I. INTRODUCTION

No attempt will be made to review all aspects of renal in vitro techniques. The focus will be on renal slices and perfusion techniques as they apply to toxicological problems. For broader coverage of in vitro procedures, especially physiological studies the reader is referred to several reviews. In addition, extensive reviews of renal slices and renal perfusion and other techniques have been published.

Both of these procedures offer the general advantages associated with in vitro techniques. Difficulties associated with undesirable changes in renal haemodynamics, generalized changes in cardiovascular function, problems of maintenance of whole animal body temperature, etc., are obviated by isolated tissue. In general, better temperature control, more precise regulation of the perfusing or bathing solution, etc., is possible when isolated tissue preparations are examined. Since the use of these techniques will be presented in the context of toxicological investigations, it is noteworthy that using isolated tissues may obviate discovery of important effects of xenobiotics, albeit indirect effects on renal function. Alterations in cardiovascular function, for example, may be caused by certain chemicals and such effects could be translated into a perturbation of renal function. This would not be observed when the isolated tissue techniques are used. Hence, in general, the advantages of the in vitro procedures are to enhance precision and control, and a disadvantage is the loss of breadth of study.

No attempt will be made here to offer a complete review of renal physiology or anatomy, but a few words pertaining to renal function are necessary. For example, for an appropriate understanding of the power of the renal slice technique, it is important to appreciate which of the normal physiological processes can be assessed and how those data can be interpreted. Further, the
isolated perfusion kidney technique will be better appreciated if some aspects of renal haemodynamics as well as transport characteristics of the kidney are at hand. Hence, a few introductory comments will be offered with the understanding that details will have to be gleaned from the published literature. The comments here can serve merely as a guide to which aspects of renal physiology and biochemistry are important.

II. RENAL SLICES

Various studies have been undertaken to demonstrate the utility of the renal slice technique to monitor organic anion and organic cation transport. These studies have been directed at a better understanding of those processes involved in the active tubular secretion of diverse chemical substances. In general, the transport mechanism located on the peritubular side of proximal tubule cells is sufficiently effective to permit the rapid movement of certain organic substances such as p-aminohippuric acid (PAH) into the cells and their ultimate passive movement from the cells into the tubular fluid. The efficiency of this process is appreciated when it is realized that the clearance of a compound like PAH can be used to monitor total renal blood flow, given an estimate of the haematocrit. Similarly, various organic bases such as tetraethylammonium (TEA) can be transported equally rapidly and can also be used to monitor renal blood flow, although the latter is usually not done for various technical and analytical reasons.

Various studies, starting with those of Cross and Taggart and Mudge and Taggart, demonstrated the correlation of the in vivo secretory activities with a renal slice accumulation of those substances. Net accumulation of these model ions by renal slices provides a quantitative assessment of the magnitude of the transport process and these uptake data correlate qualitatively with the active tubular secretion of the same compounds. Hence, in vitro studies can be used to monitor the effects of various xenobiotics on these important transport functions. Since these functions occur in the proximal tubule and since many nephrotoxins exert their primary effect on that tubule section, the renal slice procedure can be used to assess nephrotoxic actions in well controlled in vitro experiments. In some experiments, important mechanisms of action may also be investigated, although in general the technique is most useful for assessment of the likelihood of a chemical effect on renal function. As indicated above, in all probability the utility of this procedure rests with the fact that most nephrotoxins appear to exert a primary action on one or another segment of the proximal tubular epithelium where organic ion transport occurs.

III. ISOLATED PERFUSED KIDNEY

The intent of this procedure is to allow the investigator to examine intact organ function under rather rigidly controlled in vitro conditions. Accordingly, it is important to develop techniques which