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Preclinical Validation of Freeze-Dried Kit of Albumin Nanoparticles Synthesized by a Radiolytic Method

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Radiopharmaceutical kits containing human serum albumin nanoparticles (HSA-NP), which after radiolabeling with Sodium Pertechnetate solution (99mTc) results in nanocolloids, are already commercialized by international companies. These kits are used to characterize the lymphatic system and, in particular, to detect sentinel lymph nodes in breast cancer and melanoma patients. Albumin has also recently been extensively utilized to form nanoparticles for drug delivery in cancer, i.e., Abraxane®, an FDA-approved nanomedicine consisting in paclitaxel encapsulated by albumin nanoparticles (130 nm), for metastatic breast cancer treatment (2005), lung cancer (2012), and metastatic pancreatic adenocarcinoma (2013). Well-established literature data, and experimental data obtained by our CRP research, demonstrate that albumin nanoparticles synthesized by gamma radiation have the potential to become a similar product to those available on the market. As the particle size distribution is well defined and parameters such as qualitative and quantitative composition are relevant and comparable to commercial ones. The albumin nanoparticles produced by radiation synthesis were lyophilized in a radiopharmaceutical kit containing HSA-NPs, Poloxamer 188, sodium phytate, tin chloride, glucose, and anhydrous disodium hydrogen phosphate. The OECD Guidelines for the Testing of Chemicals were performed to assure the safety of using the albumin nanoparticle freeze dried kits. The development of studies included: Genotoxicity tests (OEDC 471: Bacterial Reverse Mutation Test, OECD 474: Mammalian Erythrocyte Micronucleus Test), Carcinogenicity tests (OECD 453: Combined Chronic Toxicity/Carcinogenicity Studies) and Acute Toxicity (OEDC 420). In addition, biodistribution of 99mTc radiolabeled albumin nanoparticle was performed in healthy mice. The results show that HSA-NP was not able to induce chromosomal breaks and/or chromosomal gain or loss under experimental conditions, indicating no genotoxic effect. Furthermore, it was considered non-mutagenic, as it did not induce mutations by shifting the reading frame or substitution of base pairs in the genome of the strains used (TA97a, TA98, TA100, TA102 and TA1535). The treated rats had weight gain and the blood counts showed no abnormalities, in the same way normal biochemical parameters were found indicating the nontoxicity of the product. Furthermore, the ex-vivo biodistribution study in normal mice showed rapid blood clearance with high hepatobiliary and low renal excretion, which is in agreement with literature studies and commercial products leaflets.