Abstract To monitor clinically significant isolates and their antimicrobial susceptibilities, all specimens sent to microbiology laboratory of the Kenyatta National Hospital were cultured on appropriate media. The susceptibility of the isolates was performed on Muller Hinton or diagnostic sensitivity test (DST) agar using comparative discs diffusion technique. The results were then entered into Microbe Base 2 computer programme. A total of 7416 clinically significant isolates were collected from 1991 to 1995. The most commonly isolated organisms were E.coli, Klebsiella and Staphylococcus aureus. Most of these hospital acquired infections had multiple resistance to conventional antimicrobials, namely, penicillin, tetracyclines, gentamicin, trimethoprim/sulphamethoxazole and ampicillin. The resistance pattern was high among both gram negative and positive bacteria isolates. Beta-lactamase production amongst them were 51%, 69.3%, 79.6% respectively. Prevalence of methicillin resistant Staphylococcus aureus was 39.8%. Addition of clavulanic acid to amoxycillin increased Staphylococcus aureus susceptibility three fold. The emergence of multiple drug resistance calls for a continuous monitoring and reviewing of antibiotic policy in the hospital and the country at large.