

GENERAL CLINICAL RESEARCH CENTER PROTOCOL SUBMISSION INFORMATION

For your project, the General Clinical Research Center Branch of the NIH requires the following information to be provided. This is above and beyond the current requirements for the Institutional Review Board (IRB). With your project, please attach an addendum addressing the following points:

HUMAN SUBJECTS' ADDENDUM

1. RISKS TO THE SUBJECTS

Human Subjects Involvement and Characteristics: Describe the proposed involvement of human subjects in the work outlined in the Research Design and Methods section. Describe the characteristics of the subject population, including their anticipated number, age range, and health status. Identify the criteria for inclusion or exclusion of any subpopulation. Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners, institutionalized individuals, or others who may be considered vulnerable populations.

Sources of Materials: Identify the sources of research material obtained from individually identifiable living human subjects in the form of specimens, records, or data. Indicate whether the material or data will be obtained specifically for research purposes or whether use will be made of existing specimens, records, or data.

Potential Risks: Describe the potential risks to subjects (physical, psychological, social, legal, or other) and assess their likelihood and seriousness to the subjects. Where appropriate, describe alternative treatments and procedures, including the risks and benefits of the alternative treatments and procedures to participants in the proposed research.

2. ADEQUACY OF PROTECTION AGAINST RISKS

Recruitment and Informed Consent: Describe plans for the recruitment of subjects and the process for obtaining informed consent. Include a description of the circumstances under which consent will be sought and obtained, who will seek it, the nature of the information to be provided to prospective subjects, and the method of documenting consent. The informed consent document should be submitted to the PHS only if requested.

Protection Against Risk: Describe the planned procedures for protecting against or minimizing potential risks, including risks to confidentiality, and assess their likely effectiveness. Where appropriate, discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the subjects. In studies that involve interventions, describe the plan for data and safety monitoring of the research to ensure the safety of subjects.

3. POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

Discuss the potential benefits of the research to the subjects and others. Discuss why the risks to subjects are reasonable in relation to the anticipated benefits to subjects and others.

description of how the investigator will report unanticipated adverse events to the IRB, the GCRC and other federal agencies (FDA, CDC, etc.) may be sufficient. Additional information regarding this requirement and its implementation may be found at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html> If there are questions regarding this requirement, please contact James Heubi, M.D. at 636-8046 or james.heubi@chmcc.org.

EXAMPLE OF DATA AND SAFETY MONITORING PLAN (Taken from one of Dr. Heubi's Protocols)

Data and Safety Monitoring Board:

A Drug Safety Monitoring Board (DSMB) will be assembled which will include Dr. Richard Wenstrup, a pediatric geneticist with experience using alendronate for treatment of adults with Gaucher Disease, Dr. Heidi Kalkwarf, an Assistant Professor of Pediatrics with extensive experience with bone mineral metabolism and imaging techniques and Dr. Judy Bean, a biostatistician. Reports of adverse events will be provided to this group on an ongoing basis and they will meet every 6 months to assess progress of the proposal as well as adverse events. This group will assess adverse events and evaluate trends particularly as they relate to gastrointestinal symptoms since this is the area in which the highest risk of adverse events is likely to be seen. Should a trend in increased adverse events be recognized in the area of GI symptoms, the DSMB will meet and review them and make recommendations about modifying or continuing the study to prevent or reduce the frequency of these effects. Should a large statistically significant difference of improvement become apparent between the risedronate and placebo group, and this is judged by DSMB to be clinically significant, the committee will stop the study on ethical grounds. Likewise, if the DSMB determines that one group has a significantly higher incidence of adverse effects, the study will be terminated early.

ATTACHMENT

RACIAL/ETHNIC COMPOSITION OF POPULATIONS BY CATCHMENT AREAS

(Shown as percent of total population)

<u>Ethnic/Racial Groups</u>	<u>CHMC</u>	<u>University</u>	
		<u>Hospital</u>	
White	70.82	45.0	
African-American	23.39	51.0	
Asian/Pacific Islander	0.21	1.0	
Native American/Eskimo	0.03	N/A	
Other, Including Hispanic	5.55	3.0	
Male	51.0	41.0	
Female	49.0	59.0	
	<u>United States</u>	<u>Cincinnati</u>	
	<u>2000</u>	<u>2000</u>	
White	69.2	53.0	
African-American	12.1	42.9	
Asian/Pacific Islander	3.7	1.5	
Native American/Eskimo	0.7	0.2	
Hispanic/Not Hispanic	12.5/87.5*	1.3/98.7*	
Other	1.8	1.1	
	<u>Hamilton</u>	<u>Greater</u>	
	<u>County</u>	<u>Cincinnati</u>	
	<u>2000</u>	<u>2000</u>	
White	72.9	85.3	
African-American	23.4	11.7	
Asian/Pacific Islander	1.6	1.2	
Native American/Eskimo	0.2	0.2	
Hispanic/Not Hispanic	1.1/98.9*	1.1/98.9*	
Other	0.5	0.5	
	<u>Ohio</u>		
	<u>2000</u>		
White	85.0		
African-American	11.5		
Asian/Pacific Islander	1.2		
Native American/Eskimo	0.2		
Hispanic/Not Hispanic	1.9/98.1*		
Other	0.8		

N/A = Not Available

*Persons of Hispanic origin may be of any race

Sources: U.S. Bureau of the Census, Cincinnati Chamber of Commerce, Children's and University Hospitals