2. Protocol Synopsis: *1 page maximum*

PROJECT TITLE	**Evaluation of a novel screening strategy for rheumatoid arthritis**
BACKGROUND	Rheumatoid arthritis (RA) is a disease of immunological origin, which occurs in ~1% of the population and has a high personal and societal toll and major economic impact. Once viewed as an inexorably progressive disease, RA has become a potentially curable disease with very early use of disease-modifying antirheumatic therapy. Therefore, diagnosing RA early and identifying pre-clinical RA as accurately as possible has become a high-stakes undertaking. The contemporary view of its pathophysiology is a process that starts with a pathologic activation of the adaptive immune system (or 'immune onset of the disease'), followed by an asymptomatic period (or preclinical phase), which eventually leads to the 'clinical onset of the disease'. During the preclinical phase of RA, auto-antibodies are often already present and synovitis can be demonstrated on histology in clinically uninflamed joints. Biomarkers and clinical risk factors of pre-symptomatic disease exist and suggest that screening at risk populations for early detection of RA and treatment are not out of the realm of the possible
PRIMARY OBJECTIVE(S)	Develop and evaluate a screening strategy for the development of RA in first degree relatives of patients with RA.
METHODS	We will assemble a cohort of individuals at increased risk of RA, namely first-degree relatives of patients with RA. Participants will have risk factors for RA determined and be tested for biomarkers of RA susceptibility and followed prospectively until they develop RA.
INTERVENTION	Future Aim: We plan to launch a primary prevention trial in individuals at very high risk of developing RA and determine the efficacy of a therapeutic intervention on the development of RA. But this project is dependent on an effective screening project, which is submitted herein.
FOLLOW-UP	Up to five years
ENDPOINT(S)	Development of active RA and of early undifferentiated arthritis.
STATISTICAL ANALYSIS	We will determine the optimal combination of biomarkers and patient characteristics to predict the development of RA within 3-5 years of the screening procedure. The established standards for reporting diagnostic characteristics will be used (sensitivity, specificity, positive predictive value, negative predictive value, and ROC curve analysis)
TIME FRAME	3 years to reach inclusion objectives and the follow-up goals
REQUESTED BUDGET	CHF (total for three years): 180'000 FrS TOTAL YEAR 2012-4: 60'000 FrS / year