"Environmental resource footprinting of drug manufacturing: effects of scale up and drug administration"

This cooperative study between Ghent University and Janssen Pharmaceutica proposes the learning curve of cumulative resource consumption of pharmaceutical tablet manufacturing of PREZISTA® 800 mg through Wet Granulation (WG) at four consecutive scales in both R&D and manufacturing environments (resp. WG1 = 1 kg/h, WG5 = 5 kg/h, WG30 = 30 kg/h and WG240 = 240 kg/h). Second, the authors aim at evaluating the environmental impact from a life cycle perspective of a daily consumption of PREZISTA® 2 x 400 mg tablets versus the bioequivalent PREZISTA® 800 mg tablet which was launched only recently to meet patient compliance.

Environmental sustainability assessment in this study was conducted at three different system boundaries, which enables identification, localisation and eventually elimination of environmental burdens, in this case natural resource extraction. Exergy Analysis (EA) was used at process level (α) and plant level (β) while a cradle-to-gate Exergetic Life Cycle Assessment (ELCA) was conducted at the overall industrial level (γ) by means of the CEENE method (*Cumulative Exergy Extraction from the Natural Environment*) (Dewulf, Bösch et al. 2007). Life cycle stages taken into account are Active Pharmaceutical Ingredient (API) production, Drug Product (DP) production (in this case tableting) and packaging.

At process level (α), total resource extraction for the manufacturing of one daily dose of PREZISTA® (800 mg tablet) amounted up to 0.44 MJ_{ex} at smallest lab scale (WG1) while this amount proved to be reduced by 58, 79 and 83% at WG5, WG30 and WG240 respectively. At plant level (β) total resource extraction for the manufacturing of one daily dose of PREZISTA® amounted up to 2.41 MJ_{ex} at smallest lab scale (WG1), 0.91 MJ_{ex} at WG5, 0.40 MJ_{ex} at WG30 and 0.16 MJ_{ex} at industrial manufacturing scale (WG240). Expanding the boundaries of the product system under study to the overall industrial level (γ) reveals main resource demand is at the production of Active Pharmaceutical Ingredients (APIs), excipients, packaging materials and grid electricity. From the cumulative exergetic resource extraction on smallest lab scale (WG1) which amounts up to 7.70 MJ_{ex}/daily intake, 55% is due to the API production, 35% is due to the production of cleaning media (highest impact of electricity production for the heating of cleaning media) and approximately 6% is due to the production of primary and secondary packaging materials. At the largest scale (WG240) the production of cleaning media contributes considerably less to the total resource extraction. Second, when comparing PREZISTA® 2 x 400 mg tablets and the PREZISTA® 800 mg tablet at overall industrial level (γ), the absolute amount of resource extraction did not show a significant difference (5.14 versus 5.15 MJ_{ex}/daily intake).

Overall, the effect of scale on total resource consumption from a life cycle point of view showed a decreasing exponential trend when shifting from WG1 (smallest lab scale) to WG240 (industrial manufacturing). Drug administration (2 x 400 mg versus 1 x 800 mg) did not significantly affect the environmental burden. It could be concluded that in meeting social and economic demands by launching the PREZISTA® 800 mg tablet, no trade-off in environmental burden occurred.

Auteurs UGent: Wouter De Soete, Jo Dewulf, Lieselot Boone
Auteurs Janssen Pharmaceutica NV: Filip Willemse, Bert Heirman