



To whom it may concern

All procedures in animals were performed in accordance with Guidelines and Authorization for the Use of Laboratory Animals (Italian Government, Ministry of Health) and according to the European Community guidelines for animal care (DL 116/92, application of the European Communities Council Directive of 24 November 1986 (86/609/EEC).

The animal protocol was designed to minimize pain or discomfort to the animals. The animals were housed in an animal facility with monitored temperature and light (12 hour cycle and 21 ± 2 °C). All cages were floored with sawdust and bedding was replaced on a regular basis. The animals were allowed to acclimate to the environment for at least 7 days. Rats undergoing to in vivo treatments were randomly chosen and allocated into individual cages before initiating the study, with remaining rats caged together (4 rats/cage) in the close proximity to allow experimental animals to see and smell their companions. Rats had free access to water and food when they were not under testing. All animals were handled and trained for at least 1 week to reduce the possible stress induced by drug administration procedure.

All animals were euthanized by barbiturate overdose (intraperitoneal injection, 80 mg/kg pentobarbital sodium followed by cervical dislocation) for tissue collection.

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Dr. Maria Antonietta De Salvia