To whom it might concern:

I am very glad to declare, as the person responsible for the project granted by the Italian Ministry of Foreign Affairs (Roma) under the Law 212/26-21992, that Dr. Antoaneta Trendafilova (Institute of Organic Chemistry, Centre of Phytochemistry, Bulgarian Academy of Sciences, 1113, Sofia, Bulgaria) has actively taken part to this project in Siena under my supervision and that of prof. Fabio Ponticelli, at the Institute of Organic Chemistry and the Institute of Pharmacological Sciences, University of Siena, Italy in the period 1998-1999.

Aim of this project was to perform the synthesis of novel antioxidant agents able to overcome the limits shared by the antioxidant phenol derivatives currently used in food technology. In fact, some synthetic, phenolic antioxidants beyond antioxidant features exhibit, additional, interesting pharmacological activities, which are matter of investigations at my laboratory (Sgaragli G. et al., 1993; Fusi F. et al., 2001; Saponara S. et al., 2018,), thus pointing to the pleomorphic, pharmacophoric potential of the phenolic moiety portrayed, *inter alia*, by the general anaesthetic di-*iso*-propylphenol. A food additive, however, should not share pharmacological activities, through which it can unexpectedly interact with agents in clinical, human use by antagonizing or synergizing them. To respect this basic principle of either the traditional or the precision medicine, the most attractive option is to deal with an antioxidant that, *per se* or in the form of its metabolite(s), does not get access to the human body compartments.

To accomplish this goal it was devised to modify some antioxidants, i.e. BHA and *t*-butylhydroquinone (BHQ), giving rise to novel compounds provided with such hydrophilic/lipophilic feature that their cell permeability should expectedly be impaired, thus rendering ineffective the pharmacological activity of the parent compounds. Several types of substituents can be introduced into the phenolic system, but the synthesis of glycosyl derivatives of BHA and BHQ represents a first option, that was pursued by F. Ponticelli and A. Trendafilova up to the synthesis of some novel *O*-glycosides provided with antiperoxidant activity (Ponticelli F. and Trendafilova A., 1999; Ponticelli F. et al., 2001). Furthermore, derivatization of BHA gave rise to corresponding acetylated (**α-3a** and **β-3a)** and de-acetylated (**α-6a** and **β-6a**) *O*-glycosides that exhibited in hydrophilic compartment antioxidant activity comparable to BHA, presumably by scavenging peroxyl radical $\mathbf{HO_2}\cdot$ (Alov P. et al, 2019 manuscript to be submitted). This finding is of some interest in view of the possible, irreversible binding of effective radical scavengers to organic polymeric matrices acknowledged by food container technology, as this may improve considerably the food storing capabilities of containers made of antioxidant-harnessed polymers. Finally, a series of 22 novel BHA and BHQ gluco-, or, eno-pyranosides, and D-galactosides were synthesized which proved to be provided with good antioxidant properties (Saponara S. et al., 2019, manuscript in preparation).

I can say that Dr. Antoaneta Trendafilova skilfull dedication to this project has warranted the full success of this Italian-Bulgarian scientific cooperation,



Prof. Giampietro Sgaragli , 15 july 2019.