MAKING SCIENCE WORK

Nachrichten und Mitteilungen

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

APV NEWS
02 · 2022

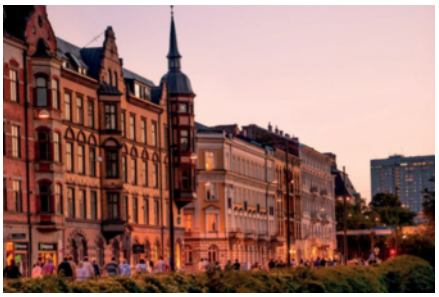
Skin Forum 2022
Annual Meeting

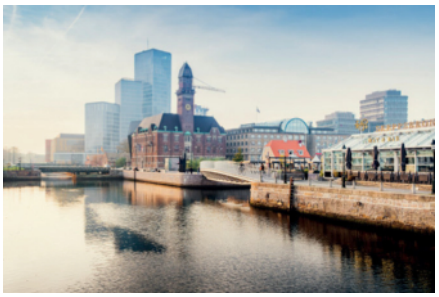
21 - 22 June 2022

Quality Hotel View, Malmö, Sweden

Course no. 6833

new venue
Malmö, Sweden





A conference organised by
The International Association for Pharmaceutical Technology
in partnership with Skin Forum

APV MAKING SCIENCE WORK

Skin Forum
international skin science network

Lokale Gruppen

Mittwoch, 25. Mai 2022

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).

Lokale APV-Gruppe Berlin

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

Lokale APV-Gruppe Ulm/Biberach/Ravensburg/Bodensee

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Martin Müller (martin.mueller@vetter-pharma.com).

Lokale APV-Gruppe Basel

Weitere Informationen und Angaben zu den nächsten Terminen erhalten Sie bei Dr. Lars Restetzki (lars.restetzki@roche.com).

Lokale APV-Gruppe Rhein-Neckar

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

Lokale APV-Gruppe Westfalen

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

Lokale APV-Gruppe Nordrhein

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

Lokale APV-Gruppe Mecklenburg-Vorpommern

Weitere Informationen und Angaben zu den nächten 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?

Elena Richert, Ludwig-Maximilians-Universität, D-München

Fasted intestinal solubility limits and distributions applied to the biopharmaceutics and developability classification systems

Qamar Abuhassan, Ibrahim Khadra, Kate Pyper, Patrick Augustijns, Joachim Brouwers, Gavin W.Halbert

After oral administration, a drug's solubility in intestinal fluid is an important parameter influencing bioavailability and if the value is known it can be applied to estimate multiple biopharmaceutical parameters including the solubility limited absorbable dose. Current in vitro measurements may utilise fasted human intestinal fluid (HIF) or simulated intestinal fluid (SIF) to provide an intestinal solubility value. This single point value is limited since its position in relation to the fasted intestinal solubility envelope is unknown. In this study we have applied a nine point fasted equilibrium solubility determination in SIF, based on a multi-dimensional analysis of fasted human intestinal fluid composition, to seven drugs that were previously utilised to investigate the developability classification system (ibuprofen, mefenamic acid, furosemide, dipyridamole, griseofulvin, paracetamol and acyclovir). The resulting fasted equilibrium solubility envelope encompasses literature solubility values in both HIF and SIF indicating that it measures the same solubility space as current approaches with solubility behaviour consistent with previous SIF design of experiment studies. In addition, it identifies that three drugs (griseofulvin, paracetamol and acyclovir) have a very narrow solubility range, a feature that single point solubility approaches would miss. The measured mid-point solubility value is statistically equivalent to the value determined with the original fasted simulated intestinal fluid recipe, further indicating similarity and that existing literature results could be utilised as a direct comparison. Since the multi-dimensional approach covered greater than ninety percent of the variability in fasted intestinal fluid composition, the measured maximum and minimum equilibrium solubility values should represent the extremes of fasted intestinal solubility and provide a range. The seven drugs all display different solubility ranges and behaviours, a result also consistent with previous studies. The dose/solubility ratio for each measurement point can be plotted using the developability classification system to highlight individual drug behaviours. The lowest solubility represents a worst-case scenario which may be useful in risk-based quality by design biopharmaceutical calculations than the mid-point value. The method also permits a dose/solubility ratio frequency distribution determination for the solubility envelope which permits further risk-based refinement, especially where the drug crosses a classification boundary. This novel approach therefore provides greater in vitro detail with respect to possible biopharmaceutical performance in vivo and an improved ability to apply risk-based analysis to biopharmaceutical performance. Further studies will be required to expand the number of drugs measured and link the in vitro measurements to in vivo results.

Adjustment of specific residual moisture levels in completely freeze-dried protein formulations by controlled spiking of small water volumes

Ken Lo Presti, Wolfgang Frieß

The residual moisture (RM) level strongly impacts the stability of freeze-dried biopharmaceuticals. On the one hand, the RM should not be too high to keep the reaction potential of water molecules low and to avoid a decrease in the glass transition temperature through the plasticizing effect of water. On the other hand, overdrying has been described to negatively impact protein stability. Consequently, an optimal RM has to be established and justified for approval by authorities. Therefore, end products with different RM are analyzed over storage. The different RM levels are typically obtained by slightly varying the lyophilization process itself; but deviations from the original process are critical. Additionally, samples can be taken during lyophilization runs, e.g. at the end of primary drying or after the ramp into secondary drying. This, however, does not allow for good control over the RM. Here we present the adaption of a headspace water spiking technique using a microliter syringe to precisely increase and adjust the RM. This technique is suitable to reproducibly introduce water in the microliter scale to achieve RM of less than 1% [w/w] with high precision depending on the dry cake weight. In addition, we show that by using different fill volumes and cake densities, an equal three-dimensional water distribution throughout the whole cake can be achieved. Furthermore, potential limitations and risks in manual RM introduction are discussed.

Towards quantification and differentiation of protein aggregates and silicone oil droplets in the low micrometer and submicrometer size range by using oil-immersion flow imaging microscopy and convolutional neural networks

Muhammad Umar, Nils Krause, Andrea Hawe, Friedrich Simmel, Tim Menzen

Biopharmaceutical product characterization benefits from the quantification and differentiation of unwanted protein aggregates and silicone oil droplets to support

risk assessment and control strategies as part of the development. Flow imaging microscopy is successfully applied to differentiate the two impurities in the size range larger than about 5 µm based on their morphological appearance. In our study we applied the combination of oil-immersion flow imaging microscopy and convolutional neural networks to extend the size range below 5 µm. It allowed to differentiate and quantify heat stressed therapeutic monoclonal antibody aggregates from artificially generated silicone oil droplets with misclassification rates of about 10% in the size range between 0.3 and 5 µm. By comparing the misclassifications across the tested size range, particles in the low submicron size range were particularly difficult to differentiate as their morphological appearance becomes very similar.

Wireless sensor networks for pharmaceutical lyophilization: Quantification of local gas pressure and temperature in primary drying

Andrew Strongrich, Alina Alexeenko

Wireless sensor networks have become prolific in a wide range of industrial processes and offer several key advantages over their wired counterparts in terms of positioning flexibility, modularity, interconnectivity, and data routing. We demonstrate their utility in pharmaceutical lyophilization by developing a series of wireless devices to measure spatial variations in gas pressure and temperature during primary drying. The influence of shelf temperature, chamber pressure, excipient concentration, and dryer configuration are explored for various representative cycles using a laboratory-scale pharmaceutical lyophilizer. Pressure and temperature variations across the shelf for these cases are shown to vary up to 1.2 Pa and 10 °C, respectively. Experimental measurements are supported by computational fluid dynamics simulations to reveal the mechanisms driving the vapor flow. The measurements and simulation data are then combined to estimate the shelf-wise sublimation rate in the inverse sense to within a deviation of 3% based on comparison with gravimetric data. We then apply the sublimation rate profile to obtain the vial heat transfer coefficient and product mass transfer resistance for a 5% w/v mannitol formulation. Finally, these parameters are applied to a one-dimensional quasi-steady heat transfer model to predict the evolution of the product temperature over the course of primary drying. Thermocouple measurements of product temperature are compared directly to the simulated data and demonstrate accuracy comparable to existing published one-dimensional models.

Impressum:

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

Vorstand der APV
Prof. Dr. Johannes Bartholomäus · Dr. Kathrin Bartscher · Dr. Karoline Bechthold-Peters · Prof. Dr. Jörg Breitkreutz · Prof. Dr. Heribert Häusler · Prof. Dr. Sandra Klein · Dr. Hans Lindner · Dr. Martin Lück

Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e. V. (APV)
Kurfürstenstr. 59 · 55118 Mainz · Germany
Telefon +49 6131 9769-0
Telefax +49 6131 9769-69
email apv@apv-mainz.de
web www.apv-mainz.de

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

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

Satz
Anna-Maria Pötzl · APV e.V.

Leasing auch für andere Investitionsgüter

Leasing und Finanzierung von Investitionsgütern zu günstigen Konditionen:

- ✓ schont das Eigenkapital
- ✓ schafft Liquidität
- ✓ ist bilanzneutral
- ✓ erhöht die Eigenkapitalquote
- ✓ verbessert das Rating
- ✓ ermöglicht den Einsatz neuester Technologie
- ✓ auch „sale and lease back“ möglich

Sehr interessant auch für Nutzer von Maschinen für die Pharmaindustrie:

- ✓ niedrige Leasingraten statt hoher Kaufpreise
- ✓ Erweiterung der Dienstleistungspalette vom Verkäufer zum Full-Service-Anbieter
- ✓ erhöhte Kompetenz als „all in one“-Anbieter
- ✓ kein Bonitäts-/Ausfallrisiko für Hersteller/Händler
- ✓ Finanzierung von Neu- und Gebrauchtmaschinen
- ✓ Abdeckung der kompletten Produktpalette

Unser Kooperationspartner bietet Leasing von Neu- und Gebrauchtfahrzeugen zu Sonderkonditionen an. Alle Marken und Modelle sind lieferbar. Die nachfolgende Tabelle gibt nur wenige aktuelle Beispiele möglicher Modelle und Marken wieder.
NEU: Vorführwagen (VfW) aus dem Leasing-Pool und Dienst-/Werkswagen (DW) zu attraktiven Konditionen erhältlich.

Alle Preise in Euro zuzüglich gesetzlicher Mehrwertsteuer. Beschaffung durch die Leasing-Gesellschaft. 36 Monate Laufzeit, ohne Anzahlung, Laufleistung 10.000 km pro Jahr, gewerbliches Leasing, Angebote freibleibend. Der Nachlass auf den Listenpreis ist in die ermäßigte Rate einkalkuliert. Der jeweilige BAFA-Anteil ist bei den Plug-In-Hybrid Fahrzeugen und den reinen Elektrofahrzeugen (ZOE) bereits wie eine Anzahlung berücksichtigt. (* = Service inklusive).

Anfragen bitte an apv@apv-mainz.de, das Leasing-Unternehmen wird sich dann mit Ihnen in Verbindung setzen.

Kfz-Leasing

Hersteller/Typ	Listenpreis	mtl. Rate
Audi A5 Cabriolet S line 40 TFSI 150kW/204PS S tronic inkl. Metallic, Infotainment-Paket Smartphone, Komfortpaket Sitze, Winterpaket, 3-Zonen-Komfortklimaautomatik, 18" LMR etc.	49.118,00 €	579,00 €
Audi e-tron S line 50 quattro 230kW inkl. Metallic, MMI Navigation plus, LED-Scheinwerfer, 2-Zonen-Komfortklimaautomatik, Einparkhilfe plus mit Umgebungsanzeige, 20" LMR etc.	58.887,00 €	359,00 €
BMW 118d Advantage 110kW/150PS inkl. Klimaautomatik, Sitzheizung Fahrer/Beifahrer, Parking Assistant, Ablagenpaket, Comfort Paket, 16" LMR Sternspeiche 517 etc.	31.891,00 €	379,00 €
BMW 330e Touring Advantage 215kW/292PS inkl. Automatic, Klimaautomatik, Parking Assistant, Sitzheizung Fahrer/Beifahrer, Sportsitze, Lordosenstütze, Live Cockpit Professional etc.	48.134,00 €	419,00 €
BMW X1 xDrive25e Advantage 162kW/220PS inkl. Automatic Getriebe Steptronic, Klimaautomatik, Parkassistent inkl. PDC, Business Paket, automat. Heckklappenbetätigung, 17" LMR etc.	41.681,00 €	339,00 €
CUPRA Born 170kW/231PS DSG inkl. Vordersitze + Scheibenwaschdüsen vorne beheizbar, Ladekabel Mode 2+3, Pilot M+ Pack, Navi, Rückfahrkamera, 19" Winterkompletträder zusätzl. etc.	40.529,00 €	389,00 €
Lexus UX 300e ELEKTRO 150kW inkl. 2-Zonen-Klimaautomatik, LED-Scheinwerfer, 7" Multi-Funktions-Monitor, Spurassistent, GRA, Fahrer-/Beifahrersitz elektr. verstellbar, 17" LMR etc.	36.588,00 €	299,00 €
MINI Cooper 3-Türer 100kW/136PS inkl. Classic Trim, Connected Navigation, Komfortpaket, Parkassistent/PDC, Sportsitze, Sitzheizung vorn, 16" LMR Revolite Spoke etc.	24.244,00 €	269,00 €
Polestar 2 Single Motor 69kWh 170kW inkl. 2-Zonen Klimatisierung, Navi, Einparkassistent vorne + hinten/Rückfahrkamera, Vordersitze beheizbar, Pilot Litle/Pilot Assist, GAP-Deckung etc.	38.172,00 €	339,00 €
Seat Arona FR 1.5 TSI 110kW/150PS DSG inkl. Metallic, 9,2" Media-System/Navi, Einparkhilfe v+h mit Kamera, Winter-Paket, Wireless Charger, Paket FR PRO, 17" LMR etc.	26.366,00 €	209,00 €
Seat Ateca Style 1.5 TSI ACT 110kW/150PS DSG inkl. Businesspaket Navigation, Parklenkassistent mit Einparkhilfe vorne und hinten, Winter-Paket, Klimaautomatik, 17" LMR etc.	29.076,00 €	279,00 €
Skoda Fabia Active 1,0 MPI 48kW/60PS inkl. Klimaanlage, Musiksystem Swing mit DAB+, Außenspiegel elektrisch einstell- und beheizbar, Fahrlichtassistent, Frontradarassistent etc.	13.101,00 €	99,00 €
Skoda Octavia Combi Active 1,0 TSI 81kW/110PS inkl. Klimaanlage, Parksensoren hinten, Ausstattungspaket Sound SmartLink Apple CarPlay/Android Auto, Bluetooth Freisprechanlage etc.	21.235,00 €	169,00 €
Toyota Yaris 1.0-l-VVT-i Comfort 53kW/72PS inkl. Klimaanlage, Einparkhilfe/-assistent hinten, Kamera, Bluetooth inkl. Musik Streaming, Tempomat, Lederlenkrad mit Multifunktion etc.	15.084,00 €	149,00 €
Toyota C-HR 1.8-l-VVTi Hybrid Business Edition 90kW/122PS AUT. inkl. 2-Zonen-Klimaautomatik, Navi mit Touch Screen, LED-Scheinwerfer, Einparkhilfe v+h/Kamera, GRA, 17" LMR etc.	26.378,00 €	239,00 €