

04 · 2020



## Nachrichten und Mitteilungen

APV NEWS

International Association for Pharmaceutical Technology  
Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V.  
Gemeinnütziger wissenschaftlicher Verein



## 12<sup>th</sup> World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology

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# Lokale Gruppen

**Dienstag, 08. September 2020**

**Lokale APV-Gruppe Berlin** um 19:00 Uhr. Der Veranstaltungsort wird noch bekanntgegeben.

Weitere Informationen und Angaben zu dem Veranstaltungsort sowie den nächsten Terminen erhalten Sie bei Dr. Andreas Sachse (andreas.sachse@cpl-sachse.de).



**Mittwoch, 30. September 2020**

**Lokale APV-Gruppe Rhein-Main** ab 19:30 Uhr. Der Veranstaltungsort wird noch bekanntgegeben.

Weitere Informationen und Angaben zu dem Veranstaltungsort sowie den nächsten Terminen erhalten Sie bei Cathrin Pauly (pauly@aspiras.de).



**Mittwoch, 30. September 2020**

**Lokale APV-Gruppe Basel** um 18:30 Uhr im Restaurant „Gifthüttli“, Schneidergasse 11, 4051 Basel (www.gifthuetli.ch).

Bitte um Anmeldung bis zum 25.09.2020 bei Dr. Lars Restetzki (lars.restetzki@roche.com).



**Lokale APV-Gruppe Rhein-Neckar**

Weitere Informationen und Angaben zu dem Veranstaltungsort sowie den nächsten Terminen erhalten Sie bei Dr. Viktoria Riedel (viktoria.riedel@schwabe.de).



**Lokale APV-Gruppe Westfalen**

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Johanna Anlahr (johanna.anlahr@bayer.com).



**Lokale APV-Gruppe Nordrhein**

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Klaus Wening (klaus.wening@grunenthal.com).



**Lokale APV-Gruppe Mecklenburg-Vorpommern**

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Katharina Tietz (katharina.tietz@uni-greifswald.de).



**Lokale APV-Gruppe Oberbayern**

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. (USA) Julia Schulze-Nahrup (jsn@pharmoveo.de).



# What's hot in European Journal of Pharmaceutics and Biopharmaceutics?

Eduard Trenkenschuh, Ludwig-Maximilians-Universität, D-München

P. Gajjar et al./ European Journal of Pharmaceutics and Biopharmaceutics 151 (2020) 32-44

**3D characterisation of dry powder inhaler formulations: Developing X-ray micro computed tomography approaches**

P. Gajjar, I.D. Styliari, T.T.H. Nguyen, J. Carr, X. Chen, J.A. Elliott, R.B. Hammond, T.L. Burnett, K. Roberts, P.J. Withers, D. Murnane

Carrier-based dry powder inhaler (DPI) formulations need to be accurately characterised for their particle size distributions, surface roughnesses, fines contents and flow properties. Understanding the micro-structure of the powder formulation is crucial, yet current characterisation methods give incomplete information. Commonly used techniques like laser diffraction (LD) and optical microscopy (OM) are limited due to the assumption of sphericity and can give variable results depending on particle orientation and dispersion. The aim of this work was to develop new three dimensional (3D) powder analytical techniques using X-ray computed tomography (XCT) that could be employed for non-destructive metrology of inhaled formulations.  $\beta$ -lactose monohydrate powders with different characteristics have been analysed, and their size and shape (sphericity/aspect ratio) distributions compared with results from LD and OM. The three techniques were shown to produce comparable size distributions, while the different shape distributions from XCT and OM highlight the difference between 2D and 3D imaging. The effect of micro-structure on flowability was also analysed through 3D measurements of void volume and tap density. This study has demonstrated for the first time that XCT provides an invaluable, non-destructive and analytical approach to obtain number- and volume-based particle size distributions of DPI formulations in 3D space, and for unique 3D characterisation of powder micro-structure.

Ruben Wälchli et al./ European Journal of Pharmaceutics and Biopharmaceutics 151 (2020) 53-60

**Relationship of PEG-induced precipitation with protein-protein interactions and aggregation rates of high concentration mAb formulations at 5 °C**

Ruben Wälchli, Francesca Fanizzi, Jan Massant, Paolo Arosio

Native protein-protein interactions can play an important role in determining the tendency of monoclonal antibodies (mAbs) to aggregate under storage conditions. In this context, phase separation of mAb solutions induced by the addition of neutral polymers such as poly(ethylene glycol) (PEG) represents a simple method to assess the tendency of proteins to self-associate in the native state. Here, we investigated their relationships between PEG-induced phase separation, protein-protein interactions and long-term aggregation rate of several formulations of four mAbs at 100 mg/mL and 5 °C over 12 weeks of storage. We observed that the location of the phase boundary correlated well with the osmotic second virial coefficient

determined in absence of the polymer, indicating that for our solutions PEG primarily leads to depletion forces between protein molecules, which are additive to protein-protein interactions.

However, limited correlation between aggregation rate at 5 °C and phase behavior was observed across different mAbs, pH values and ionic strengths, indicating that colloidal stability is not the only determinant of aggregation even at such low temperature and high protein concentration. Our results contribute to the growing realization that aggregation propensity in the context of antibody developability is a complex feature, which depends on a variety of biophysical properties rather than one single parameter.

Juliana Radtke et al./ European Journal of Pharmaceutics and Biopharmaceutics 153 (2020) 43-51

**Real-time monitoring of multi-layered film coating processes using Raman spectroscopy**

Juliana Radtke, Peter Kleinebudde

Raman spectroscopy was used as an in-line PAT tool to predict the applied coating mass of three different coating layers on caffeine cores. The different coating suspensions contained titanium dioxide in the anatase and rutile modification and iron oxide as Raman markers. Partial least squares-regression (PLSR) and multivariate curve resolution-alternating least squares (MCR-ALS) were used for multivariate analysis. The acquired Raman spectra were correlated to the applied coating mass. MCR-ALS models were built and applied offline, while PLS-regression was implemented in the coating process to enable a real-time monitoring. Inline-measurements were optimized by a higher frequency of the spectral measurements and the implementation of a moving average. By PLS-regression analysis, all three layers could be predicted with root mean square errors (RMSEP) of less than 2.3%. Inline implementation and optimization resulted in RMSEPs less than 1.9%. MCR-ALS analysis was able to predict the application of the first and the second layer with RMSEPs less than 2.9%, but failed in predicting the application of the third layer. In conclusion, a real-time monitoring of a multi-layered coating process was achieved, PLS-regression was found to be superior to MCR-ALS and smoothing by the implementation of a moving average enhanced the predictability.

Marco Carfagna et al./ European Journal of Pharmaceutics and Biopharmaceutics 153 (2020) 84-94

**Heat flux sensor to create a design space for freeze-drying development**

Marco Carfagna, Monica Rosa, Matthias Lucke, Andrea Hawe, Wolfgang Frieß

Freeze-drying methodology requires an in-depth understanding and characterization for optimal processing of biopharmaceuticals. Particularly the primary drying

phase, the longest and most expensive stage of the process, is of interest for optimization. The currently used process analytical technology (PAT) tools give highly valuable insights but come with limitations. Our study describes, for the first time, the application of a heat flux sensor (HFS) to build a primary drying design space and predict the process evolution. First, the heat transfer coefficient ( $K_v$ ) generated by HFS and by the most accurate, but time-consuming and invasive, gravimetric method were compared. Second, the applicability to generate a design space was tested and verified. Obtained results revealed a good agreement of the values generated from this new and fast HFS compared to the gravimetric determination. Additionally, residual moisture assessed by Karl-Fischer titration and frequency modulated spectroscopy (FMS) support the quality of the obtained predictions. Thus, the HFS approach can substantially accelerate evaluation, development and transfer of a freeze-drying cycle.

In-Jeong Choi et al./ European Journal of Pharmaceutics and Biopharmaceutics 153 (2020) 150-157

**Patchless administration of canine influenza vaccine on dog's ear using insertion-responsive microneedles (IRMN) without removal of hair and its in vivo efficacy evaluation**

In-Jeong Choi, Woonsung Na, Aram Kang, Myun-Hwan Ahn, Minjoo Yeom, Hyung-Ouk Kim, Jong-Woo Lim, Seong-O Choi, Seung-Ki Baek, Daesub Song, Jung-Hwan Park

Microneedles provide the advantages of convenience and compliance by avoiding the pain and fear of needles that animals often experience. Insertion-responsive microneedles (IRMN) were used for administration to a hairy dog without removing the dog's hair. Canine H3N2 vaccine was administered with IRMN attached to the dog's ears ex vivo and the conventional microneedle system (MN) was administered for 15 min to compare puncture performance and delivery efficiency. The vaccine was also administered to compare antibody formation using IRMN with the use of intramuscular injection. The veterinarian observed the behavior of the dog during the course of the administration and compared the response to IRMN with that of intramuscular administration.

The tips of IRMN were separated from the base and delivered into the hairy skin successfully. Puncture performance of IRMN were the same as that of coated microneedles (95%), but delivery efficiency of IRMN were 95% compared to less than 1% for coated microneedles. The H3N2 vaccine inoculated into the dog's ears showed the same antibody formation as the intramuscular injection. The dog appeared to be more comfortable with IRMN administration compared to syringe administration. IRMN are the first microneedle system to deliver a canine vaccine successfully into a hairy dog without removal of the dog's hair. The use of IRMN can provide both convenience and compliance for both the dog and the owner.

## Impressum:

### Redaktion

Prof. Jörg Breitkreutz (Präsident der APV)  
Dr. Martin Bornhöft (Leiter der Geschäftsstelle der APV)

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### Verlag

ECV · Editio Cantor Verlag für Medizin und Naturwissenschaften GmbH  
Baendelstockweg 20 · 88326 Aulendorf · Germany  
Telefon +49 7525 940-0  
Telefax +49 7525 940-180  
email info@ecv.de  
web www.ecv.de

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### Druck

Holzmann Druck GmbH & Co. KG  
Gewerbestr. 2 · 86825 Bad Wörishofen · Germany

### Satz

Anna-Maria Pötzl · APV e.V.

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Anfragen bitte an [apv@apv-mainz.de](mailto:apv@apv-mainz.de), das Leasing-Unternehmen wird sich dann mit Ihnen in Verbindung setzen.

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Toyota Aygo 5-Türer 1,0-I-VVT-i 5-Gang "Team Deutschland" 53kW/72PS inkl. CarPlay, x-connect Smartphone-Integration, PDC hinten/Rückfahrkamera, 15" LMR etc.	11.748,00 €	115,00 €
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