

## Agar difusion cytotoxicity assay for medical devices evaluation

### *Ensaio de citotoxicidade por difusão em ágar para avaliação de utensílios médicos*

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Polyvinyl chloride (PVC) is widely used in medical devices because of its specific properties, including flexibility, obtained after the addition of plasticizers (phthalates). Latex is a natural elastomer used for surgical gloves and condoms. Either PVC and latex devices should be non-toxic, eliciting no adverse response.<sup>1</sup>

Phthalates present in PVC cause adverse effects in rodent liver, kidney, and - for selected phthalates - in thyroid gland tissue and testes. Medical devices containing di-(2-ethylhexyl) phthalate are a source of significant exposure in a susceptible subpopulation of individuals, especially those undergoing intensive care, platelet transfusion, hemodialysis and extracorporeal membrane oxygenation (ECMO) in newborns.<sup>2</sup>

Thirteen latex allergens have been identified and isolated from natural rubber latex. Latex proteins present in surgical gloves and condoms can cause type I immediate hypersensitivity reaction, besides of type IV delayed hypersensitivity reaction caused by the chemicals added to latex during processing. Chemicals present in latex surgical gloves and condoms comprise accelerators like mercapto-benzothiazole, thiurams and carbamates, and antioxidants such as various amines. Clinical manifestations of latex allergy depend on the route of exposure and occur by direct contact either with skin, mucosa, or by inhalation.<sup>2</sup>

Biomaterials are assigned cytotoxicity ratings based on visual evidence of morphological cellular changes, including cell lysis, rounding, spreading, and proliferation. An accurate and precise in vitro cytotoxicity assay reduces the number of animal studies needed to develop a new medical device. The US FDA guidelines for medical device evaluation are in concordance with ISO-10993 requirements (FDA G95-1,1995)<sup>3</sup> so that medical device cytotoxicity may be evaluated according to ISO-10993-5 recommendations, with a visual scoring method. In contrast, the Japanese Ministry for Health and Welfare applies a more stringent standard for medical device approval and specifies that medical device cytotoxicity be evaluated using a quantitative assessment of surviving cells (MHW notification no. 99, 1995). In this issue the article "Evaluation of Brazilian Medical Devices using Agar Difusion Cytotoxicity Assay" by Mirian Noemi Pinto Vidal, Claudia Aiub, Shirley Abrantes and Helena P. da S. Zamith<sup>4</sup> it is described the use of L-929 mammalian fibroblast cells cushioned in red agar (viable cells depicted by the red presence on its citoplasm), in contact with PVC and latex samples no more than 25mm<sup>2</sup> (blood bags, catheters,

intravenous equipos, condoms) to evaluate cytotoxicity (cellular degeneration and malformation) which was scored from 0 to 4. Using this method it was observed an increase in the quality (citotoxicity decrease) in the quality of the Brazilian Medical Device products from 2000-2007 which can lead to an improvement in the population health.

### References

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