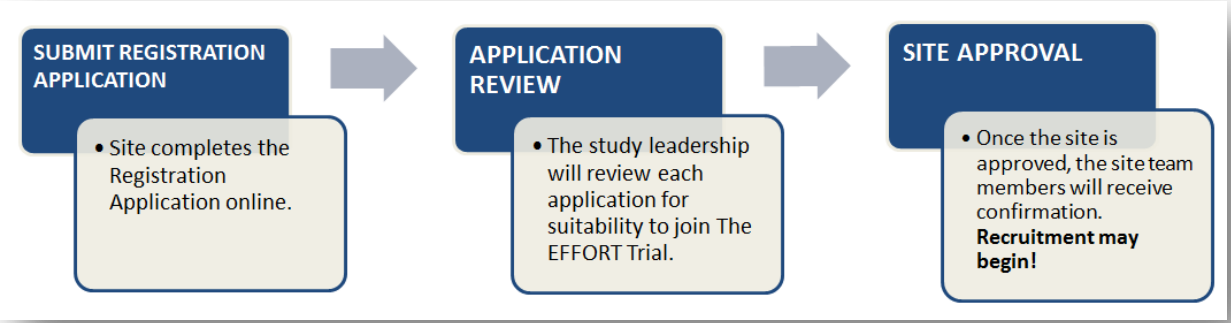
SECTION 2: REGISTER YOUR ICU

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 of an interested site submitting an application to join. Once the registration application has been reviewed by the study leadership, 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.
  - **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.
  - **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 overfeed the patient with too much energy in order to achieve high levels of protein intake.

- ❑ **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.

- ❑ **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.

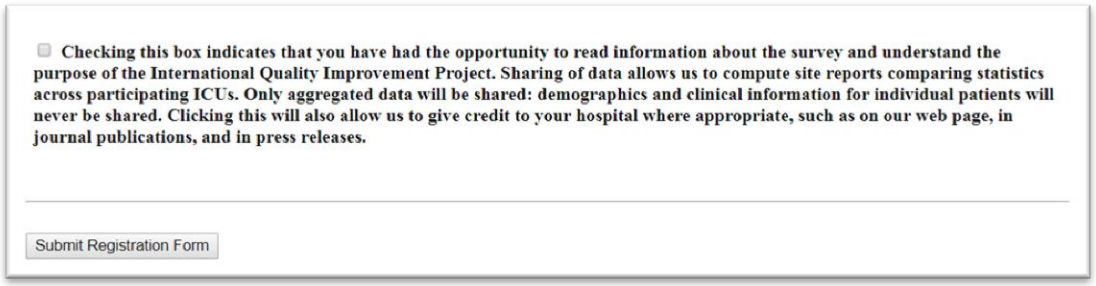
- ❑ **Ethics clearance has been obtained.**
  The Ethics Clearance (i.e. Approval Letter) must be submitted at the time of ICU registration. The section below provides ICUs with direction in seeking ethics clearance.

- ❑ **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 ethic approval.

The final step in the application submission process requires you to confirm you understand the purpose of the EFFORT Trial, 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 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.

Obtaining Ethics Clearance

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

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

Regional Central 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. 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	TBA	TBA
Canada – Ontario	Jennifer Korol Jennifer.Korol@kingstonhsc.ca	To join the Clinical Trials Ontario (CTO) application, your institution must have a Participation Agreement in place. ***CTO Provincial Approval for use of 'waived consent' has been obtained.***
Canada – Quebec	TBA	A central provincial application is underway.
United States	Charlene Compher compherc@nursing.upenn.edu Jayshil Patel jpatel2@mcw.edu	***A central IRB approval, allowing for the use of a waived consent model, has been obtained in the US (Vanderbilt University).*** Sites in US may join this central IRB application by following the steps in the SOP. The ***US Ethics SOP*** can be downloaded from the website.
United Kingdom	Danni Bear Danielle.Bear@gstt.nhs.uk	A central ethics application is currently underway. Further details available soon.

Consent Types: Waived vs. Standard 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.

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.

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.

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 (i.e. Waived or Standard Consent) at their institution 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
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 ready now 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

If you have multiple ICUs that you wish to include, each ICU must be registered separately. Even if you anticipate enrolling the 30 participants (minimum) across all of your ICUs combined, you should register each ICU separately.

If you have registered multiple ICUs, please note that each team member will receive separate login credentials for REDCap for each ICU.