Cromos Pharma's update on registration of medical devices in Russia

The purpose of this white paper is to discuss the new regulatory requirements for registration of medical devices that were put forth by the Russian government on December 27, 2012[1].

January 1st, 2013 has *supposedly* marked the end of the era of vagueness in the field of medical device registration in Russia. Prior to this date, device manufacturers had no clear understanding of what processes to follow when it came to submission; what questions, quarries and deadlines to anticipate. The guidelines as to which governmental agency was responsible for which step of registration process were unclear. All these uncertainties are now in the past, or are they not?

What has changed?

1. Now device registration essentially follows the path of drug registration (please also see our recent white paper on new rules in drug registration[2]).

2. RosZdravNadzor[3] (RZN, Russia's equivalent of FDA) is now in charge of registration process.

3. The process of registration can be separated into 3 phases:

   - Application to assess feasibility of clinical trial of the device;

   - Permit to conduct such a trial followed by a "halt" of registration process;

   - Removal of a "halt" when the study is completed, followed by data analysis and the final decision.

4. In much the same way as established the current guidelines for drug trials, the Central Ethics Committee (CEC) of the Ministry of Health (MoH) will be responsible for the "Central IRB" approval. What is different is that the CEC approval does not appear to be a necessary prerequisite of the clinical trial approval by the RZN.

5. New guidelines clearly specify the timelines for each step of registration process. If these guidelines are adhered to, then the "regulatory" part should not exceed a total of 3 months.

6. Certificates of use for currently registered devices will be "grandfathered" and will not require recertification: certificates with a fixed term of validity will remain valid until the expiry date, while those with no fixed term will only need to be replaced by January 1, 2014 on the basis of an application letter and information specified in the new guidelines.

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1 http://www.government.ru/gov/results/22216/

2 http://cromospharma.com/en/whitepapers

3 http://www.roszdravnadzor.ru/

7. Medical devices submitted for registration before the enactment of the new guidelines will be registered on the basis of documents already submitted and an application letter which has to conform to the new guidelines (i.e. old submission dossier + new application letter).

What is still unclear?

1. What processes and which guidelines need to be followed when making a decision on which device will be allowed to undergo clinical testing? This is critical as refusal to allow clinical testing automatically disqualifies the device for any further consideration for regulatory approval.

2. The aforementioned issue of parallel MoH ethics approval and RZN approval of clinical trial conduct. It appears that current regulations do not view ethics approval as a prerequisite for the latter. We find this to be rather perplexing. How the MoH and RZN will resolve this issue remains to be seen.

3. Only selected medical centers will be allowed to conduct clinical trials of medical devices and will have to meet certain criteria, which are to be set forth by the MoH. There is no clarity on how these criteria are going to be determined. What makes this issue even less unambiguous, is the fact that RZN, and not the MoH, will be responsible for assessing the eligibility of these sites.

4. The process of replacement of existing certificates of use. While the certificates without expiry date will not require a full-scale "re-registration", the information contained in the application for replacement has to meet the new guidelines. The process of how this will be determined and what action will be necessary if the information is not complete is not addressed.
   The process of renewal of existing certificates that do have an expiry date is not defined either. One should worry that at the time of recertification the regulatory body may request the medical device in question to undergo a full registration procedure. While this scenario is not very likely, this subject is not addressed in the current set of rules and regulations.

5. Neither there is a defined framework for the sample size, duration, nor for the statistical power of the trials that must be performed. It is also unclear what type of studies will be requested. The glossary that describes clinical trials is rather imprecise[4]. This leaves a lot of leeway for the expert groups within the regulatory bodies and may significantly influence the complexity of requested studies.

6. Unlike drug registration, where participation of Russian patients in the pivotal international clinical trial allows for fast track registration, this rule does not appear to apply to medical devices.

Conclusion

While the new regulatory requirements offer some guidance to the medical device companies, the number of unknowns remains prohibitively high. Historically, based on the experience of recent changes in drug registration procedures[5], such lack of clarity may result in confusion within the regulatory agencies and could lead to significant overall delays in registration process.

We will continue to monitor this topic and will provide you with all pertinent updates as soon as they become available.

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[4] "clinical trials" - designed and planned systematic studies, ***including those involving human subjects*** undertaken to evaluate safety and effectiveness of medical devices

[5] http://www.government.ru/gov/results/22216/