For BP clinical features, including bone marrow and cytogenetic examination, results will be reported to the patient's attending physician and be entered into the study database. Newly diagnosed cases of BP will be reported to the subject's physician and the SMCDCP for entry into the BP registry. Newly diagnosed and follow-up cases of BP will be cross-checked with SMCDCP to confirm removal from benzene- exposure environments.

11.3 AML

Cases of AML will not be subject to follow-up, AML being a final diagnosis in the Disease Progression Study. Moreover, no cytogenetic or molecular analyses of clonal abnormalities will be entered into the study database after chemotherapy has been initiated. However, additional follow-up of AML cases will be conducted by the clinical laboratory as requested in support of clinical management of the patient.

12 DIFFERENTIAL DIAGNOSIS AND DISEASE CLASSIFICATION

12.1 AA/MDS

Mild AA clinical features include gradual onset, easy fatigue, mild anemia, infection and/or mild bleeding. If the disease becomes progressively worse over 1-2 year history it is re-designated as severe AA. Peripheral blood parameters are characterized by a gradually decreasing hemoglobin, decreased reticulocyte counts, decreased white count, granulocytes, lymphocytes or platelets.

Severe AA is usually a fulminant illness and may be accompanied by acute symptoms of fatigue, shortness of breath, tinnitis, bleeding, shortness of breath or congestive heart failure. While serious infections are usually rare early in the disease the severity of bleeding is usually related to the degree of thrombocytopenia present. Peripheral blood counts usually reveal markedly reduced numbers of reticulocytes, granulocytes and/or platelets, while monocytes and lymphocytes are variably reduced, and bone marrow cellularity is markedly reduced. Cases of AA can be further characterized with respect to the involvement and severity and of individual cytopenias, i.e. granulocytopenic, lymphocytopenic, thrombocytopenic, or pancytopenic.

Severe MDS can be, and AML is almost always, a fulminant illness that may be accompanied by varying degrees of fatigue, shortness of breath, dizziness, bleeding or infection. Peripheral blood changes can involve anemia and variously either a marked increase or decrease in individual while blood cell counts. It is virtually impossible to distinguish among AA, MDS, CML or AML solely on the basis of clinical presentation, the differential diagnosis requiring morphologic, cytochemical, immunochemical and cytogenetic/molecular analysis of blood and bone marrow (WHO, 2001).

12.2 Mild AA and/or MDS

Peripheral blood parameters in mild AA are characterized by a gradually decreasing hemoglobin, decreased reticulocyte counts, decreased white count, granulocytes, lymphocytes or