Pharmacokinetic profile assessment studies in male and female healthy volunteers comparing two new OD oral formulations of *Bacillus clausii* Enterogermina (4 x10^9 spores oral suspension or 6 x 10^9 spores powder for oral suspension) vs current formulations

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Enterogermina is an over the counter medicinal product for oral administration, whose active ingredient consists of spores of 4 strains of *Bacillus clausii* (strains O/C, T, N/R and SIN). Enterogermina is a probiotic widely used in Italy since the 1960s for bacterial and alimentary diarrhea in children and for antibiotic related side-effects. Up to now Enterogermina has been available on the market in vials for oral suspension or in capsules containing 2 billions spores of *B. clausii*.
Two new formulations containing *B. clausii* were developed in Origgio (VA) in one of the Italian industrial sites of Sanofi: vials 4 x 10^9 spores and sachets (powder for oral suspension) 6 x 10^9 spores.
A once a day (OD) administration of these formulations may represent a suitable alternative to the twice a day (BID) or to the three times a day (TID) administration of the current formulations in order to improve the compliance and the adherence to the therapy.
Two studies were designed by Sanofi Medical and Scientific Department in cooperation with Centro Ricerche Cliniche di Verona, the single center where the studies were performed with Dr. Milleri as principal Investigator. Primary objective was the comparison of the pharmacokinetic profile of these two new formulations and dose regimens with the existing ones. The secondary objectives were to evaluate the survival/persistence of *B. clausii* spores in the intestine of healthy volunteers by comparison of bacterial count (spores and vegetative forms) in fecal recovery after the administration of the two new formulations vs the existing ones and to evaluate the safety of the investigational products.
Both studies were performed according to a randomized, open label, cross-over design.
Conclusions: the pharmacokinetic profile of the newly developed Enterogermina formulations (4 x 10^9 *B. clausii* spores OD and 6 x 10^9 spores OD) resulted similar to that observed with the current oral formulations considered as reference:
• a superimposable AUC and daily curve profile of spore forms was observed up to the 8th day postdose;
• the survival/persistence profile of *B. clausii* spores in the intestine of healthy volunteers did not differ with the two new formulations in comparison with the existing ones;
• all Enterogermina formulations were well tolerated in terms of adverse events, laboratory parameters and vital signs.