# Pharmaceutical aspects of subvisible particles in protein formulations

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## Abbreviations

| | |
|---|---|
| % | percent |
| %RH | Percent relative humidity |
| °C | Degree Celsius |
| µg | Microgram |
| µL | Microliter |
| µm | Micrometer |
| ABD | Area based diameter |
| ACS | American Chemical Society |
| ADA | Anti-drug antibody |
| AF4 | Asymmetric flow field flow fractionation |
| Al | Aluminum |
| ANN | Artificial neuronal networks |
| APC | Antigen-presenting cell |
| API | Active pharmaceutical ingredient |
| Asp | Asparagine |
| AU | Absorption unit |
| AUC | Analytical ultracentrifugation |
| C | Carbon |
| Ca | Calcium |
| CD4+ | Cluster of differentiation 4 positive |
| CFR | Code of federal regulations |
| cIEF | Capillary isoelectric focusing |
| cP | Centipoise |
| cSt | Centistokes |
| CTA | Clinical trial authorization |
| DLS | Dynamic light scattering |
| DNA | Deoxyribonucleic acid |
| DP | Drug product |
| DS | Drug substance |
| DSC | Differential scanning calorimetry |
| DSF | Dynamic scanning fluorimetry |
| ECD | Equivalent circular diameter |
| EDX | Energy dispersive X-ray spectroscopy |
| ELISA | Enzyme-linked immunosorbent assay |

| | |
|---|---|
| Exp. | Expiration date |
| FDA | Food and Drug Administration |
| Fe | Iron |
| FTIR | Fourier transform infrared spectroscopy |
| g | Gram |
| Glu | Glutamine |
| h | Hour(s) |
| H | Hydrogen |
| $H_2O_2$ | Hydrogen peroxide |
| HCl | Hydrogen chloride |
| His | Histidine |
| HLA | Human leukocyte antigen |
| HMW | High molecular weight |
| HPLC | High performance liquid chromatography |
| HTF | High throughput formulation |
| ICH | International Council for Harmonization |
| IgG | Immunoglobulin G |
| IgG1 | Immunoglobulin G1 |
| IgM | Immunoglobulin M |
| IL | Interleukin |
| INF | Interferon |
| K | Potassium |
| kDa | Kilo Dalton |
| LA | License application |
| LDE | Laser Doppler electrophoresis |
| LMW | Low molecular weight |
| LO | Light obscuration |
| LOD | Limit of detection |
| mAb | Monoclonal antibody |
| MDa | Mega Dalton |
| MFI | Micro-Flow Imaging |
| mg | Milligram |
| Mg | Magnesium |
| MHC | Major histocompatibility complex |
| min | Minute(s) |
| mL | Milliliter |

| | |
|---|---|
| mM | Millimolar |
| mm | Millimeter |
| MS | Mass spectrometry |
| NaCl | Sodium chloride |
| nDSF | Intrinsic dynamic scanning fluorimetry |
| ng | Nanogram |
| NIST | National Institute of Standards and Technology |
| NK | Natural killer cells |
| nm | Nanometer |
| NPI | Nanoparticulate impurities |
| NTA | Nanoparticle tracking analysis |
| O | Oxygen |
| P | Phosphorus |
| Part./mL | Particles per milliliter |
| PBMC | Peripheral blood mononuclear cells |
| PDI | Polydispersity index |
| Ph.Eur. | European Pharmacopeia |
| PK/PD | Pharmacokinetics / pharmacodynamics |
| pKa | Acid dissociation constant |
| PVDF | Polyvinylidene fluoride |
| QC | Quality control |
| $R^2$ | Coefficient of determination |
| RI | Refractive index |
| RMM | Resonant mass measurement |
| RNA | Ribonucleic acid |
| rpm | Rounds per minute |
| s | Second(s) |
| S | Sulfur |
| SEC | Size-exclusion chromatography |
| SEM | Scanning electron microscopy |
| Si | Silicon |
| SLS | Static light scattering |
| SMR | Suspended microchannel resonator |
| TCR | T cell receptor |
| TFF | Tangential flow filtration |
| Tg’ | Glass transition temperature of the frozen state |

| | |
|---|---|
| Tm | Melting temperature |
| TNF | Tumor necrosis factor |
| UPLC | Ultra performance liquid chromatography |
| US | United States |
| USP | United States Pharmacopeia |
| UV | Ultra-violet |
| v/v | Volume per volume |
| w/v | Weight per volume |
| w/w | Weight per weight |
| λ | Wavelength |

## List of publications

**Weinbuch D***, Zölls S*, Wiggenhorn M, Friess W, Winter G, Jiskoot W, Hawe A. Micro-flow imaging and resonant mass measurement (Archimedes) - complementary methods to quantitatively differentiate protein particles and silicone oil droplets. *Journal of Pharmaceutical Sciences* 2013 Jul;102(7):2152-65.

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**Weinbuch D**, Jiskoot W, Hawe A. Light obscuration measurements of highly viscous solutions: sample pressurization overcomes underestimation of subvisible particle counts. *AAPS Journal* 2014 Sep;16(5):1128-31.

**Weinbuch D**, Cheung JK, Ketelaars J, Filipe V, Hawe A, den Engelsman J, Jiskoot W. Nanoparticulate impurities in pharmaceutical-grade sugars and their interference with light scattering-based analysis of protein formulations. *Pharmaceutical Research* 2015 Jul;32(7):2419-27

**Weinbuch D**, Hawe A, Jiskoot W, Friess W. Introduction into formulation development of biologics. In: *Challenges in Protein Product Development* by Mahler HC & Warne NW (editors). Manuscript accepted for publication.

**Weinbuch D**, Fogg M, Ruigrok M, Jiskoot J, Hawe A. Nanoparticulate impurities in pharmaceutical-grade sucrose are a potential threat to protein stability. Manuscript submitted for publication.

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## *Curriculum vitae*

Daniel Weinbuch was born on May 1st 1985 in Illertissen, Germany. In September 2004, he started his career by earning an associate degree as a pharmaceutical production technician at Merckle in Ulm, Germany and further gained experience in fill-finishing processes by working at the validation/qualification department for sterile dosage forms at ratiopharm in Blaubeuren, Germany, until August 2015. He subsequently pursued an academic study in Pharmaceutical Biotechnology at the Biberach University of Applied Sciences in Germany from which he graduated in January 2010. During this study, he wrote his Bachelor thesis on the development of human monoclonal antibodies by phage display at Boehringer Ingelheim in Ridgefield, CT, USA. He further worked as a scientist at the Kobe Pharma Research Institute in Japan in 2010 before earning his Master's degree in Biopharmaceutical Sciences from the Leiden University in the Netherlands in September 2012, where he focused on protein aggregation and unwanted immunogenicity. In February 2013, Daniel Weinbuch started his PhD project under the supervision of Prof. Dr. Wim Jiskoot at the Leiden Academic Centre for Drug Research (LACDR) in the Netherlands in collaboration with Dr. Andrea Hawe at Coriolis Pharma in Munich, Germany. While focusing on the topic "pharmaceutical aspects of subvisible particles in protein formulations", he (co-)authored seven peer-reviewed publications and gave podiums presentations at international conferences on several occasions. During the PhD project-collaboration, Daniel Weinbuch worked part-time as a formulation scientist at Coriolis Pharma. Since March 2016, he is employed as the Manager GRP (Good Research Practice) at Coriolis Pharma.