Parental Permission

Parental Permission to Participate in a Clinical Research Study and Authorization to Use Protected Health Information

Children's National Hospital

111 Michigan Ave NW,
Washington, DC 20010

STUDY TITLE: Biomarker-enhanced Artificial Intelligence Based Pediatric Sepsis Screening Tool Towards Early Recognition and Personalized Therapeutics, version 1.0, version date 04 February 2022

INVESTIGATOR: Ioannis Koutroulis, MD, Division of Emergency Medicine

SUMMARY AND KEY INFORMATION

We are inviting your child to be part of a research study at Children's National Hospital.

The reason we are doing this study is to find out if a new blood test to identify sepsis in children may provide more timely and accurate information beyond what is available using currently available blood tests. In addition to a blood sample, data from your child's medical record will be collected and used for the study.

Study participants are children who are suspected to have sepsis and for whom a blood test has been ordered to help your child's doctor determine if sepsis is present. We are asking for your consent to allow us to collect a small additional blood sample (1-5ml) while your clinical team draws blood as a part of your child's standard care. This additional blood sample will be tested to see if it can help doctors identify and treat pediatric sepsis faster. If we are not able to get blood at the same time as the clinical team's routine blood collection, we would like your consent to allow us to collect your child's leftover, unused blood from the lab that would otherwise be discarded. The blood is needed to see if the new test works.

Taking part in this study and providing a blood sample and access to your medical record information is voluntary. You can choose to take part, or you can choose not to take part in this study. You also can change your mind about participating at any time. No matter the choice you make, your child will not lose access to any medical care or give up any legal rights or benefits.

To help you decide if you would like to participate, we want you to know why you are being asked to participate, why we are doing the study, what you will be expected to do, and the possible risks and benefits of being in the study. This form has information to help you make your choice about whether or not to participate.

(PI or Investigator) listed above is the person responsible for this research study at (institution), assisted by (research assistants) and is available to answer any of your questions.

Why am I being invited to take part in this research study?

We invite you to take part in this research study because we are seeking children (17 years old or younger) who fall within one of the two following categories for suspicion of sepsis:

1) following an examination by a physician, your child has been found to be at risk of sepsis and a blood sample has been ordered and/or sepsis treatment has been started; or

2) there is suspicion of sepsis, and a blood sample has been ordered based on your child having one or more of the signs or symptoms of sepsis that may include:

a) one or more abnormal vital signs that include: a fever, difficulty breathing, low blood pressure, or an abnormal heart rate and/or pulses
b) abnormal capillary refill (a test for assessing blood flow through peripheral tissues)
c) abnormal mental status (e.g., new confusion, abnormal irritability, inappropriate crying or drowsiness, poor interaction with parents, lethargy, decreased arousability or alertness
d) abnormal skin (e.g., red, or purple spots caused by bleeding below nipple, any purple looking rash, any patchy or irregular colors of the skin)
e) history of a condition that puts your child at especially high risk of sepsis when there is an infection (e.g., history of cancer, sickle cell disease, organ transplant) or your child has a catheter or other device under the skin/inside the body that could cause a serious infection.

Purpose of the Research

Sepsis in children can progress quickly from an infection to a life-threatening medical emergency. Prior research has shown that the best outcomes and highest chances of successful recovery occur when sepsis is recognized early by doctors, and patients receive appropriate antibiotics and other treatments during the early stages of this condition. However, the screening tools available today that are designed to assist in early recognition of emerging sepsis and identify the best treatment needed for the patient do not work well. The purpose of this research study is to determine if new blood tests called "biomarkers" can be used to improve the ways clinicians screen for sepsis early on during a hospital visit. Early detection of sepsis may help identify the type of treatment that might be more effective for an individual patient.

If you decide to participate, we will collect a minimum of 1ml and a maximum of 5ml of blood within 24 hours of your child's arrival to the hospital. We will ask your child's treating nurse to draw the additional blood when they are collecting a sample for routine care. We may also request our lab to provide us with a left over, unused blood sample that is no longer needed if we are unable to get blood with your routine labs. We will only collect research blood one time during your study participation either as part of your routine lab collection or leftover blood from the lab.

The completion of all aspects of this study (blood collection) will not add any time to your stay in the hospital. We will use information from your child's medical record such as history, laboratory and imaging information, vital signs, and medications to examine their response to treatment and whether, combined with the results of the biomarker tests, we can develop a screening tool that can accurately recognize sepsis earlier.

What are the risks and possible discomforts from being in this research study?

We will not draw blood clinically for research purposes only. Blood collection for this study will take place only if a regular blood draw or an intravenous or arterial line placement is required as a part of standard care. If we are unable to collect blood at that time, we will use leftover, unused blood from our laboratory.

There are some risks to your child participating in this study, but they are minimal: 1) the blood test will require a small amount of blood to be drawn. Most children will need to have no more than one

teaspoon of blood drawn as required for the research. The proposed amount of 1-5 mL of blood is very low in order to avoid causing any harm to your child's health. Current guidelines allow for blood draws in infants and children that do not exceed 5% of their total blood volume. The total amount of blood needed to perform both the required test and research test is well within this guideline. Consequently, the amount of blood to be drawn for research is not enough to have any significant effect on your child; 2) since we will not draw blood for research purposes only, participation will not involve any additional discomfort over the usual risks (e.g., discomfort, bleeding, bruising, or infection at the puncture site of the blood draw) associated with a routine blood draw. You or your doctor will not receive the results of your child's blood analysis because the analysis is for research purposes only.

Beyond the low-risk collection of a blood sample, this study also involves the collection of medical information which is also low risk since we will take steps to protect your child's privacy as described later in this document.

There could also be un-identified risk that we are not yet aware of for this project but we are closely monitoring for any adverse events.

Is there any way participating in this study could be good for me?

Participating in the study will not benefit you/your child directly. However, the information we gather regarding your condition may help improve the treatment of septic patients in the future.

Alternatives to Participation

Your/your child's participation in the study is voluntary. You do not have to join the study. You may change your mind and stop being in the study at any time. There will be no penalty or loss of benefits to which you/your child are otherwise entitled if you decide to not participate or to withdraw from this study at any point in time. Choosing not to participate or to withdraw will not affect your/your child's regular medical care.

If you are interested in learning more about this study, please continue reading below. The rest of this form gives you more important information you need to know about the study before you decide if you want to participate. The study doctor or a member of the research team will talk to you about the study and answer all of your questions. We encourage you to discuss this study with your family, your child's doctor, and anyone else you trust before making a decision. It's important that you have as much information as you need and that all of your questions are answered.

The PI may also withdraw a participant if he/she believes it is in the participant's best interest, the participant was found ineligible for the study based on the inclusion criteria or for any reason. If the PI withdraws you from the study your blood and data will not be used and there will be no penalty to you. We will reach out to you and inform you if you are withdrawn from the study.

Your participation in this research is voluntary.

There will be no penalty or loss of benefits to which you are otherwise entitled if you decide not to be in the study or withdraw from the study later. This means that:

- You/your child do not have to join the study.
- You may change your mind and stop being in the study at any time.
- We will tell you if we make any important changes to the study or if there are any important new findings so that you can decide if you still want to be in the study.

Will everyone participating in this study have pediatric sepsis?

Patients 0-17 years who are eligible to participate in the study will have "suspected sepsis" as a result of having one or more of the symptoms of sepsis as listed above and their doctor will have ordered a

blood test to confirm a sepsis diagnosis. However, not everyone who is eligible to participate in the study will have sepsis. There may be other reasons besides sepsis that can cause these same signs or symptoms. Many children with suspected sepsis will be "false positives", i.e., appear to have sepsis but in fact will not have sepsis as determined by outcomes of blood tests and a response to treatment. Your child might be in this group, or your child may be in the "true positive" group that receive a confirmed clinical diagnosis and treatment of sepsis, severe sepsis or septic shock. For our research, we need data and samples from both groups of patients.

How many people will be in the study?

The study will involve up to 400 people taking part at 6 sites nationally: Children's National Hospital, Cincinnati Children's Hospital, Johns Hopkins, Johns Hopkins All Children's Hospital, UH Rainbow Babies and Children's Hospital, Emory University Hospital.

What will happen in this research study?

If you choose to participate in this research study, we will collect medical information (history, vital signs, lab results, x-ray results, and medications given) about your child for as long as they are in the hospital. We will do this by recording the information we need from your child's medical record and will keep it in the PI's office in a secure location.

Only children who, as part of their standard care, require a blood draw or have received an intravenous or arterial catheter that can be used to draw blood without any additional needle sticks will be asked to participate. We will ask your nurse to draw an extra sample of blood for this study. The sample taken will be no more than 5 ml (one teaspoon) for research purposes. In the event that an intravenous or arterial catheter is no longer available, the research tests will be drawn at the same time as the regularly scheduled blood draws ordered by your doctor. Blood will only be collected if it is thought to be safe by your doctor(s).

If we are unable to get blood during a routine clinical blood draw, we may also use leftover, unused blood from the laboratory that was sent for other routine tests and is no longer necessary for medical care.

All the samples collected from participating sites will be de-identified (blood sample labels will not contain any personal identifying information) and shipped to be processed at Children's National Research Institute.

How long will my participation in the research study last?

We will only collect blood once. Since we will also be collecting your child's medical record information, your child's participation ends when your child is discharged from the hospital. We will ask you to drop out of the study if either you or your study doctor thinks it is in your/your child's best interest.

Secure Sample Storage

All samples are given a code number and your child's name will be removed from the samples (deidentified) before they are stored. Any information that could link the sample to your child (like a name or birthday) will be kept in a password protected file on the hospital server. All personal medical information given to the study doctor will be strictly confidential and will be kept in a locked cabinet on a secure and restricted research floor.

What are the possible benefits from being in this research study?

If you agree for your child to take part in this research study, there will be no direct medical benefit for you or your child. The children who are part of this study will help us find out if combining the

information in the electronic medical records with markers from blood tests will lead to screening tools that identify patients at risk for sepsis sooner, and whether current treatments in sepsis are better for certain patients than others. If the research is successful, future patients may benefit from the information discovered.

What kinds of information will the study collect? Will any information be shared with me?

The blood samples will be collected and will undergo research tests to determine how to identify sepsis early. We will collect demographics information as well as clinical data from your child's medical record to be studied. No DNA or other genetic information will be collected or studied.

Most tests done on samples as part of research studies are only for research and have no clear meaning for health care. While it may be possible that some study data and test results have meaning for your health care, we are not planning to share data or test results from this research study with you or your doctors.

Will the information that I give you be shared with others? How will you protect my privacy?

Efforts will be made to limit the use and disclosure of your child's personal information, including research records, medical records, and Protected Health Information (PHI), to authorized members of the study team and to people who have a need to review this information. Your child's identifiable personal information will not be given to anyone unless we get your permission in writing, except as described in this consent form or if the law requires it. This information will also only be given for regular hospital care, payment, and hospital management activities. We will make every effort to keep your child's information private, but no one's privacy can be totally guaranteed.

Your child's medical record is confidential, but just like any medical record, there are some exceptions under state and federal law.

There are some third parties such as government agencies or other groups within (institution) that may check records that identify your child without your permission. They might review the study records and your child's medical records to make sure our results are correct and that we are following the law and protecting the people in the study. The agencies or groups who might see these records are the sponsor and the (institution's) Institutional Review Board (the ethics board that reviewed and approved this research study) and the Office for the Protection of Human Subjects.

The results of this research may be presented at meetings or in publications. You will not be personally identified.

Information that your child is participating in this study will be entered into his/her electronic medical record. This information will be seen by any medical provider caring for your child at (institution) and its affiliated institutions. In the uncommon event that your child is treated outside of this research study by a medical provider affiliated with (institution), there is a possibility that the medical provider may contact the Principal Investigator regarding your child's participation in this research study. The Principal Investigator will carefully decide on the type and amount of information he/she gives to the medical provider and will maintain your child's privacy and the confidentiality of the information to the greatest extent possible.

Finally, data and samples collected during this research with identifiers like your child's name, address, date of birth and phone number removed could be used for future research studies or given to another investigator for future research studies without your additional informed consent.

Certificate of Confidentiality

Sometimes people tell us some very personal information about themselves when they participate in a study, and it becomes part of their research record. To help us protect your privacy, the investigators have obtained a Certificate of Confidentiality from the Department of Health and Human Services (DHHS).

With this Certificate, the investigators cannot be forced (for example, by a court order or subpoena) to give information that may identify you in any federal, state, or local civil or criminal court, or in any administrative, legislative, or other proceedings.

It is important that you know that a Certificate of Confidentiality does not stop you or a member of your family from voluntarily giving information to others about yourself or your taking part in this research. You should also know that if an insurer or employer learns about your participation and you give them permission to receive research information about you, we cannot use the Certificate of Confidentiality to keep your information private from them. This means that you must also actively protect your own privacy.

Finally, it is important that you know that we are not prevented from taking steps to prevent serious harm to you or to others. If we learn that you or someone else is harming you or others around you, we may be required by law to report this to the police or a social services agency to get emergency help if it is needed.

A Federal law called "HIPAA" provides additional protections of your medical records and related health information. These protections are described below.

What other choices do I have if I don't want to take part in the study?

If you do not want to participate in the study, there are no other choices except not to take part. If you choose not to participate, it will not be held against you/your child and it will not affect the care you will receive in any way. If you choose not to participate, you can withdraw at any time without penalty. You may do so in writing or by contacting the research team. If you withdraw, we will not use your sample or data unless they are already analyzed.

Will it cost me anything to take part in the study?

There are no costs to you or to your insurance company for taking part in this study. You or your insurance company will have to pay for the costs of any routine or standard medical care that is not part of the study. This may include, but is not limited to, visits to the clinic, having to stay in the hospital, laboratory tests, x-rays, or other tests. If your insurance company does not pay for the routine or standard care, you will be responsible for paying for it.

Will I be paid for taking part in this study?

You will not be paid for taking part in this study.

Your child's information and samples (both identifiable and de-identified) may be used to help researchers create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you or to pay you or your family.

Blood Specimen Collection:

We are asking for your consent to allow us to collect a small additional blood sample (1-5ml) while your clinical team draws blood as a part of your child's standard care. If we are not able to get blood at the same time as the clinical team's routine blood collection, we would like your consent to allow us to collect your child's leftover, unused blood from the lab that would otherwise be discarded.

Please indicate your approval of any or all of the following by checking a box next to each statement and initialing your choice:

- I agree that the research team may ask the clinical team to draw an additional 1ml -5ml blood (based on weight, age and health) during a routine clinical care blood draw.

  ☐ Yes ☐ No Initials _____

- I agree that the research team may collect and unused, leftover blood from the (Insert hospital name) lab if the blood cannot be collected at the same time as clinical care blood draw.

  ☐ Yes ☐ No Initials _____

HEALTH INSURANCE PORTABILITY AND ACCOUNTABILITY

In 1996 the government passed a law known as The Health Insurance Portability and Accountability Act (HIPAA). This privacy law protects your individually identifiable health information (Protected Health Information or PHI). The privacy law requires you to sign an agreement so researchers can use or share your PHI for research purposes. This describes to you how information about you may be used or shared if you are in a research study. It is important that you read this carefully and ask a member of the research team to explain anything you do not understand.

I authorize the Investigator, (institution investigator) and his research staff to create, access, use, and disclose my PHI for the purposes described below.

Protected Health Information that may be used and shared includes:

- Information that identifies your child such date of birth, date of service, date of admission and discharge, gender, race, and other demographic information
- Information that relates to your child's health or medical condition from your child's medical records
- Information obtained from the study procedures outlined in this consent form, for example: things done to see if your child can join the study such as physical exams, blood and urine tests, x-rays and other tests, and any other medical information we learn from your child about your child's health history and family history
- Laboratory results obtained on specimens collected from you child (blood, urine, tissue)

The Researchers may use and share my child's Protected Health Information with:

- The Principal Investigator, other Investigators, Study Coordinators, and all administrative staff in charge of doing work for the study
- Government agencies that have the right to see or review your PHI including, but not limited to:
  - The Department of Health and Human Services (DHHS) Office of Human Research Protections (OHRP)
  - The Food and Drug Administration
- Institutional Review Board
- Institutional Quality Assurance Program, if applicable

In addition to the above people and organizations, the Researchers may also use and share my child's Protected Health Information with:

- Doctors and staff at multiple locations are participating in the study. The name(s) of the place(s) that are participating in this study are Computer Technology Associates, Children's National Hospital, Cincinnati Children's Medical Center, Johns Hopkins Children's Center, Emory

University/Children's Healthcare of Atlanta, and Case Western Reserve University/Rainbow Babies Hospital
- The Sponsor of the study and people that the Sponsor may contract with for the study. The name of the Sponsor is National Institute of Allergy and Infectious Diseases.

Also, your child's primary physician will be contacted if, during the course of your participation in the study, the researcher learns of a medical condition that needs immediate attention.

Should your child's health information be disclosed to anyone outside of the study, that information may no longer be protected by HIPAA and this Authorization. However, the use of your child's health information will still be regulated by applicable federal and state laws.

Banking of Blood Specimens:

We would like to store blood specimens collected from your child in this study in a tissue bank for future research as identified below. The blood bank is maintained by Center for Genetic Medicine, Children's National Research Institute. We will not conduct whole genome sequencing and no DNA or other genetic information will be collected or analyzed.

Please indicate your approval of any or all of the following by checking a box next to each statement and initialing your choice:

- My child's blood may be stored in the above-named bank for future analysis related to this study.

  ☐ Yes ☐ No Initials _____

You may change your mind at a later time and request that your tissue specimen be destroyed. If you change your mind and want to request that your blood sample be destroyed, you must do so in writing to:

Ioannis Koutroulis
Children's National Medical Center
Emergency Medicine
111 Michigan Avenue, N.W.
Washington, DC 20010-2970

Storage of PHI in a Database:

We would like to store personal health information collected from your child in this study in a database for future research. The database is maintained by Center for Genetic Medicine, Children's National Research Institute and Computer Technology Associates.

Please indicate your approval of any or all of the following by checking a box next to each statement and initialing your choice:

- My child's personal health information may be stored in the above-named database for future analysis related to this study.

  ☐ Yes ☐ No Initials _____

If you agree to participate in this research study, the research team, the research sponsor (when applicable) and the sponsor's representatives may use Personally Unidentified Study Data. The Personally Unidentified Study Data does not include your/your child's name, address, telephone, or social security number. Instead, the researcher assigns a code to the Personally Unidentified Study Data. Personally Unidentified Study Data may include your child's date of birth, initials, and dates your child received medical care. Personally Unidentified Study Data may also include the health information used, created, or collected in the research study. The research team or the research sponsor may share

the Personally Unidentified Study Data with others to perform additional research, place it into research databases, share it with researchers in the U.S. or other countries, or use it to improve the design of future studies. They may also publish it in scientific journals or share it with business partners of the sponsor and to file applications with U.S. or foreign government agencies to get approval for new drugs or health care products.

You do not have to sign this Consent/Authorization. If you decide not to sign the Authorization, your child will not be allowed to participate in the research study.

After signing the Consent/Authorization, you can change your mind and revoke this Authorization.

- If you revoke the Authorization, you must send a written letter to the institutional Investigator to inform him of your decision.

Ioannis Koutroulis, MD
Children's National Hospital
Emergency Medicine
111 Michigan Avenue, N.W.
Washington, DC 20010-2970

- If you revoke this Authorization, researchers may only use and disclose the PHI that was collected for this research study before you revoked the Authorization.
- If you revoke this Authorization, your child's PHI may still be used and disclosed if you should have an adverse event (unexpected side effect).
- If you change your mind and withdraw the Authorization, you child will not be allowed to participate in the study.

You will not be allowed to review the information collected for this research study until after the study is completed. If you are not allowed to review your information during participation in the study, when the study is over you will have the right to access the information.

This Authorization does not expire.

If you have not already received a Notice of Privacy Practices from (institution)**, you may request a copy and will be given one. If you have any questions or concerns about your privacy rights, you may contact us at (phone number).**

Whom can I contact if I have questions about this research study?

We want you to ask questions about any part of this research study at any time.

For questions about the study or the information in this informed consent/parental permission document, call the site Investigator, Ioannis Koutroulis at 202.476.8877 or you can email at EDResearchDirect@childrensnational.org. Or you may contact Pearl IRB. See below for contact information.

Pearl IRB
Monday through Friday 9-5 EST/EDT
29 East McCarty Street
Suite 100
Indianapolis, IN 46225
info@pearlirb.com
317-899-9341 (main)
317-602-6554 (fax)
https://www.pearlirb.com/ [pearlirb.com]

Whom can I call if I have questions or concerns about my rights as a research study participant?

We are available to talk with you about:

- Your rights as a research participant
- Your concerns about the research
- A complaint about the research

This is the administration office for the Institutional Review Board, which is a group of doctors, nurses, and non-medical people who review research studies for safety and the protection of people who participate in research. You can contact us at (phone number).

CONSENT/PARENTAL PERMISSION:

- I am authorized to act on behalf of the participant.
- I have read this consent form or had it read to me.
- I have been invited to take part in a research study. I was told why the research is being done and how long my child's participation in the study is expected to last. I was told about what will happen in the study.
- I was told that taking part in this research is voluntary. I also was told that I can decide not to take part or stop being in it at any time without any penalty to me or any change to the quality of care I receive at (Institution)
- I was told about the risks and possible discomforts of taking part in this research study. I was also informed that there will be no direct benefits to my child if my child is in this study.
- I have been given the chance to ask questions about the study, and my questions have been answered. If I have questions later, I can ask one of the people listed in this form.
- I agree to take part in this research study.
- I will receive a signed copy of this Informed Consent/Parental Permission form to keep.

Signature of LAR, Parent(s)/Guardian(s) for participant under the age of 18 years

Printed Name of Participant: _____

Printed Name of Parent/Guardian: _____

Signature of LAR, Parent/Guardian: _____

Date and Time: a.m. / p.m. (circle one) _____

AFFIDAVIT OF PERSON OBTAINING CONSENT / Parental Permission:

I certify that I have explained to the above individual(s) the nature and purpose of the study, possible risks, and potential benefits associated with participation in this study.

I have answered any questions that have been raised.

Printed Name of Person Obtaining Consent: _____

Research Role: _____

Signature: _____

Date and Time: _____