authorities to find ways to raise clinical research awareness to improve the society's understanding.

Advertisement to patient through social media will soon be required for COVID-19 vaccination studies.

Additionally, extended discussion with educators should be developed to address these challenges.

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