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**LIFESPAN EXPOSURE TO LOW DOSES OF ASPARTAME BEGINNING DURING
PRENATAL LIFE INCREASES CANCER EFFECTS IN RATS**

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Short running head: Carcinogenicity of Aspartame

Key words: artificial sweeteners, aspartame, carcinogenicity, lymphomas/leukemias, mammary cancers, prenatal exposure, Sprague-Dawley

Abbreviations:

ADI	acceptable daily intake
APM	aspartame
BW	body weight
CMCRC	Cesare Maltoni Cancer Research Center
EFSA	European Food Safety Authority
ERF	European Ramazzini Foundation
EU	European Union
FDA	Food and Drug Administration

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ABSTRACT

Background. In a previous study conducted at the Cesare Maltoni Cancer Research Center of the European Ramazzini Foundation (CMCRC/ERF), we demonstrated for the first time that aspartame (APM), administered with feed at various doses to 8 week-old Sprague Dawley rats for the lifespan, is a multipotent carcinogenic agent. **Objective.** The aim of this second study is to better quantify the carcinogenic risk of APM, beginning treatment during fetal life. **Methods.** The study was conducted on groups of 70-95 male and female Sprague Dawley rats, administered APM with feed at concentrations of 2000, 400, or 0 ppm from the 12th day of fetal life until natural death. **Results.** The results of the study show: a) a significant dose-related increase of malignant tumor-bearing animals in males ($p < 0.01$), in particular in the group treated at 2000 ppm ($p < 0.01$); b) a significant increase of the incidence in lymphomas/leukemias in males treated at 2000 ppm ($p < 0.05$) and a significant dose-related increase of the incidence of lymphomas/leukemias in females ($p < 0.01$), in particular in the group treated at 2000 ppm ($p < 0.01$); c) a significant dose-related increase of the incidence of mammary cancer in females ($p < 0.05$), in particular in the group treated at 2000 ppm ($p < 0.05$). **Conclusions.** The results of this carcinogenicity bioassay not only confirm, but also reinforce the first experimental demonstration of APM's multipotential carcinogenicity at a dose level close to the acceptable daily intake (ADI) for humans. Furthermore, the study demonstrates that when lifespan exposure to APM begins during fetal life, its carcinogenic effects are increased.