Inflammatory Response to Trauma – Does Early Cytokine Modulation Improve Patient Outcome?

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IRB Approval
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IRB1

KEY INFORMATION FOR Inflammatory Response to Trauma – Does Early Cytokine Modulation Improve Patient Outcome?

You are being invited to take part in a research study about early inflammatory modulation to improve surgical patient outcomes in trauma patient population

WHAT IS THE PURPOSE, PROCEDURES, AND DURATION OF THIS STUDY?

Dr. Aneja, MD, PhD, and his colleagues are asking you to participate in this research study because you suffer a traumatic injury to either your arm or leg or both due to a high energy mechanism, such as a car accident, farm injury, gun accident, a fall from > 15 feet, etc. This research is being done because accidental trauma is the 4th leading cause of death in the United States, and it is associated with a complex inflammatory response (you body's response after an injury). We are attempting to see if a drug (Ketorolac) given early after trauma alters the clinical outcome of trauma patients.

By doing this study, we hope to learn how to provide the best care for all of our patients in the state of Kentucky. Your participation in this research will last about 1 year.

WHAT ARE REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You are being asked to participate in this study because you are aged between18 to 75 and you have suffered a long bone fracture, meaning a broken bone in your upper or lower extremity (i.e. arm or leg), and you are currently admitted to the University of Kentucky Chandler Hospital Surgical Service.

WHAT ARE REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You should not participate in this study if you:

1. Are under the age of 18 or older than the age of 75
2. Had your injury more than 24 hours prior to transfer to University of Kentucky
3. Are currently in hemorrhagic shock or have significant risk of hemorrhage
4. Suffered a thermal injury
5. preexisting inflammatory medical condition such as: inflammatory arthropathy, inflammatory bowel disease (rheumatoid arthritis, crohn's, ulcerative colitis, etc)
6. Have acquired immunodeficiency syndrome (AIDS)
7. Have active GI bleed or ulceration
8. Chronically use steroids or immune modulating drugs or history of organ transplantation
9. Have chronic liver, kidney, or lung disease
10. Have a history of heart attacks or heart failure
11. Are pregnant or incarcerated
12. Have tested positive for H. pylori

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering. If you decide not to take part in this study, your decision will have no effect on the quality of medical care you receive.

Your alternative is to not take part in the study. If you choose not to take part, your healthcare at University of Kentucky will not be affected.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of this study is Arun Aneja, MD PhD of University of Kentucky, Department of Orthopaedic Traumatology There may be other people on the research team assisting at different times during the study.

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his contact information is:

Dr. Arun Aneja, MD PhD
Department of Orthopaedic Surgery and Sports Medicine
740 S Limestone, K400
Lexington, KY 40536
(859) 629-1970

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The research will be conducted at UK Hospital. The screening visit will take place while you are hospitalized for your injury. You will need to come to the Kentucky Clinic 740 S. Limestone Street, Lexington KY, for your regular follow up visits (3 week, 6 week, 3 month, 6 month, 1 year after initial surgery or hospital discharge). Each of those visits will take about 1 hour. The total amount of time you will be asked to volunteer for this study overlaps with your regular medical care, therefore, no additional time outside of your routine medical follow up visit is necessary. We will observe and record information regarding your care conducted at the University of Kentucky.

WHAT WILL YOU BE ASKED TO DO?

If you agree to participate in this study, we will treat your broken bone as we normally would. The only change to normal care would be to randomize you to one of two groups and additional blood samples taken as part of your routine labs.

If you agree to participate and are included in the study, you will be randomized into one of two groups:

- Group 1 will get a brief and low dose administration of a non-steroidal anti-inflammatory drug Ketorolac (Toradol) 3 times a day for the initial 5 days of hospital admission
  OR
- Group 2 will get the standard post surgery protocol, which you will **NOT** receive non-steroidal anti-inflammatory drug Ketorolac(Toradol).

Randomization is like the flipping of a coin (based on chance). Randomization for this study will be in a 1:1 fashion. This means that there is a 1 out of 2 (50%) chance that you will receive Toradol.

After consent, we will collect the first blood sample. This will involve two tubes and we will make our best efforts to coordinate this with you next scheduled blood draw. Each day following your enrollment for five days total we will collect two additional tubes of blood that we will use to determine the level of inflammatory markers you're your body is releasing. In total, we will collect 10 additional tubes of blood over a 6 day period.

After your orthopaedic surgery consultation in the emergency room, your medical care will be exactly the same as if you were not in the study. You will be asked to come back to the clinic and follow up with us at 2 weeks, 3 months, 6 months, and 1 year after your surgery or hospital discharge. These visits coincide with times you would normally come back to see your physician for a check-up. During these visits the following things will happen:

- You will have a physical exam
- Because you are in the study, you will be asked additional questions by a member of the study team. These questions will typically take about 5 minutes of your time and will usually be asked while you are waiting to see your surgeon.
- Wewill check to see if you have been re-hospitalized for your injury since your last follow-up visit. If you have, we will gather the details about the hospitalization from your medical record.
- We will ask you if you have had any problems with your treated fracture and if you have been told you have an infection by any of your doctors outside of this facility.
- You will also be asked if you are taking any kind of medication for any kind of infection.
- You will be evaluated by your primary orthopaedic surgeon for radiographic evidence of bone healing
- You will be evaluated by experienced research coordinator, who will administer a patient center survey that will ask you about your daily pain level and functional status.

In addition, at the 6 month study visit we would like to ask you some questions about pain, your health and general well-being. These questions are widely used in research and have been found to be useful in finding out how you are doing after your injury. These include the Short Form Musculoskeletal Assessment (SMFA) and Patient Reported Outcomes Measurement Information System (Promis). These questions should take you approximately 10 minutes to answer.

Finally, we would like to contact you by phone for the final study visit at 12 months following your injury. At that

time we will check to see if you:

- have been re-hospitalized for your injury since your last follow-up visit.
- have had any problems with your treated fracture and if you have been told you have an infection by any of your doctors outside of this facility.
- are taking any kind of medication for any kind of infection.

This call should last approximately 5 to 10 minutes.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There are standard risks with surgery. These will be explained to you along with your consent for surgery.

The risks associated with getting Toradol treatment are low. Depending on your treatment group, you will be either receiving Toradol treatment for 5 days or just the standard of treatment. There is minimal risk associated with taking Toradol. The dose we provide is very low, and the duration is brief. If at any time you experience any discomfort, such as difficulty breathing, stomach pain, or bloody stools, please notify your health provider There is always a chance that any medical treatment can harm you, and the investigational treatment in this study is no different. There is always the possibility that taking Toradol may make worse your diagnosed medical comorbidities, such as peptic ulcer disease, or bleeding disorder. In addition to exacerbating pre-existing conditions, Toradol can also cause a new ulcer or bleeding incident to occur. Please alert your health care provider any prescription medication you are currently taking, or any family history of bleeding disorders. There will be orthopedic surgery resident physicians, nurses, physical therapists, and/or medical students that will check on you daily to prevent that from happening while you remain an inpatient.

All treatments have potential to cause some side effects or other reactions; however, there are no treatments, therapies, or procedures directly involved with your participation in this research study. All treatments, therapies, or procedures you are receiving are part of standard of care and possible risks and discomforts from standard of care should be discussed with your primary care physician and your orthopaedic surgeon.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

There is no guarantee that you will get any benefit from taking part in this study. Your willingness to take part, however, may help doctors better understand and/or treat others who have similar injuries in the future.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of the overall care and treatment you receive during this study that you would normally receive for the treatment of your injury. By enrolling in the present study, no additional cost will be added to your overall medical cost. The University of Kentucky may not be allowed to bill your insurance company, Medicare or Medicaid for the medical procedures done strictly for research. The study sponsor will be paying for the 5 days of the study drug and its delivery

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

The information we collect from you will be kept private to the best of our ability. Your name, birth date, medical record number and any other information that could identify you as an individual will be removed from all study forms. Instead, we will label your forms with a unique study number. The link between your name and your study number will be kept confidential to the greatest extent provided by law and removed once your final follow up has been completed. The information collected for the study will be stored in a password protected, HIPPA verified computer database that only authorized members of our research team can use. When we report the results of the study, we will combine the information about you with similar information about forty other patients so your individual information will not be identifiable in any reports or publications.
We will make every effort to safeguard your data, but, the security of data obtained through commercial survey companies cannot be guaranteed. It is also possible the data collected for research purposes may be used for

marketing or reporting purposes by the company, depending on the company's Terms of Service and Privacy policies. We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. You should know that there are some circumstances in which we may have to show your information to other people such as the The University of Kentucky's Institutional Review Board/Office of Research Integrity, Law enforcement agencies when required by law, University of Kentucky representatives when situation arises, such as if you report information about a child being abused, or if you pose a danger to yourself or someone else.

We will use your information only for the purposes of this study. The data from the study may be published. However, you will not be identified by name. People designated from the institutions where the study is being conducted will be allowed to inspect sections of your medical and research records related to the study. This includes people designated by the Institutional Review Board at the University of Kentucky who is overseeing this study. Everyone using study information will work to keep your personal information confidential. Your personal information will not be given out unless required by law.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?

Your participation in this study is voluntary. You have the right to withdraw from the research study at any time without penalty. Your decision will not affect the medical care you receive. If you decide to stop participating, you should notify the study doctor or the research coordinator.

Dr. Arun Aneja, MD PhD
Department of Orthopaedic Surgery and Sports Medicine
740 S Limestone, K400
Lexington, KY 40536
(859) 629-1970

Your participation in this research study could be ended without your consent. Possible reasons could include our decision to end the study early or other reasons. If you choose to leaqve the study early, the data up to that point will remain in the database and will not be removed.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may not take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should discuss this with the investigator/your doctor before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Arun Aneja, MD PhD at (859) 629-1970 immediately. If you are hurt or become sick after normal business hours or on the weekend or holiday please call 859-323-5321 and ask to speak with the orthopaedic resident on call. Arun Aneja, MD PhD will determine what type of treatment, if any, that is best for you at that time.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

If you are injured or become ill because of your participation in this study, you will receive emergency medical care if needed and you will receive assistance in getting other medical care as needed. You or your insurance carrier will be billed for the cost of care, just as you would be billed for any other medical care. If you have any costs that are not covered by insurance, they are your responsibility.

You do not give up any of your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will not be compensated by participating in the present study. However, the information and knowledge learned from the present study has the potential to benefit millions of trauma patients in the future.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the researcher learns of new information regarding to your medical care, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

Do you give permission for Drs. Aneja and Bernard to contact you with information about research results or incidental findings that are determined to be important to you/your family's health? (Incidental findings are unforeseen findings discovered during the course of the research that may affect you or your family's health).

☐ Yes ☐ No _____Initials

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

- You will send a written letter to Arun Aneja, MD PhD (mailing address: K401 Kentucky Clinic 740 S. Limestone, KY 40536-0284) to inform him of your decision.
- Researchers may use and release your health information **already** collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).

WHAT ELSE DO YOU NEED TO KNOW?

There is a possibility that the data collected from you may be shared with other investigators in the future. If that is the case the data will not contain information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal, state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued. If you volunteer to take part in this study, you will be one of about 200 people at the University of Kentucky. A description of this clinical trial will be available on ClinicalTrial.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Mon-Fri at: (859) 323-1184.

You are the subject or are authorized to act on behalf of the subject. You have read this information, and you will receive a copy of this form after it is signed.

FUTURE USE OF YOUR PROTECTED HEALTH INFORMATIOON OR SPECIMEN(S)

Identifiable information such as your name, medical record number, or date of birth may be removed from the information or samples collected in this study. After removal, the information or samples may be used for future research or shared with other researchers without your additional informed consent.

In addition to the main study, you are being asked to allow us to keep and use your information and/or specimens for future research that involves surgical complications and patient outcome research in trauma patient population.

AUTHORIZATION TO DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. The following sections of the form describe how researchers may use your health information.

Your health information that may be accessed, used and/or released includes:

- Demographic information (name, initials, gender, race, age, height, weight, study number, mailing address, email address, and home/work cell initials, Social Security Number, Medical Record number, insurance information, marital status)
- Medical history, Type of injury, Smoking Status, BMI, Activities you usually did before your injury, circumstances of your injury, X-rays of your fracture, length of time in ICU,
- Medications taken prior to Injury, Medications used to treat your injury
- Employment status, Workers compensation status, Income
- Current Military Service

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity.
- Law enforcement agencies when required by law.
- University of Kentucky representatives.
- University of Kentucky Center for Clinical and Translational Science and/or Orthopaedic Trauma Association if grant(s) are funded
- Wake Forest University Clinical and Translation Science Institute (CTSI) if grant(s) are funded

Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws. You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign the form, it will not affect your:

- **Current or future healthcare at the University of Kentucky**
- **Current or future payments to the University of Kentucky**
- **Ability to enroll in any health plans (if applicable)**
- **Eligibility for benefits (if applicable)**

The registry will remove all information that could identify you such as your name, address, medical record number, etc., before sharing with investigators. The registry will not share information that could identify you without your permission.

After Signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). IF you revoke the authorization:

- You will send a written letter to: Arun Aneja, MD to inform him of your decision.
- Research may use and release your health information **already** collected for this research study.
- Your protective health information may still be used and released should you have a bad reaction (adverse event).

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5 pm EST, Monday-Friday at (859)323-1184.

Appendix A: Study Visits/Procedures

Upon arrival to the emergency room, you will be treated according to the standard Advanced Trauma Life Support (ATLS) protocol. After careful screening by Dr. Aneja and the research team, you will be asked to enroll in our study group. Once you are discharged from the hospital, trained research personnel will follow up with you and document any subjective pain scores and additional pain modulating medication intake. At 6 weeks after your hospital discharge, the principal investigator will evaluate for evidence of bone healing on radiographic imaging. Please see table below for detailed project timeline and schedule of activities.

Tentative time table of the proposed project											
Procedures	Daily Screen	Day 1	Day 2	Day 3	Day 4	Day 5	2 wk	6 wk	3 mon	6 mon	12 mon
Inclusion/Exclusion Review	x										
Informed consent	x										
Blood Sample		x	x	x	x	x					
Ketorolac intervention		x	x	x	x	x					
Pain assessment		x	x	x	x	x	x	x	x	x	x
Radiographic evaluation for fracture nonunion								x	x	x	x
Data Analysis											x
Years 1								Years 2 (12-18 mo)			
Active patient screening, enrollment, and data evaluation								Data Analysis and Manuscript preparation			

Appendix B: Risks

There are standard risks with surgery. These will be explained to you along with your consent for surgery.

The risks associated with getting Toradol treatment are low. Depending on your treatment group, you will be either receiving Toradol treatment for 5 days or just the standard of treatment. There is minimal risk associated with taking Toradol. The dose we provide is low, and the duration is brief. As a matter of fact, Toradol is a standard adjunctive pain medication in patients who receives colorectal surgery. If at any time you experience any discomfort, such as difficulty breathing, stomach pain, or bloody stools, please notify your health provider because it is our mission at UK that your health care will always come first.

There is always a chance that any medical treatment can harm you, and the investigational treatment in this study is no different. There is always the possibility that taking Toradol may exacerbate your diagnosed medical comorbidities, such as peptic ulcer disease, or bleeding disorder. In addition to exacerbating pre-existing conditions, Toradol can also cause a new ulcer or bleeding incident to occur. Please alert your health care provider any prescription medication you are currently taking, or any family history of bleeding disorders. There will be orthopedic surgery resident physicians, nurses, physical therapists, and/or medical students that will check on you daily to prevent that from happening while you remain inpatient.

All treatments have potential to cause some side effects or other reactions; however, there are no treatments, therapies, or procedures directly involved with your participation in this research study. All treatments, therapies, or procedures you are receiving are part of standard of care and possible risks and discomforts from standard of care should be discussed with your primary care physician and your orthpaedic surgeon.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Toradol (Ketorolac Tromethamine) is a nonsteroidal anti-inflammatory drug (NSAID) that is used to treat moderately severe pain and inflammation, usually after surgery. Toradol works by blocking the production of prostaglandins, compounds that cause pain, fever, and inflammation. The brand name Toradol is no longer available in the U.S. Generic versions may be available. Common side effects of Toradol include:

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- Headache
- Heartburn
- Upset Stomach
- Nausea
- Vomiting
- Diarrhea
- Stomach Pain
- Bloating
- Gas
- Constipation
- Dizziness
- Drowsiness
- Sweating
- Ringing in the ears.

Stop taking ketorolac and seek medical attention or call your doctor at once if you have any of these serious side effects:

- Chest pain, weakness, shortness of breath, slurred speech, problems with vision or balance;
- Black, bloody, or tarry stools;
- Coughing up blood or vomit that looks like coffee grounds;
- Swelling or rapid weight gain;
- Urinating less than usual or not at all;
- Nausea, stomach pain, low fever, loss of appetite, dark urine, clay-colored stools, jaundice (yellowing of the skin or eyes);
- Fever, sore throat, and headache with a severe blistering, peeling, and red skin rash;
- The first sign of any mouth sores or skin rash, no matter how mild;
- Pale skin, easy bruising, severe tingling, numbness, pain, muscle weakness; or
- Fever, headache, neck stiffness, chills, increased sensitivity to light, purple spots on the skin, and/or seizure (convulsions).

Less serious side effects may include:

- Upset stomach, mild nausea or vomiting, diarrhea, constipation;
- Mild heartburn, stomach pain, bloating, gas;
- Dizziness, headache, drowsiness;
- Sweating; or
- Ringing in your ears.

Appendix C: Subject information to be stored for future research

WHAT IS A REGISTRY AND WHAT IS THE PURPOSE OF THE REGISTRY?

A registry is a collection of medical information with pre-set definition of inclusion criteria. The purpose of the registry is to collect and store contact and/or health information for research purposes. Investigators can then use the stored information for future research studies to learn more about future treatment directions for providing the optimal care for trauma patients. The registry provides a ready supply of information, so investigators do not have to look for participants for each newstudy.

The registry will enroll 200 participants.

Participant Confidentiality: It is the investigator's responsibility to conduct the protocol under the current version of Declaration of Helsinki, ICH Guidelines, Good Clinical Practice, and rules of local IRBs. The investigator will ensure that the patient's anonymity be maintained in their data collection and submission.
Patients will be identified only by an identification code but not by their name, SSN, or hospital medical record number. Study Site Investigators will maintain a separate confidential enrollment log which matches identifying codes with the patients' names and addresses available only to local clinic staff to participate in the study.

All study forms, reports, and other records that are part of the study data collection materials will be identified by coded number to maintain patient confidentiality. All paper records will be kept in locked file cabinets. All electronic records of study data will be identified by coded number. Clinical information will not be released without written permission of the patient, except as necessary for monitoring by the Institution Review Board (IRB). Consent procedures and forms, and the communication, transmission and storage of patient data will comply with University of Kentucky IRB requirements for compliance with The Health Insurance Portability and Accountability Act (HIPAA).

Data Management: Following initial enrollment, each patient will be assigned a unique patient identifier. All electronic medical documentation will be associated with this unique patient identifier during analysis. All protected health information will be stored in a separate, password-protected research file that will not be accessed regularly. Following our secondary analysis, all personal health information will be removed from our electronic files and destroyed in accordance with patient privacy guidelines.

Data obtained at University of Kentucky during the study will be recorded that will be maintained at the hospital by the research staff. Final analysis will be conducted using Excel spreadsheets. All documents will be stored on a password-protected research drive and only research personnel will have access to its content. Paper documents, including consent forms, will be stored in a locked cabinet in a secure research room.

Each researcher on the project has passed the exam on ethical conduct of research and has received training and supervision regarding patient confidentiality. Only approved research personnel will administer consents and perform phone surveys. All efforts will be made to maintain the confidentiality of the patient reported data. Only study personnel listed will have access to identified study data.

All other research-related files including but not limited to copies of consents and surveys will be stored on a password protected research drive or locked research cabinet. Research personnel also have allocated space with locked drawers for source document files and secure workspace apart from patient or public areas that is also locked.

DOES TAKING PART IN THE REGISTRY COST ANYTHING?

There will be no additional costs or charges to you for taking part in the registry.

WHAT IF YOU CHOOSE NOT TO PARTICIPATE OR CHANGE YOUR MIND AND WANT TO WITHDRAW FROM TAKING PART IN THE REGISTRY?

Taking part in the registry is voluntary. Choosing not to take part will not affect your care or cause you to lose benefits to which you are entitled. You may withdraw your permission to continue taking part in the registry at any time. To do so, you must send a written withdraw request to Arun Aneja, MD PhD (mailing address: K401 Kentucky Clinic 740 S. Limestone, KY 40536-0284) to inform him of your decision.

The registry will destroy any remaining information that has been stored. In addition, it may be possible for the registry to destroy the code that links you with your medical information. However, the information that has already been shared with other investigators or placed in shared databases cannot be withdrawn.

INFORMED CONSENT SIGNATURE PAGE

You are a participant or are authorized to act on behalf of the participant. This consent includes the following:

- **Key Information Page**
- **Detailed Consent**
- **Appendices A, B, and C. Please refer to above for further details**

You will receive a copy of this consent form after it has been signed.

_____ _____

Signature of research subject *or, if applicable,* **Date**
**research subject's legal representative*

_____

Printed name of research subject *and, if applicable,*

_____

**Printed name of research subject's legal representative*

**If applicable, please explain Representative's relationship to subject and include a description of representative's authority to act on behalf of subject:*

_____

_____

_____ _____

Printed name of [authorized] person obtaining informed consent/HIPAA authorization Date

_____

Signature of Principal Investigator or Sub/Co-Investigator