tem that will allow the investigator to examine the etiology, at the molecular level, of the toxicity of certain classes of chemicals and obtain more information on the predictability of the cutaneous irritancy potential of such chemicals.

Mainly for these reasons, in vitro systems are being developed to study cutaneous toxicity. Such systems include mammalian cells and tissues maintained in vitro by using standard tissue culture techniques, as well as cell-free systems prepared from living tissue for assay of subcellular changes caused by xenobiotics. Valuable information is currently being generated with these systems. One of the more promising contributions of in vitro systems anticipates the use of human biological material in designing models for studying toxicity.

Correlations between in vitro cytotoxicity and local irritancy in vivo were described by Schmidt, et al. (5), who used established cell lines of mouse liver and connective tissue, for a system assaying anesthetics. Another early developed cell culture system was described by Guess et al. (6) in which cytotoxicity was determined after exposing agar-overlay monolayer cultures to chemical irritants of varying potency. The test was reported to correlate well with implantation, intradermal, dermal, and intraocular tests in rabbits.

Some investigators have used cells derived from the skin in developing cutaneous toxicity in vitro assays. It is felt that the response of cells from this tissue would more closely reflect skin irritation. Early experiments by Hu and co-workers (7) demonstrated a correlation between in vitro cytotoxicity of topical medicants to keratinocyte cultures and local irritancy in vivo. Kao and associates (8) employed an organ culture system composed of full-thickness mouse skin to quantitate cutaneous toxicity. The 48-hr organ culture was treated topically with a xenobiotic and deleterious morphological changes were correlated with the incorporation of radiolabeled DNA and protein precursors, as well as with the leakage of intracellular enzymes into the culture medium.

As a result of these, and other earlier studies, some desired characteristics of mammalian cell systems have come to the forefront. For example, it has been established that, in some instances, cell types that become permanent lines with indefinite mortality through genetic alterations, lose much of the metabolic activity expressed by their progenitors. As a result, many cell culture systems currently under study use primary cells, which generally have retained many of the original genetic markers of the parent cell. Another example of the desirability of specialized in vitro cellular activity is the observation that cells cultivated and maintained in a microenvironment similar to that in vivo tend to display similar morphological and metabolic activities. Tissue cell types growing as monolayers sub-