

# Scientific Update on Benzene<sup>a</sup>

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## INTRODUCTION

Benzene has been used in industrial applications since the 1800s. The first toxicity studies were described by Santesson<sup>1</sup> and Selling<sup>2,3</sup> as disrupting normal hematopoiesis in humans and animals. There have been several reports documenting bone-marrow hypoplasia and aplasia produced by benzene exposure.<sup>4</sup> Several reports of benzene-induced leukemia were made as early as the 1920s,<sup>5,6</sup> but characterizing the specific mechanism of toxicity will remain a challenge for the next century. Problems with exposure measurements in epidemiology studies and the lack of an animal model of benzene-induced leukemogenesis have prevented an accurate, dose-response assessment of toxicity. However, the advent of novel molecular biology techniques, improved analytical detection, biomarker identification, and stratification of clinical endpoints have greatly reduced the uncertainty regarding benzene-induced leukemia.

## OVERVIEW OF BENZENE TOXICITY/LEUKEMOGENESIS

Over the past century, the chronic disease end points of benzene have typically been described as aplastic anemia or acute myeloid leukemia (AML). The progression of benzene toxicity was first observed in the workplace. The first signs of hematotoxicity, such as leucopenia, were reversible upon cessation of benzene exposure. However, prolonged exposure to high doses led to irreversible bone-marrow damage. Workers exposed to benzene solvent showed a range of hematotoxic effects including anemia, leucopenia, and thrombocytopenia.<sup>4</sup> Each of these is associated with the depression of one type of blood cell. In some cases, a depression in all types of blood cells results in pancytopenia, which is commonly associated with irreversible bone-marrow aplasia or aplastic anemia.

Benzene-induced AML is frequently, if not always, preceded by functional abnormalities in the bone marrow and in the growth of blood precursor cells well before the onset of leukemia. These abnormalities are heterogeneous but have been collectively described as a preleukemic syndrome<sup>7</sup> or myelodysplastic syndrome<sup>8</sup> (MDS). MDS is characterized by anemia, leukopenia, and thrombocytopenia in various combinations.

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