Applicability of Roll Compaction for Mannitol Based Ibuprofen Formulations
C. M. Wagner ¹, L. Tobies ¹, M. Pein ¹, G. Moddelmog ², J. Breitkreutz ¹
¹ University of Dusseldorf, ² Merck KGaA

Purpose
To investigate roll compaction (RC) behavior of various mannitol grades in combination with the poor flowing and highly cohesive model drug ibuprofen.

Methods
Ibuprofen (70%) was blended for 10 minutes (Turbula®) with two spray-dried mannitol grades (A and B) and unprocessed, crystalline δ-mannitol (C), respectively. In a second series 2% crospovidone (Polyplastone®) was added as disintegrant. The powder mixtures were granulated using an instrumented roll compactor (Mini-Pactor®, Gerteis, specific compaction force 8 kN/cm, 2 mm gap between the rolls, 3 rpm roll speed). Tablets containing 1% magnesium stearate were produced on a rotary tablet press Pressima (IMA Kilian) equipped with concave 12 mm punches (Ritter Pharma-Technik) applying compression forces of 27, 44 and 76 MPa. The tablets were characterized with respect to their mass (MC210P, Sartorius), height, diameter (Digimatic Caliper, Mitutuyo), crushing force (TBH210, Erweka), abrasion (TAH120, Erweka) and disintegration (Sotax DT2). Tensile strength (σ) was calculated from crushing forces.

Results
RC of the first blends led to robust tablets with low abrasion applying compression forces ≥ 44 MPa (A: 0.75 ± 0.06 %, B: 0.82 ± 0.02 %, C: 0.81 ± 0.06 %). Nevertheless, disintegration behavior was insufficient. None of the produced tablets met the pharmacopoeial requirements for immediate release tablets (900 s). The addition of 2% disintegrant led to significant reduction of disintegration times (44 MPa, A: 187 ± 15 s, B: 113 ± 11 s, C: 114 ± 15 s). Tablets containing mannitol A reached the highest values for tensile strength (76 MPa, 1.06 ± 0.09 N/mm²), followed by mannitol B (0.93 ± 0.06 N/mm²) and C (0.88 ± 0.05 N/mm²). These findings confirm the results of our compactability studies of roll compacted granules made from pure mannitol powder, where spray-dried grades with a large BET surface area showed advanced compactability. However, these differences are less pronounced in ibuprofen granules than in drug-free formulation.

Conclusion
High dosed ibuprofen with poor manufacturing properties was roll compacted with various mannitol grades, spray-dried and crystalline δ-mannitol. Concerning flowability and the amount of fines granules with desired properties were obtained. Fast disintegrating tablets could be produced.