7 CONCLUSIONS

Drug resistance in trypanosomes appears to be an increasing problem in the tsetse-infested area of sub-Saharan Africa. Isometamidium is the only recommended prophylactic drug. In the current study the isometamidium sensitivity of stocks and clones of *T. congolense* from East and West Africa were assessed using a standardised protocol. An attempt was also made to understand the role of drug pressure in the development of isometamidium resistance in immunosuppressed animals, through induction of isometamidium resistance in a *T. congolense* clone in mice. Furthermore, possible involvement of the TbAT1 transporter gene in isometamidium resistance in *T. b. brucei* and *T. congolense* was assessed using field and laboratory stocks. The need to identify molecules that could serve as markers for this phenotype as well as to reveal the mechanisms by which drug resistance arises in nature is of paramount importance. Besides revealing new drug targets, this may serve as a good epidemiological tool for the early detection of drug resistance and design effective control strategies. Within the limits of the current study, the following conclusions are made:

1. The clones of *T. congolense* from Ethiopia and Burkina Faso expressed high level of resistance to isometamidium, with the clones from Burkina Faso expressing a significantly higher level of resistance than those from Ethiopia. There was no clonal variation in expression of resistance detected.
2. A series of *T. congolense* populations with varying degrees of isometamidium resistance can be generated by progressive sub-curative treatment of immunosuppressed mice. This will contribute to the understanding of the mechanism of isometamidium resistance in *T. congolense*, and the isogenic clones derived can be used for further comparative molecular studies. This may serve as a useful tool in experimental chemotherapy and has potential applications in the primary screening of candidates of new trypanocides.
3. There is a link between the presence of mutations in the nucleotide transporter gene (TbAT1) in *T. b. brucei* and isometamidium resistance.
4. The point mutations in the TbAT1 gene fragment in isometamidium-resistant *T. b. brucei* result in a change in Sfa NI restriction site. Thus, Sfa NI-RFLP, if validated with a large scale screening of field isolates, may serve as a convenient diagnostic tool for rapid identification of isometamidium-resistant *T. b. brucei*.

5. Attempts made to amplify the TbAT1 gene fragment described for *T. brucei* from the genomic DNA of *T. congolense* failed.