WCG Foundation Pilot Expanded Access Project
Request for Proposals

Statement of Purpose

WCG Foundation wishes to engage several organizations with institutional review boards (IRBs) to conduct full board reviews of single-patient expanded access (compassionate use) applications. Currently, some IRBs are reluctant to review single-patient expanded access applications because they lack experience or expertise with such applications and/or because of the costs associated with a full board review. At the same time, there are both institutionally based and independent IRBs that established and have procedures to conduct high-quality reviews of single-patient expanded access applications efficiently. The purpose of the Pilot Expanded Access Project, therefore, is to provide a standardized regulatory review for expanded access applications with the intent to increase access for desperately ill patients in need of these treatments. WCG Foundation wishes to engage IRBs who will use standard procedures to conduct high-quality reviews with a timely turn-around time.

Organizational Background

WCG Foundation is a public charity (501(c)(3)) with a mission to strengthen research protections and improve health and well-being worldwide. The Foundation has two initial priorities: 1) To get experimental medicines to patients in desperate need and 2) To support research ethics education so that, no matter where a study is conducted, it is overseen by skilled professionals whose first commitment is to the safety of the research participants.

This request for proposals is part of WCG Foundation's first priority to get experimental medicines to patients in desperate need with the aims to advance IRB practice and reduce the financial burden on patients.

Background Information

Clinical trials are the best way to discover new safe medicines. Use of an investigational medical product by a patient enrolled in a clinical trial is preferable to use outside of a trial because well-run clinical trials with sufficient numbers of participants can generate data that lead to the approval of products and, subsequently, to wider availability for all patients.

The Food and Drug Administration (FDA) has an expanded access program, often referred to as "compassionate use," which provides a pathway for patients to gain access to investigational drugs, biologics, and medical devices for patients in **non-emergency** situations, but with serious diseases or conditions, who are ineligible or unable to enroll in a clinical trial.

Patients are eligible for FDA's expanded access program when they have a serious or immediately life-threatening disease or condition and their physician has found an investigational new drug (IND) that the physician believes could be beneficial to the patient. FDA requires that the patient's physician seek approval from the pharmaceutical company, the sponsor, to obtain the IND. If the sponsor approves the request, the physician applies to FDA for

approval to access the IND. On June 2, 2016, FDA released Form 3926, a streamlined submission form, for physicians to use to make these requests.

FDA must determine for these patients that:

- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
- The patient cannot obtain the drug under another IND or protocol.
- The potential benefit to the patient justifies the risks of the treatment use and those risks are not unreasonable in the context of the disease or condition to be treated.
- Providing the IND will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the expanded access use or otherwise compromise the potential development of the expanded access use.
- The patient's physician is willing to manage the use of the IND and the patient's medical care. This includes discussing risks and benefits, obtaining all required informed consent and IRB approval, reporting adverse events and outcomes, and submitting the necessary paperwork to FDA (including Form FDA 3926).

IRBs must follow the requirements in 21 CFR 56 to approve the request for single-patient use and ensure that an appropriate consent process and document are used.

General principles governing informed consent include:

- Adult patients with capacity must give informed consent (i.e., should understand and be willing to accept the known and unknown risks and unknown effectiveness associated with the investigational product and understand any costs for using the product that may be required).
- Pediatric patients must have the permission of at least one parent. The patient's assent is preferred, but not essential (e.g., treatment will be based on the parent's authorization).
- Adult patients without capacity must have the permission of a representative who is authorized under FDA regulations and state law to give such permission (documented by attestation from the treating facility legal counsel).

This Request for Proposal (RFP) does not include expanded access for intermediate size patient groups or widespread treatment use. This RFP does not include emergency requests where treatment may begin without prior IRB approval, provided the IRB is notified of the emergency treatment within five (5) working days of treatment (in accordance with 21 CFR 56.104(c)) .

Project Goals and Target Audience

In this Pilot Expanded Access Project, WCG Foundation has three goals: 1) provide a core group of experienced IRBs to assist physicians whose patients are seeking access to experimental treatments but are unable to pay for the cost of IRB review; 2) through the core group of IRBs, streamline the IRB process by standardizing the IRB application, provide guidance to the IRB community on how to review expanded access applications, and ensure that IRBs have mechanisms to conduct reviews quickly; and 3) educate the broader national IRB community on

using a streamlined IRB process so that standard, efficient IRB practices are used throughout the U.S.

The immediate target audience is independent and institutionally based IRBs. WCG Foundation will engage with several different types of IRBs in order to evaluate procedures to ensure high-quality and timely reviews that occur in a manner that is the least burdensome to physicians/investigators, treatment facilities and IRBs. The ultimate outcome is to improve the quality and accessibility of IRB review, and decrease the IRB approval time for desperately ill patients who seek access to experimental medicines, thereby maximizing their chances for a positive outcome.

Scope of Work and Deliverables

There are three components to the scope of work: 1) publication of service availability on IRB's website, 2) process to review and approve single-patient expanded access applications, and 3) evaluation of the process.

1. Publication of service availability:

Each recipient of the award by WCG Foundation will publish on its website that it will provide IRB reviews of single-patient expanded access applications for patients/physicians who are not able to pay the IRB fee or who do not have ready access to an IRB. The organization may advertise in other venues that it is a recipient of the award by WCG Foundation.

All text about the award must be approved by WCG Foundation prior to its publication.

2. Process to review and approve single-patient expanded access applications:

Upon submission of a single-patient expanded access application to an IRB operating in accordance with FDA regulations, the IRB must:

- Confirm the medical evaluation of the patient's condition based on the information provided by the requesting physician. This evaluation must be completed by an IRB member or consultant who is a physician and experienced in the condition/disease. This individual must be able to confirm or deny the claim that there is no comparable or satisfactory alternative available.
- Ensure that informed consent or appropriate permissions will be obtained and documented. Given the compassionate nature of the request and FDA's involvement, consent documents should meet the requirements listed in 21 CFR 50.25, using plain language that is specifically aimed at "patients" who expect direct benefit, as opposed to "subjects" who may not expect benefit.
- Receive documentation that FDA has made its determinations regarding safety and effectiveness and has given clearance for the use.
- Review the physician's treatment plan (or sponsor-provided treatment protocol) and determine that it makes adequate provision for ensuring the safety of the patient including

adequate monitoring (timing and type of tests/exams, etc.) and appropriate plans for collecting and reporting the data.

- Use a reasonable process to determine whether the patient or the patient's treating provider or institution has the ability to pay the IRB fee, when the IRB charges a fee.
- Confirm the provisions of 21 CFR 56.111 (and, for INDs to permit single-patient use with children, 21 CFR 50.52) are met.

In addition, under this RFP the IRB must:

- Use FDA Form 3926 along with a draft consent document as the IRB application form. Do not require the submission of a protocol beyond the physician's treatment plan.

- Use the above guidance to conduct the IRB review to determine that FDA requirements at 21 CFR 50 and 56 are satisfied.

- Have a mechanism to convene an IRB meeting to review such applications and respond to the physician/investigator within 72 hours, from date of receipt of the application. In addition, the IRB must be able to conduct a review and respond within 24 hours when disease or condition requires an immediate response.

3. Evaluation:

Submit a quarterly report to WCG Foundation that describes the number of single-patient expanded access applications reviewed under the services agreement. The IRB may report other such reviews that are conducted, but not reimbursed by WCG Foundation. Describe in the quarterly report any problems in the use of FDA Form 3926 as the IRB application form, any problems in using the guidance above in conducting IRB review, and any other problems in conducting reviews. Provide a tabulation of the turn-around time from receipt of submission until decision is reported to the physician/investigator. Provide any suggestions or comments that might be helpful in streamlining the IRB process for future review of such applications.

Services Agreement

Selected IRBs shall be required to enter into a Services Agreement with WCG Foundation in form and substance required by WCG Foundation. Such Services Agreement shall typically have a term of one year, renewable for additional one year terms based on availability of funds and performance by IRB. The Services Agreement may be cancelled by either party without cause with thirty (30) days advanced written notice.

Payments

IRBs will be paid $1,000 for each review that is conducted for a patient reasonably determined to be unable to pay, up to 15 reviews during the contract period.

Invoices are to be submitted quarterly. Payment of the invoice will occur within 30 days provided the appropriate documentation is submitted with the invoice.

Invoice must include the number of reviews conducted and justification that each IRB review meets the financial criteria described in policies and procedures.

Contractual terms and conditions

The Services Agreement will contain customary terms and conditions required by WCG Foundation, including requirements that the IRB and organization provide WCG Foundation with access to relevant policies, procedures, and information regarding services rendered pursuant to the Services Agreement, provided that any such policies and procedures will remain the property of the IRB or organization

Evaluation and Award Process

Proposals will be evaluated by an external review committee established by WCG Foundation. Criteria for scoring applications include, but are not limited to, the following:

- General IRB policies and procedures meet FDA regulatory requirements found at 21 CFR 50 and 21 CFR 56. If the organization is AAHRPP-accredited, indicate the date of the most recent accreditation and status of accreditation. If not AAHRPP-accredited, submit general IRB policies and procedures.

- IRB policies and procedures to conduct initial and continuing review of single patient expanded access applications meet FDA regulatory requirements found at 21 CFR 812.305 and 310. Policies and procedures should differentiate between non-emergency expanded access and emergency expanded access.

- Policies and procedures to convene a full board meeting and communicate to physician/investigator within 72 hours (within 24 hours if immediate response is required).

- Policies and procedures to accept single-patient expanded access applications during non-business hours.

- Policies and procedures for communicating directly with, and monitoring of the treatment site and physician.

- IRB's experience in reviewing single-patient expanded access applications.

- Policies and procedures for determining that neither the patient nor the physician submitting the single-patient expanded access application can pay for the review.

- Number of and experience of staff who handle single-patient expanded access applications.

- Number of and expertise of physician IRB members who review single-patient expanded access applications.

Format for Proposals

Proposals must be submitted in PDF format and are limited to five pages. Proposals must address all the evaluation criteria in the proposal. Policies and procedures are submitted as a supplement. All policies and procedures must be clearly labeled and correspond to one of the selection criteria. Do NOT submit all IRB policies and procedures; they will not be reviewed and the application will be considered non-responsive.

Structure of Proposal

1. Description of organization/IRB
2. Approach to address the scope of work
3. Policies and procedures to review, approve, and monitor, as needed, single-patient expanded access applications
4. Plan to publish announcement of award on website, if selected
5. Evaluation and reporting plan
6. Experience with single-patient expanded access
7. Staff capacity and expertise
8. IRB expertise

Process Schedule

August 29, 2016	Proposals in PDF format are due electronically by 5 pm EDT.
September 20, 2016	Follow-up with finalists
September 30, 2016	Announcement of awards

Point of Contact

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