Informed Consent Form

INFORMATION TO PARTICIPANTS

NAME OF STUDY:	A Phase 4, Open-Label, Single-Dose, Parallel-Group Study to Evaluate the Safety of 1 g of Cefazolin in Pediatric Subjects With a Weight of at Least 25 kg but Less Than 60 kg Scheduled for Surgery and the Safety of 2 g of Cefazolin in Pediatric Subjects With a Weight of at Least 60 kg Scheduled for Surgery
STUDY NUMBER:	HC-G-H-1601
STUDY SPONSOR:	B. Braun Medical Inc. 824 Twelfth Avenue Bethlehem, PA 18018 USA
STUDY DOCTOR (INVESTIGATOR):	[Investigator Name] [Site Address] [Office Hours Tel] [Out of Hours Tel]
[ETHICS COMMITTEE (EC) or INVESTIGATIONAL REVIEW BOARD (IRB):]	[EC/IRB Name] [EC/IRB Address] [Office Hours Tel] [Out of Hours Tel]

Why are you receiving this information?
As the parent, Legally Authorised Representative (LAR), the legal guardian(s), of _____ (enter patient/child's name), you are being asked to consider whether you would like your child to participate in a clinical research study. This research study is sponsored by a company called B. Braun Medical Inc., and B. Braun Medical Inc. is also providing the study drug. The following information describes the study and your child's role as a possible participant. Please read this information carefully and do not hesitate to ask your study doctor any questions to ensure that you are able to make an informed decision as to whether to participate.

What is the purpose of this clinical research study?
The purpose of this study, which involves research, is to check the safety of a study drug, named cefazolin, in children who are scheduled for surgery, who are 10-17 years of age. The dose of study drug given to your child will be either a 1 gram or 2 gram dose and will depend on your child's weight. The study drug is given by a needle inserted into a vein. Cefazolin, the study drug, is a widely used antibiotic medication and has been given to over one million patients. It is given to prevent infections that might happen during and after surgery. Ancef®, which is the version of cefazolin that can be given by an injection (a shot), has been FDA-approved for use in children over a month old. This study is required by the FDA as part of the Pediatric Research Equity Act to check the safety of the 1 gram and 2 gram doses of cefazolin in children scheduled for surgery. It is expected that approximately 110 subjects will participate in this study.

What procedures are involved?
If you decide for your child to take part in this study, your child will be asked to make a total of 2-3 visits to the study [hospital/location] over the next approximately 39 days, including today's visit called the Screening Visit.

At the first visit (Screening), the following procedures will be done to confirm if your child is able to participate in the study:

- The child's legally authorized representative (LAR), for example: the parent, will be required to sign this Informed Consent Form (ICF).
- Depending on age, your child may also be required to sign a form that confirms his or her agreement to participate in the study.
- A subject identification number will be assigned to your child.
- The following information about your child will be collected:
    - Gender
    - Date of birth
    - Ethnicity (Hispanic/Latino or not Hispanic/not Latino)
    - Race (White, American Indian/Alaska Native, Asian, Native Hawaiian or other Pacific Islander, Black/African American)
    - Height (without shoes)
    - Weight (with indoor clothing and without shoes)
- Your child's medical history will be reviewed by the study doctor or study nurse.
- Your child's medication history will be reviewed by the study doctor or study nurse.
- A physical examination will be done by the study doctor.
- Your child's vital signs including blood pressure, pulse, temperature, and breathing rate will be taken by the study doctor or study nurse.
- An Electrocardiograph, also called an ECG, will be done by the study doctor or study nurse. An ECG is a test that records the heart's electrical activity. The test is used to detect and study heart rhythms and disorders that affect heart function. The study nurse or technician will attach soft, sticky patches called electrodes to the skin on your child's chest, arms, and legs; these patches will then be hooked up to wires attached to an ECG machine. After the patches are in place, your child will be asked to lie still on an examination table while the machine records the heart's electrical signals on a graph paper or digital screen. Skin reactions to the sticky patches may occur, such as redness, itching, or discomfort. Some temporary hair loss may be associated with the removal of the patches like when a band-aid is removed. It is also possible that there may be an allergic reaction to the patches from the sticky glue.
- Blood samples for laboratory assessments will be collected. An amount equal to about 1.5 teaspoons (8 mL) of blood will be taken during this collection. Collecting blood samples involves inserting a thin needle into a vein, which could cause slight discomfort and possible bruising or pain at the area where the blood is drawn, occasional lightheadedness, rarely an infection and sometimes feeling faint from the procedure.
- Medications that your child is taking or has taken recently will be reviewed.
- If your child is a female of childbearing potential (if she has started getting her period), a urine pregnancy test will be done. If it is positive, pregnancy will be confirmed with a blood test. If your child is pregnant, she will not be able to take part in the study.

*Please note that in some cases the Screening Visit and surgery can happen on the same day. In those cases the study procedures for the Screening Visit and the study procedures for the day of surgery will be combined. Duplicate procedures will only be done once. The study doctor will decide if surgery will happen on the day of the Screening Visit.

If the study doctor decides your child is eligible and if you agree for your child to enter the study, the following study procedures will be done according to the study schedule starting on the day of surgery. If you are not familiar with any of these procedures, please ask your study doctor to explain how they are done.

Procedures before surgery begins on the day of surgery:

- Your child's weight will be taken.
- Your child's medical history will be reviewed.
- A brief physical examination will be done.
- Your child's vital signs will be taken.
- Blood samples for laboratory assessments will be collected. An amount equal to about 1.5 teaspoons (8 mL) of blood will be taken during this collection.
- Study drug will be given through a needle inserted into a vein.
- The study doctor or nurse will check your child for any side effects from the study drug.
- If your child is a female of childbearing potential (if she has started getting her period), a urine pregnancy test will be performed. Confirmation with a blood test will be done if the urine pregnancy test is positive. If your child is pregnant, she will not be able to participate in the study.

Procedures during surgery:

- Your child's vital signs will be taken.
- The study doctor or nurse will check the area on your child's body where the study drug is being given.
- The study doctor or nurse will check your child for any side effects from the study drug.

Procedures 24 hours after surgery or at discharge:

- A brief physical examination will be performed.
- Your child's vital signs will be taken.
- An ECG will be done.
- The study doctor or nurse will check the area on your child's body where the study drug was given.
- Blood samples for laboratory assessments will be collected. An amount equal to about 1.5 teaspoons (8 mL) of blood will be taken during this collection.
- The study doctor or nurse will check your child for any side effects from the study drug.

Procedures 7 days after surgery for safety follow-up:

- Your child will have to return to the study doctor's office.
- A brief physical examination will be performed.

- Your child's vital signs will be taken.
- Blood samples for laboratory assessments will be collected. An amount equal to about 1.5 teaspoons (8 mL) of blood will be taken during this collection
- The study doctor or nurse will check the area on your child's body where the study drug was given.
- The study doctor or nurse will check your child for any side effects from the study drug.
- Medications that your child is taking or has taken recently will be reviewed.

The total amount of blood collected during the study for all the study procedures will be about 6.5 teaspoons (32 mL). This total amount is well within the guidelines for safe blood collection amounts for children.

In addition to all the procedures outlined above, your child is invited to participate in another optional part of the study. The FDA has asked that approximately 40 children from this study agree to 4 additional blood collections taken during surgery to check the levels of the study drug in the blood. This check is called pharmacokinetics which is abbreviated PK. The amount of blood collected for the 4 additional PK blood collections totals about 3 teaspoons (16mL). The total amount of blood collected for the study plus this separate PK part of the study is still well within the guidelines for safe blood collection amounts for children. A separate consent form will be provided for this optional, PK part of the study.

Your child will be assigned to receive either 1 gram or 2 grams of cefazolin (the study drug) based on your child's weight taken before surgery starts. The study drug will be given over 30 minutes as an infusion (fluid given through a needle in a vein) starting 30 minutes to 1 hour before surgery begins and following the guidelines of the [hospital/location]. If your child weighs between 25 to 59 kg (approximately 55 pounds to 130 pounds), your child will receive the 1 gram cefazolin dose. If your child weighs 60 kg or more (approximately 130 pounds or more) your child will receive the 2 gram cefazolin dose. If the surgery unexpectedly goes beyond 3 hours, the study doctor may decide that an additional dose of study drug is needed and an additional dose will be given.

How will study drug be given?
Cefazolin will be given to your child intravenously (through an IV) by placing a thin needle into a vein in your child's arm (or leg). The needle is connected to plastic tubing leading to an IV bag holding the study drug. The needle and tubing will stay in place for approximately 30 minutes while your child is given the study drug. Administration of the cefazolin will begin 30 minutes to 1 hour before the start of your child's surgery.

What is expected from you?
When deciding whether or not your child should enter the study, consider whether you and your child are able and willing:

- To follow the study rules, including the study procedures and restrictions.
- To not use any medication (for example, prescription, herbal, OTC [over the counter] medication or dietary supplements) known to interact with cefazolin within 5 days before the scheduled surgery until after the final study visit (Safety Follow-up Visit). This includes use of probenecid, which is a medication that is typically used to treat gout (form of inflammatory arthritis) and hyperuricemia (abnormally high level of uric acid in the blood). The study doctor will check your child's medications.

- To commit the time required to keep appointments.
- To tell the study doctor truthfully about your child's complete medical history.
- To report any new problems, illnesses, or changes in any medication (prescription drugs, herbal products, vitamins, minerals, and OTC medications) during the study.
- If your child is a female of childbearing potential (if she has started her period), and is sexually active she must be willing to use an effective method of birth control during the study period, for example: oral contraceptives (pill), double barrier methods (for example, condom and spermicide), hormonal injectable (for example, Depo-Provera) or implanted contraceptives (for example, Nexplanon), tubal ligation ("having tubes tied"), or have a partner with a vasectomy (surgical procedure for male sterilization).

What will happen at the end of the study?
There are no required actions for you or your child after your child's participation in the study is complete, however, there may be follow-up procedures related to the surgery itself. The study doctor will tell you what happens next.

What are the potential risks and discomforts?
All drugs may cause certain side effects and discomforts. Although it does not occur very often, the most common side effect reported for cefazolin is an allergic reaction which may be mild like a skin rash or hives or severe like anaphylaxis. The study doctor will ask you about other medications that your child is allergic to, like penicillin, which might indicate that they could be allergic to cefazolin. Your child will not be able to participate in the study if they are allergic to penicillin or cefazolin. Other infrequent side effects of cefazolin are loss of appetite, mild diarrhea, nausea, or stomach cramps. There may also be side effects or discomforts that are not yet known.

When a needle is inserted into a vein for giving the study drug or for blood collections, your child may experience some temporary discomfort, bruising, swelling and/or, in rare circumstances, infection at the needle site.

Are there any reproductive risks?
Women: cefazolin is safe for use during pregnancy and while breast-feeding. However, pregnant or nursing women are not allowed to participate in this study. For this reason, if your child is breast-feeding a child, is pregnant or plans to become pregnant, she may not participate in this study. If your child is capable of becoming pregnant and is sexually active, your child must use an acceptable method of birth control throughout the entire study (see examples listed below).

Birth Control: Birth control methods that are acceptable for this study include oral contraceptives (pill), double barrier methods (for example, condom and spermicide), hormonal injectable (for example, Depo-Provera) or implanted contraceptives (for example, Nexplanon), tubal ligation ("having tubes tied"), or have a partner with a vasectomy (surgical procedure for male sterilization). It is important that you tell the study doctor immediately if your child becomes pregnant during the study.

Pregnancy: If your child becomes pregnant during her participation in the trial, her participation in the study will be stopped, however, details about the pregnancy may be collected.

What are the advantages and disadvantages of participation in the study?
Cefazolin is a widely used medication and is often given to children and adults to prevent infections that might occur during and after surgery. As participants in this study will be recruited from those who are already scheduled to have surgery in which cefazolin will have already been chosen as the pre-surgery antibiotic, your

child may not receive any additional benefits from participation in this study. However, by taking part, your child will provide new information that will help confirm the safest and best doses of this drug to use in children who have surgery and may benefit other patients in the future.

Are there any alternative treatments?
If you and your child decide to not take part in this study, your child may receive the same or a similar option for prevention of infection. Your study doctor will discuss the options with you, including important potential risks and benefits for the other option(s).

Will you be informed if new information becomes available during the study?
Your study doctor will inform you and your child in a timely manner of any new information learned during the study that may affect your willingness to continue your participation.

Who can you contact with further questions?
You and your child may ask questions about this consent form or the study at any time (before or during the course of the study). If you have additional questions, or if your child experiences a study-related injury, contact the study doctor using the details provided in the table on the first page of this information sheet.

If you have a complaint or question about your child's rights as a research subject, you may contact the [Ethics Committee (EC) or Institutional Review Board (IRB)] using the details provided in the table on the first page of this information sheet. This is a group of scientific and non-scientific individuals who review research studies with the safety and welfare of research subjects in mind.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by US Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What happens if you change your mind?
Your child's participation in this study is voluntary. Your child does not have to take part, and may discontinue participation at any time and for any reason without prejudice to your child's future medical care by the study doctor or at the study site, and without penalty or loss of benefits to which your child is otherwise entitled. If your child decides to leave the study before the last study visit, tell the study doctor and follow instructions. It may be helpful if you/your child could explain your reasons. Your child may receive standard treatment and no prejudice will be shown towards you for medical care or participation in future research.

In addition, your study doctor or the sponsor may withdraw your child from the study for your child's own safety, even if you/your child wish to continue to participate, for example:

- If your child does not meet the protocol eligibility criteria
- If you/your child do not follow the study rules
- If your child experiences a serious or intolerable side effect that in the study doctor's opinion requires withdrawal from the study
- If your child becomes pregnant
- If you or your child request to withdraw informed consent or Health Insurance Portability and Accountability Act (HIPAA) authorization
- Any other reason warranting withdrawal at the discretion of the study doctor with approval of the sponsor, B. Braun Medical Inc.

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If your child's participation in the study is stopped early, you may be asked to complete end of study procedures (safety follow-up procedures) for your child's safety.

Are there any costs if you decide to participate?
The study drug will be made available to your child at no charge and you will not be required to pay for any study procedures. You or your insurance company may be billed for any standard medical care that is not required for the research study.

Is there a payment if you decide to participate?
You/your child will not receive payment for participation in this study. You may be reimbursed for any reasonable travel expenses (bus/train/taxi fares) incurred as a result of taking part in this study upon production of a receipt.

Will you receive compensation if you are injured as a result of the study?
If any injury or illness should occur to you that is reasonably judged by the Investigator and Sponsor to be a direct result of the study treatment, medical treatment will be provided. The Sponsor of this study will pay for reasonable and routine costs of such treatment (a) if not covered by your personal insurance, by a governmental program or by any third party and (b) provided you have followed the directions given by the study doctor. The sponsor does not offer to provide compensation other than that described above. If you would like further information about compensation for research-related injuries, please contact the study doctor. Please be aware that some insurance plans may not pay for research-related injuries. You should contact your insurance company for more information. You and your child do not give up any of your legal rights by agreeing to this and signing this form.

Will the personnel involved in the study receive any payment?
The [investigator] receives payment from B. Braun Medical Inc. who is the sponsor of this study.

Statement of Consent
- I have read and understand the statements in this informed consent form
- I have had the opportunity to ask questions and I am satisfied with the explanations provided
- I voluntarily agree to allow my child to take part in this study
- I will receive a copy of this signed consent form to keep. I understand that the signed original will remain on file with the study doctor

_____

Legally Authorized Representative or Legal Guardian
Printed Name Signature Date

_____

Witness (if applicable)
Printed Name Signature Date

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- I have presented the study and answered the Legally Authorized Representative or Legal Guardian's questions
- I will give the subject/legal representative a copy of this signed and dated Informed Consent

_____

Presenter (Investigator/Delegate)

Printed Name Signature Date

HIPAA Authorization

Confidentiality and Authorization to Access and Use of Medical Information

This research study may be performed only by collecting and using your child's medical information. Your child's study records will be kept as confidential as possible. Only a number will be used to identify your child. (This is will be referenced as your child's coded medical information.) Your child will not be personally identified in any reports or publications that may result from this research study.

Because of the research goals of this study, however, study records cannot be kept completely confidential. The sponsor of this study is B. Braun Medical Inc.

The study personnel and the sponsor and its agents will need to review the medical information collected from your child for use in this study in order to accurately record information for this study. In addition, in order to review the study findings, the U.S. Food and Drug Administration (FDA) and other regulatory agencies may review your child's medical records. The following sections provide a specific description of how information will be used and disclosed if you participate in this research study. By signing this consent form, you are authorizing such access. If you do not sign this form to authorize access, you will not be able to participate in this research study.

Your child's medical records may identify your child by name, address, telephone number, social security number, health plan number, study number, date of birth, dates relating to various medical procedures, and/or other identifying information. Your child's name, address, telephone number, social security number, health plan number will NOT be retained by B. Braun Medical Inc. as part of the data for this study, but it may be retained by the study doctor.

The medical information that will be collected from your child if your child participates in the study includes:

- Information obtained from procedures to determine your child's eligibility to participate in the study, including a routine medical history, physical exam, ECG, and blood tests.
- Information that is collected from you during your child's participation in the study, including the results of the tests and any other procedures performed during the study.
- Information contained in your child's underlying medical records related to your child's medical history and treatment.

If you sign this form and allow your child to participate in the study, the study personnel will be authorized to use the information described above to carry out the purposes of the research study. The study personnel will also be authorized to disclose the relevant information described above to the following parties involved in the research study:

- B. Braun Medical Inc., the study sponsor
- PPD, which is a company hired by B. Braun Medical, Inc., and PPD's affiliates designated to collect and review study data for verification of study procedures and/or adverse event (side effect) reporting.
- Other agents designated by B. Braun Medical Inc. to collect or review study data for verification of study.
- The Institutional Review Board (IRB) or Independent Ethics Committee (IEC) that oversees the research study at your site.
- Government regulatory agencies including the FDA.

Once your child's coded medical information is disclosed to the study sponsors, its agents, the IRB/IEC or government agencies as described above, there is a potential that your child's medical information will be re-disclosed and will no longer be protected by US federal privacy regulations. In addition to disclosures to the entities identified above, PPD may further electronically disclose your child's coded health information to others involved in the research study, such as:

- To laboratories or offsite testing facilities for clinical tests required by study protocols.
- To approved offsite storage facilities or cloud service providers to meet study record retention and storage requirements.
- To study B. Braun Medical Inc. who directs the medical research study.
- To other third parties contracted by PPD and/or B. Braun Medical Inc. to provide services related to study.

The study data may be transferred to other countries for processing, including countries not covered by data protection legislation. The laws of your state may provide further protection.

**Edit the expiration date in the 2nd sentence of this paragraph if a specific date of expiration is required by state law (e.g., CA, MN, IL)*

Study data, including your child's coded medical information, may be used and shared for pharmaceutical research purposes related to this study. This authorization has no expiration date. In signing this form, you authorize the use and disclosure of your child's coded medical information for purposes of the study at any time in the future.

You/your child may withdraw your authorization at any time by sending a written request to [insert name of responsible study personnel] at [insert address]. If you/your child withdraw your authorization, data collected prior to your withdrawal may still be processed along with other data collected as part of the study. Normally no new information will be collected for the study database unless you specifically authorize that. However, the law does require that any side effects your child may suffer are documented and reported.

Statement of Consent and Authorization

I have read and understand the statements in this informed consent. I have had the opportunity to ask questions and I am satisfied with the explanations provided by the consent process. I voluntarily consent my child to participate in the study and I authorize the use and disclosure of my child's information in connection with the study. I understand that I will receive a signed copy of this consent and authorization form.

_____

Legally Authorized Representative or Legal Guardian

Printed Name Signature Date

_____

Witness (if applicable)

Printed Name Signature Date