

Animal-free and chemically-defined media for cell culture: an ethical and scientific duty.

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In the last fifty years, advances in cell culture techniques have allowed propagation and maintenance of eukaryotic cells from different tissues and organs in a highly differentiated state. Fetal bovine serum has been, until recently, an important and often essential supplement in cell culture media, providing important factors for cell adhesion, growth and differentiation. However, its widespread use has increasingly been criticized for both ethical and scientific reasons. Strong ethical objections for its use arise from the collection procedures from bovine fetuses that do not rule out animal suffering. But there are also many scientific reasons that advise against using it. Among the disadvantages of fetal bovine serum are the chemically undefined and variable composition in different commercial lots, the high costs, the risk of transmitting unknown pathogens, and the high protein concentration that interferes with purification procedures of recombinant cell culture products. The rapid increase in the production from cultured mammalian cells of biopharmaceuticals (recombinant proteins, monoclonal antibodies, viral vaccines) and in the therapeutic use of stem cells has boosted the development of chemical-defined media without animal-derived products, to reduce the risk of potential contamination from known and still unknown pathogens. Among the problems of developing a chemically-defined animal products-free medium is the need to adapt it to the specific needs of the different cell lines in the proliferative and differentiation stages. This is particularly relevant in the case of stem cells that need to maintain in culture both their proliferative capacity and their pluripotential ability to differentiate into distinct cytotypes.

For *in vitro* toxicology the use of chemically defined cell culture media is particularly important to guarantee a high reproducibility in dose-response curves of toxic substances, to allow more accurate prediction of *in vivo* toxicity. In addition, the presence of serum or other undefined proteins in the medium can interfere with the assays by binding and reducing the availability of the substance under investigation.