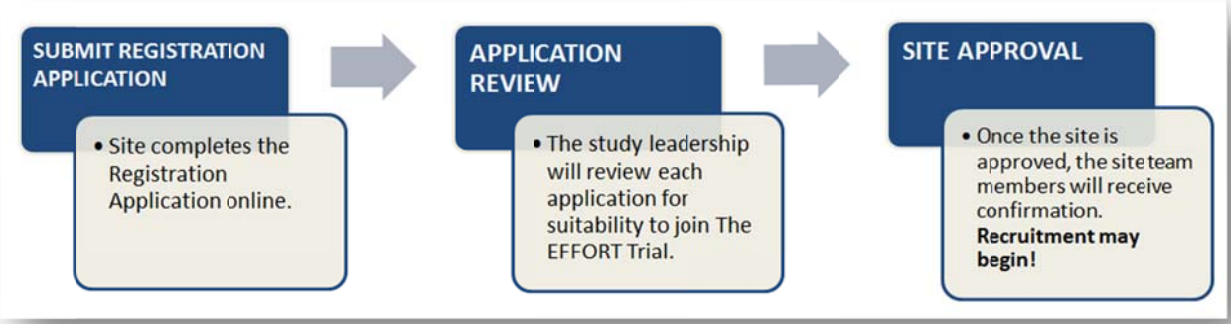
SECTION 2: REGISTER YOUR ICU

Contents

Site Registration and Activation

ICUs from around the world will voluntarily register their interest in participating in the EFFORT Trial. Site registration is the formal process where an interested site submits an application to join. Once the study leadership has reviewed the registration application, formal approval will be granted and the site may begin study recruitment activities. The figure below outlines this process.

Figure 3: Overview of Site Registration



Before you register

Is your Site Suitable?

The first thing to consider before deciding to register is whether your ICU is suitable to participate in the EFFORT Trial. To be considered suitable to join EFFORT, all of the criteria that are noted below must be present.

- ❑ **ICUs must assign two (2) Study Leaders**
  One study leader should be an ICU physician and the other can be either an ICU dietitian or research coordinator. In general, we believe a multidisciplinary team consisting of a physician and a dietitian (and others) will be more effective in implementing the EFFORT study procedures; for this reason we recommend a physician and dietitian as study leaders however, exceptions can be allowed. What is critically important is that each of the study leaders have the following qualifications:

  - o **The Study Leaders must be knowledgeable about critical care nutrition.**
    Study Leaders must submit their curriculum vitae (CV) or other document that demonstrates their knowledge of critical care nutrition as part of the application process.

  - o **The Study Leaders must have Good Clinical Practice (GCP), or similar training**.
    Study Leaders must submit their training certificate as part of the application process. See below for information regarding a free online GCP training course.

- ❑ **The ICU will abide by the randomization scheme and arm assignment AND avoid overfeeding for each randomized patient.**
  Confirm their site has overall equipoise and is willing to abide by the randomization schema of high versus low protein prescription. In addition, they are confirming that if the patient is randomized to the high protein group, they will not over feed the patient with too much energy in order to achieve high levels of protein intake.

  Check out a NIBBLE (i.e. nutrition information memo) posted on our website that discusses the current literature regarding this very issue: ***Should We Have Equipoise (or Clinical Uncertainty) About How Much Protein to Provide to Critically Ill Patients?***

- ❑ **The ICU uses a standardized feeding protocol in their ICU for enteral and parenteral nutrition**
  By standardized feeding protocol, we mean a form or policy that enables the bedside staff to manage the nutrition in a standardized way. These protocols are usually implemented by pre-printed or automatic order sets, printed algorithms or other beside tools. The specific nature of the protocol is not important. ICUs that have standardized protocols are much more likely to deliver high quality nutrition. If you do not have a written policy or algorithm but do take a standardized approach to enteral nutrition, this is acceptable. (Consider reducing this standard practice into writing).

- ❑ **The ICU has access to a range of commercial enteral and parenteral feeding products that they will use to achieve protein targets without providing excessive calories.**
  This includes products such as high protein enteral nutrition, protein supplements, and parenteral nutrition or amino acids.

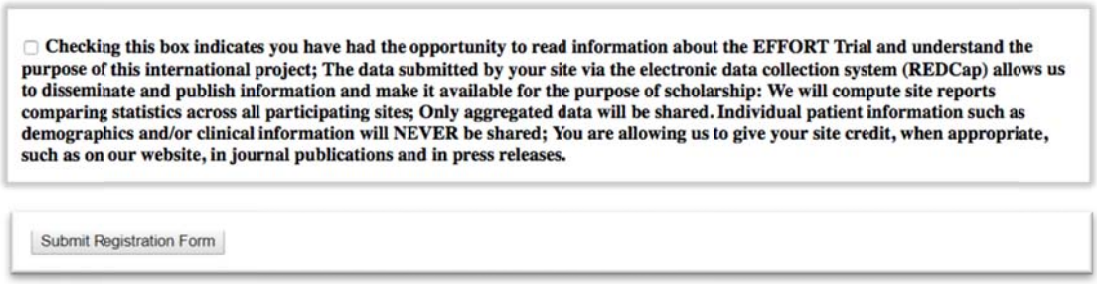
- ❑ **Ethics clearance has been obtained.**
  The Ethics Clearance (i.e. Approval Letter) must be submitted at the time of ICU registration. The section below provides ICUs with direction in seeking ethics clearance.

- ❑ **The ICU is committed to enrolling a minimum of 30 eligible patients in 2-3 years.**
  The ICU has the local resources to enrol at least 30 eligible patients. ICUs are welcome to enrol as many as they can!

The ***Site Suitability Checklist*** can be downloaded from the website. Use this checklist as a tool to speak with team members and ICU stakeholders to ensure your site will be able to meet these criteria.

At the time of registration, the above criteria must be confirmed, with associated documentation submitted (i.e. CV, GCP and ethics). Please do not proceed any further in the trial if you cannot provide or commit to the statements in the site suitability section above. If you are able and committed (and we hope you are!), please proceed first with obtaining ethics approval.

The final step in the application submission process requires you to confirm you understand the purpose of the EFFORT Trial; have committed to review the implementation and support materials on our website; and that you will be submitting data via the electronic data capture system (REDCap); and will receive a site benchmark report.



Good Clinical Practice (GCP) Training Course

The National Institutes of Health (NIH) in the United States has free interactive online GCP training course available to anyone (i.e. US and non-US) who is interested in taking the course. You can access the course here: https://gcp.nidatraining.org/.

Simply create an account to access this 12-module course. Please note this course is only offered in English. Upon completion you will be provided with a GCP Certificate.

Other GCP certification courses are also acceptable. Please contact the Project Leader if you have any questions about if a specific course will satisfy this requirement.

Obtaining Ethics Clearance

As noted above, before an ICU may formally register to join EFFORT, they must secure ethics clearance.

Ethics submission procedures and requirements will vary by region and institution therefore, each ICU is responsible for making sure they follow applicable procedures, laws and regulations when preparing their ethics submission for the EFFORT Trial.

Centralized Ethics

In some countries and/or regions, there are lead ICUs/investigators that can support and advise other ICUs with joining an existing central ethics approval. For example, in the US, Vanderbilt is the lead site for the Single IRB process. The table below lists each region with the appropriate contact person to inquire about how to do this.

Country/Region	Contact Person	Brief Information
Brazil	Ricardo Rosenfeld	rsrosenfeld@hotmail.com
Canada – Ontario	Jennifer Korol jennifer.korol@kingstonhsc.ca To join the Clinical Trials Ontario (CTO) application please contact	***CTO Provincial Approval for use of 'waived consent' has been obtained.***

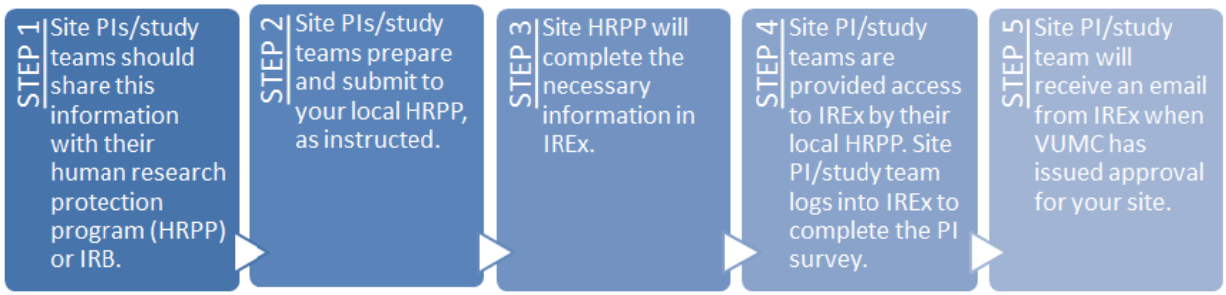
	Jennifer Korol	
Canada – Quebec	Danaë Tassy danae.tassy.cemtl@ssss.gouv.qc.ca To join the Quebec application please contact Danaë Tassy.	***Quebec Provincial approval for use of 'waived consent' has been obtained.***
United States	Jennifer Korol jennifer.korol@kingstonhsc.ca Sites in the US may join this SIRB application by following the steps outlined here. Also, see below for further details.	***A single IRB (reliance) process is available from Vanderbilt University Medical Center. The approval allows for the use of a waived consent model.***
United Kingdom	Danni Bear Danielle.Bear@gstt.nhs.uk	A central ethics application is currently underway.

US Single IRB (Reliance) Process

Vanderbilt University Medical Center (VUMC) will serve as the single IRB of Record ("sIRB") using the SMART IRB Master Common Reciprocal Institutional Review Board Authorization Agreement ("SMART IRB Agreement") and the sIRB Letter of Indemnification (LOI) to establish reliance between all participating sites and Vanderbilt.

Once a participating site contacts the coordinating center Project Leaders and signals their intent to join the sIRB, the Project Leaders will provide the site with a start-up package (also available for download from the study website). The Site should follow the steps outlined in the diagram below.

sIRB Process Steps



Detailed instructions for each of the steps can be downloaded from the EFFORT Study website.

A Case for the use of Waived Consent

Given the study treatment groups are within the range usual nutrition practice in ICUs, The EFFORT Trial presents no greater risk than typical management of feeding in ICU patients today. Additionally, the safety characteristics of the trial and the time sensitivity of protein administration in the patient population, provide a strong rationale for the use of ***waived consent***. It is therefore recommended that participating ICUs seek ethics clearance for waived consent.

In cases where an ICU is seeking waived consent, they may use the ***Patient Information Sheet*** as part of their local ethics submission and consent process.

We have prepared a slide deck "***A justification for use of waived consent in EFFORT***" that local study leaders can use to present the rationale for requesting the use of waived consent to their ethics committees and other local stakeholders. It can be downloaded from our website.
Also, feel free to contact the Project Leader to obtain a current list of the ICUs that have joined EFFORT and been successful in obtaining waived consent. This information may be useful to your ethics committee in their deliberations regarding this issue.

For ICUs in jurisdictions where written informed consent (i.e. Standard Consent) from the patient/family member is required, ICUs will need to adapt the ***Informed Consent Form template*** to local standards before submitting.

Each site will be required to identify the consent type being used at their institution (i.e. Waived or Standard Consent) at the time of registration.

Further details regarding how to use these consent types can be found in SECTION 4: Patient Recruitment.

Documents Needed for Ethics Submissions

All documents necessary for preparation of the ICU ethics applications are available for download from the website.

Document	Version Date	File Format
The EFFORT Trial Protocol	1-Oct-2017	.pdf
Patient Proxy Information Sheet template *(applicable when 'waived' consent is used)*	1-Oct-2017	.docx

FDA 45 CFR 46.116 – Waived Consent

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;

(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;

(3) The research could not practicably be carried out without the waiver or alteration; and

(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

Informed Consent Form template *(applicable when 'standard' consent is used)*	1-Oct-2017	.docx
Study Synopsis	17-Oct-2017	.docx

Please contact the regional/country ethics leader to obtain regionally specific copies of these documents (e.g. centrally approved templates).

Each ICU should file one (1) ethics clearance letter and associated consent/information form for each version of the protocol over the 3 years of the trial. In addition, any annual renewals will also need to be retained in the site study files. Contact your local ethics committee for guidance if you have any questions about which documents should be filed.

Time to Register!

Once you have completed the activities outlined in the 'Before you Register" section above, you are now ready to complete the online registration application.

REGISTER HERE! https://ceru.hpcvl.queensu.ca/randomize/EFFORT/registration.php

Registration Instructions and a paper version of the ***Application Form*** can be downloaded from the website.

Registration Tips

Each ICU should be registered **once**. Take special care to coordinate with all study team members to ensure that only one person completes the online registration, and provides the contact details for all team members that require REDCap login credentials (i.e. user name and password).

All team members must log onto the REDCap using their personally assigned credentials. Please keep track of your password.

How to Register Multiple ICUs in 1 institution

If you want an individualized site performance report for each ICU in your institution, then each ICU must be registered separately and strive to enroll at a minimum of 30 patients per each ICU. If you register multiple ICUs, please note that each team member will receive separate login credentials for REDCap for each ICU.

If you anticipate enrolling the 30 participants (minimum) across all of your ICUs combined, then you should register only the one ICU. You will then receive one site report for the mix of patients across the ICUs.