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European Federation of Pharmaceutical Industries and Associations

Position Paper

EFPIA Russia network Position Paper: Redundant Quality Control Testing of Pharmaceutical Products as Part of the Clinical Trial Authorisation – Final, 19th March 2013

Background

Clinical trial sponsors are required by international regulation and guidance to ensure consistent quality control of clinical trial product manufacturing and supply in compliance with Good Manufacturing Practice (GMP). In Russia, according to Federal Law #61, implementation of local cGMP standards is expected for 2014.

Key Statements

Additional local quality control testing of pharmaceutical products as part of a Clinical Trial Authorisation is considered redundant for companies already manufacturing under GMP. Such redundant quality testing has the potential to delay the start of clinical trials without increasing public health. It could delay or impede early patient access to life saving medicines, and create an unnecessary burden for regulatory authorities and sponsors. Due to the added complexity and delays to obtain clinical trial data in Russian patients, industry is concerned that this proposed change to the legislation could potentially lead to exclusion of Russia from clinical development.

Clinical trial materials are manufactured and controlled in compliance with GMP

In line with EU guidance and Regulation, all pharmaceutical products intended for use in European clinical trials have to be manufactured according to GMP. Thus, manufacturers/sponsors conducting trials in Russia (or globally) are subject to risk-based periodic Agency inspections, to demonstrate ongoing compliance with GMP requirements and quality control regulations as recommended by the World Health Organization (WHO). The rationale for conducting inspections is to provide regulatory agencies with the confidence that a manufacturing site, the relevant quality system and its related processes are under regular control and thus proven to consistently manufacture products of high quality according to agreed specifications.

Product quality control strategies extend beyond the sponsors manufacturing facility. Manufacturers/sponsors also have to provide assurance that product quality is controlled with the transport and distribution network by using qualified transport containers and impact assessment of potential temperature excursions during transportation and storage on the quality of the clinical trial material. This part of the quality supply chain is also subject to guidance and regulation.

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Global Clinical Trials

In almost all countries where global clinical trials are conducted, a prerequisite to start a clinical trial is the Ethics and Health Authority approval of the CTA.

In EU member states, the approval timeline for a CTA is usually within 60 days. Other major and emerging markets have a similar timeline. Such rapid assessment and approval is crucial to ensure participation of the country in global trials and is therefore essential for local patients' access to innovative medicines.

No country worldwide requests additional governmental quality control testing, as part of the clinical application, except for China which currently retains testing for biological/biotechnology products. This re-testing at the Chinese governmental laboratories significantly contributes to the prolongation of the approval process (to approximately 18 to 20 months) which makes it very difficult for China to participate in global clinical programs. A similar effect, i.e. significantly prolonged approval timelines and potential exclusion from clinical development, is anticipated with the proposed change to the Russian legislation to include the local retesting of clinical trial material as part of the approval process.

Challenges related to implementation of test methods in governmental laboratories

The current legislative proposals will impose additional cost and logistical complexity to ensure continuity of supply for both local and multinational manufacturers as well as Russian Ministry of Health. Re-testing during clinical development takes significant time in order to implement all the test methods at governmental laboratories. This may result in a lack of access, or delayed access of medicines to patients. In addition, clinical trial material typically has a limited shelf-life. Additional time taken to locally test and release clinical material will effectively further shorten this time. Additional time can be required to resolve false out of specification results, due to inappropriate reproducibility of tests and thus potentially causing interrupted patient supply.

Additional product testing may be expensive, difficult to implement and to perform, especially for biological/biotechnology products. Consequently, the Russian Authorities will need to allocate significant resources for equipment and personnel to perform this testing, which may be extremely complex given the nature of many assays (e.g. biological potency assays). Further, government laboratories may not have the proper equipment and biological-originated materials (e.g. indicator cell, antibody). In any case, a huge effort will be needed to established the set of methods, which may be used only once for the release of one clinical batch. Given the changes during development, the final QC methods used for testing of commercial products (in case of marketing) may be significantly different from the clinical methods.

Conclusion

Industry is concerned that this proposed change to the legislation to implement governmental QC testing of clinical trial materials may have the opposite effect of trying to attract clinical studies and investment in Russia. The proposed change will significantly delay CT assessment and approval, resulting in restrictive or almost prohibitive approval timelines, which is not competitive with the EU, the US or other emerging markets.

In order to include Russia early into global clinical programs and/or to ensure that Russian patients can benefit from access to innovative medicines as fast as possible, we strongly propose, that an exemption to local quality re-testing is granted under circumstances where a manufacturer or a manufacturing facility of a pharmaceutical product:

- Provides evidence that their product manufacturing, testing and storage/transportation systems are well controlled;
- Has implemented a proper quality system to assure compliance; and
- Is under regular control of globally recognized inspectorates

A clear and timely waiver request process would ensure continuous inclusion of Russian sites in clinical studies sponsored by industry. This would subsequently allow for exposure of Russian investigators to global clinical trials, would ensure early patient access to innovative and life-saving drugs, provide an opportunity for Russian authorities to query product quality, and as described above, provide further incentive for full GMP implementation in Russia.

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