Accepted Manuscript

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PII: S0022-3549(18)30154-0

DOI: 10.1016/j.xphs.2018.03.014

Reference: XPHS 1109

To appear in: *Journal of Pharmaceutical Sciences*

Received Date: 9 September 2017

Revised Date: 23 January 2018

Accepted Date: 8 March 2018

Please cite this article as: Schack MM, Møller EH, Carpenter JF, Rades T, Groenning M, A platform for preparing homogeneous proteinaceous sub-visible particles with distinct morphologies, *Journal of Pharmaceutical Sciences* (2018), doi: 10.1016/j.xphs.2018.03.014.

A platform for preparing homogeneous proteinaceous sub-visible particles with distinct morphologies

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Regulatory authorities and scientific communities are increasingly attentive to the known and universal presence of small particulates in biological drug products. The underlying concern is that these particulates may cause unwanted formation of anti-drug antibodies in patients Pharmacological studies, however, have to date not succeeded in unambiguously identifying risk-prone particle properties. This lack of success may be partly due to a lack of available, well-defined, homogenous particle material. Protein particles arising from stress of protein drug products are by nature often highly heterogeneous in size, morphology, and structure of the constituent protein in the particles. Here, we present simple and pharmaceutically relevant stress conditions to produce eight different highly homogenous micrometre-sized protein particles from human insulin, representing very different morphologies and conformation of the constituent protein molecules in the particles generated. Insulin's self-association patterns were varied by formulation approaches to create diverse starting materials. The resulting collection of homogenous particles underlines that the particle formation is not necessarily a random process but a consequence of formulation and specific stress condition. Due to the inherent homogenicity of these populations, the particle materials can act as a standard platform for further studies on sub-visible particles in insulin drug products.