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PART I: Background Information

The Clients approached the Attorney with the request to provide legal opinion on the matters related to conducting of Clinical Trials in the territory of Georgia. After reaching an agreement on provision of legal services as described in the Proposal of December --, 2016 (representing integral part of this Opinion Letter), the Attorney and the Clients engaged into the confidential arrangement. It is therefore understood that the person receiving this document for any purpose from the Clients are bound to keep this document private and confidential and do not disclose its content to the third parties without prior approval of the Clients or the Attorney.

This Opinion Letter describes the rules and procedures applicable to conducting of the Clinical Trials in the territory of Georgia. It does not extend to the regulations relevant to obtaining general license of medical activities by the laboratory or facility or the individuals to be engaged in the Clinical Trials. Neither is this Opinion addressing the issues related to import or export of pharmacological products or obtaining any permit/authorization for realization of such products on the market.

PART II: Documents Reviewed and Inquires Made

In rendering the Opinion Letter, we have examined and relied upon the following normative acts, documents and inquires made:

1. Law of Georgia on Licenses and Permits, dated July 18, 2005;
2. Resolution 176 of the Government of Georgia Approving Rules for Issuance Permits and Conduct of Clinical Trials of Pharmacological Products, Pharmaceutic Manufacturing, Authorized Pharmacy, Import or Export of Special Control Substances, dated October 14, 2005;
3. Law of Georgia on Medicines and Pharmaceutical Activities, dated April 17, 1997;
4. Order #233/o of the Minister of Labor, Health and Social Protection of Georgia on Recognition of Standards and Guidelines for Clinical and Pre-Clinical Trials of Medicines, dated August 4, 2010;
5. General Administrative Code of Georgia, dated June 25, 1999;
6. Law of Georgia on License and Permit Fees, dated August 12, 2003;

7. Law of Georgia on Personal Data Protection, dated December 28, 2012;
8. ICH Harmonised Tripartite Guideline for Good Clinical Practice E6(R1), dated June 10, 1996;
9. ICH Harmonised Tripartite Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals M3(R2), dated June 11, 2009.

PART III: Assumptions and Limitations

- The Opinion Letter is based on the facts and information communicated to us by the Clients;
- Decisions of the regulatory authorities to grant or revoke the permits under the applicable legislation fall within the discretion of respective administrative bodies; therefore, this Opinion Letter may not be interpreted as the guarantee that the respective permit will be issued even if the rules and procedures described below are fully met;
- The Opinion Letter is addressed to the Client at the explicit request and may not be disclosed or relied to any other person or the company without the prior approval of the Attorney;
- The Opinion Letter is strictly limited to the matters addressed herein and is not to be used or extended by implications of any other matters, whether in connection with the Opinion Letter or otherwise;
- The date of e-mail to which the opinions expressed herein apply is December 19, 2016 unless otherwise specified herein.

PART IV: Legal Overview

1. Applicable Legislation & Regulatory Supervision

Conduct of the Clinical Trials represents one of the limited types of activities requiring the special permit under the Law of Georgia on Licenses and Permits (*hereinafter* the Law on Permits). [1] Consequently, the Law on Permits represent the major law determining the procedures for obtaining the permit for conducting the Clinical Trials in the territory of Georgia.

[1] Art. 22.44 of the Law of Georgia on Licenses and Permits, dated July 18, 2005 (as amended) (official English translation available at: https://matsne.gov.ge/en/document/view/26824).

Specific rules and procedures applicable for obtaining the clinical trial permit is regulated by the Resolution #176 of the Government of Georgia (*hereinafter* the Resolution #176). [2] The Resolution #176 is a sub-legislative normative act setting out the detailed rules for issuing clinical trial permits.

While the Law on Permits and the Instruction establish the legal regime for obtaining the required permit, conduct of the Clinical Trials do also fall under the general scope of application of the Law of Georgia on Medicines and Pharmaceutical Activities (*hereinafter* the Law on Pharmaceutical Activities). [3] As the main legislative act in this field, the Law establishes a legal framework for regulating the circulation of pharmaceutical products and the rights and obligations of natural and legal persons. [4]

Georgia is part of international cooperation in this field. Except for its membership of World Health Organization (WHO), it also enforces standards adopted by International Conference on Harmonization (ICH). On August 4, 2010, the Ministry of Labor, Health and Social Protection (*hereinafter* the Ministry) enforced the two documents adopted by ICH: Guideline for Good Clinical Practice GCP E6, 1996 and Guidance on NonClinical Safety Studies M3, 2009. [5] According to this Order, the two standards became the officially applicable to conducting the clinical and pre-clinical trials of medicines in Georgia.

Conduct of clinical trials is regulated by the Legal Entity of Public Law – State Regulation Agency for Medical Activities (*hereinafter* the Agency) under the Minister of Labor, Health and Social Protection of Georgia. The Agency is responsible for issuance the clinical trial permits and supervision and control of the regulated activities in the Country. [6]

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[2] Resolution 176 of the Government of Georgia Approving Rules for Issuance Permits and Conduct of Clinical Trials of Pharmacological Products, Pharmaceutic Manufacturing, Authorized Pharmacy, Import or Export of Special Control Substances, dated October 14, 2005 (as amended) (Georgian version available at: https://matsne.gov.ge/ka/document/view/10492).
[3] Law of Georgia on Medicines and Pharmaceutical Activities, dated April 17, 1997 (as amended) (official English translation available at: https://matsne.gov.ge/en/document/view/29836).
[4] Art. 1.2 of the Law on Pharmaceutical Activities.
[5] Order #233/o of the Minister of Labor, Health and Social Protection of Georgia on Recognition of Standards and Guidelines for Clinical and Pre-Clinical Trials of Medicines, dated August 4, 2010.
[6] Georgian language web-page of the Agency is accessible at: http://rama.moh.gov.ge/geo).

2. Major Terminology and Definitions

Before describing the rules and procedures applicable to obtaining the clinical trial permit, we would like to provide definitions of major terms in the Georgian legislative framework.

> *Pharmaceuticals (therapeutic agents) - medicine or a physiologically active substances derived naturally or by synthesis, or their combination, allowed for medical use, including complementary medicinal products, biologically active additives and paratherapeutic products that are voluntarily registered under the National Regime of State Registration of Pharmaceutical Products.*[7]
>
> *Pharmacological Product - a substance or a combination of substances of an established pharmacological activity and safety, which is an object of a clinical trial.*[8]
>
> *Pre-clinical trial of a pharmacological product - a pharmacological, toxicological and other type of study of a pharmacological product to determine its specific activity and the level of impact on the physiological system, which is not conducted on humans.* [9]
>
> *Clinical trial (testing, research) of a pharmaceutical product – the study of the impact of a pharmacological product on a human organism to identify adverse reactions and to assess the efficacy and safety levels.* [10]

3. Rules & Procedures for Obtaining the Clinical Trial Permit

As already mentioned above, the body authorized to issue the clinical trial permit is LEPL – State Regulation Agency for Medical Activities. The Agency administers the process nationwide and ensures maintenance of the permitted clinical trials around the Country. [11]

Unlike the licenses, which are issued to authorize specific activities by the license-seekers, [12] permit is an authorization to carry out specific action for the definite or indefinite term. [13] Unless

[7] Art. 1^1.13 of the Law of Georgia on Pharmaceutical Activities.
[8] Art. 1^1.35 of the Law of Georgia on Pharmaceutical Activities.
[9] Art. 1^1.36 of the Law of Georgia on Pharmaceutical Activities.
[10] Art. 1^1.45 of the Law of Georgia on Pharmaceutical Activities.
[11] The Registry may be accessed at: http://pharmacy.moh.gov.ge/Default.aspx in Georgian language).
[12] Art. 3(a) of the Law of Georgia on Permits.
[13] Art. 3(e) of the Law of Georgia on Permits.

otherwise determined by the law, permit is generally transferrable and is evidenced by the permit certificate issued by the authorized body. [14]

As the major legal act regulating issuance of permits, the Law of Georgia on Permits determine the basic procedures and documents required for the permit seeker to consider the request. According to art. 25 of the Law of Georgia on Permits, the following documents shall be submitted by the clinical trial permit seeker:

a) Written application, including the following data: [15]

i. Title of the administrative body authorized to issue the permit – the Agency;

ii. Identity and address of the applicant;

iii. Request;

iv. Date of application and signature of applicant;

v. List of annexes, if any.

b) Identity/corporate documents of the applicant shall be attached;

c) Certificate proving payment of the permit fee – GEL 200. [16]

Except for the documents mentioned above, the permit seeker shall also submit the following documents for obtaining the clinical trial permit under art. 4 of the Resolution #176:

e) Clinical trial protocol: describing basis, goal, objective, research methodology, organization and conditions of the clinical trial. The protocol shall include the following basic data:

i. Title of the clinical trial;

ii. Phase of the clinical trial;

[14] Art. 3(e) and 3(f) of the Law of Georgia on Permits.
[15] Art. 25.1 and 25.2 of the Law of Georgia on Permits; art. 78 of the General Administrative Code of Georgia, dated June 25, 1999 (official English translation is available at: https://matsne.gov.ge/en/document/view/16270).
[16] Art. 724 of the Law of Georgia on License and Permit Fees, dated August 12, 2003 (official English translation is available at: https://matsne.gov.ge/en/document/view/12880).

iii. List of the research facilities conducting the trial;

iv. Goal of the trial;

v. Description of the trial procedures;

vi. Rule for taking medicine by the patient;

vii. Description of laboratory and diagnostic procedures;

viii. Criteria for engaging and dismissing patients from the trial;

ix. Number of patient visits and overall duration of the trial;

x. Sample of informational letter for the patient;

xi. Sample patient consent letter;

xii. Decision of ethics commission;

xiii. Materials of pre-clinical trial or pharmacopeia article considering safety risks of pharmacological product. In case of international trials, pre-trial materials may be submitted in English or Russian language;

xiv. Sample individual profile for patient;

xv. Information about qualification and experience of the researcher;

xvi. Document proving license or accreditation of the medical facility conducting clinical trial.

Clinical trial permit is issued for the term of the trial as per the request of the permit seeker. [17]

Procedures applicable to issuance of the permit:

[17] Art. 8(b) of the Resolution #176.

a) Submission of application – application shall be registered and given special registration number; proof of registration shall be given to the permit seeker immediately upon request. [18]

b) Checking technical compliance of the application – authorized body shall verify technical compliance of the application within three business days after application; if the application is technically deficient, additional time shall be given to the applicant, which cannot be less than five days; this time may be extended once up to fifteen days upon request of the applicant. [19]

c) Rendering decision on granting the permit – shall be made within twenty days after application; the term may be extended up to six months if the special circumstances justify additional term; decision on extension shall be made within fifteen days after application. [20] Failure of the authorized body to issue or reject permit within the determined time equals granting of the permit. In such case, the permit certificate shall be issued immediately. [21]

Permit may be refused only if: [22]

a) The application is not duly submitted and the applicant fails to correct the defect within the time determined by the administrative body;

b) The applicant fails to meet the criteria for obtaining the permit as established under the law;

c) The applicant is prohibited from carrying out the relevant activities based on the guilty verdict of the court.

Refusal to grant the permit may be appealed in the higher administrative body or the court of law. [23]

[18] Art. 79.2 of the Administrative Code of Georgia.
[19] Art. 83 of the Administrative Code of Georgia.
[20] Art. 26 of the Law of Georgia on Permits.
[21] Art. 26.10 of the Law of Georgia on Permits.
[22] Art. 27 of the Law of Georgia on Permits.
[23] Art. 28 of the Law of Georgia on Permits.

4. Compliance Control

After obtaining the clinical trial permit, the permit seeker may commence the activities immediately. However, conduct of the trials in accordance with the permit terms and the applicable legislation is supervised and controlled by the permit issuing authority, namely the Agency. The supervision may be carried out in the form of random selective site visits.

Georgian law does not determine specific rules and procedures for conducting clinical trials in the Country. However, according to the Order #233/o of the Ministry, standards established under the two ICH documents: Guideline for Good Clinical Practice GCP E6, 1996 [24]and Guidance on NonClinical Safety Studies M3, 2009 apply. [25]

Except for the international standards to be followed during the clinical trials, general laws applicable to the process should also be observed. One of the most relevant normative acts in this field may be the Law of Georgia on Personal Data Protection. [26] The Law requires due observation of personal data processing regulation and reporting with the Personal Data Inspector in accordance with the applicable legislation.

Should you have any question or need for additional information, do not hesitate to contact us anytime!

Regards,

Jaba Gvelebiani

[24] ICH Harmonised Tripartite Guideline for Good Clinical Practice E6(R1), dated June 10, 1996 (available at: https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf).
[25] ICH Harmonised Tripartite Guidance on Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals M3(R2), dated June 11, 2009 (available at: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Multidisciplinary/M3_R2/Step4/M3_R2__Guideline.pdf).
[26] Law of Georgia on Personal Data Protection, dated December 28, 2012 (as amended) (English translation is available at: https://www.ilo.org/dyn/natlex/docs/ELECTRONIC/90399/118656/F1892628043/GEO90399%20Eng.pdf).