USP Workshop on In vitro Testing for Meeting Future Challenges for Veterinary Dosage Forms
March 14–15, 2016
USP Meetings Center, Rockville, MD USA

Agenda

DAY ONE: Monday, March 14, 2016

8:00 – 8:30 a.m.	**Registration & Coffee**
8:30 a.m.	**Welcome** Margareth Marques, Ph.D., *USP Principal Scientific Liaison, General Chapters*
8:30 – 9:15 a.m.	**USP Revision Process** John Mauger, Ph.D., *Member, USP General Chapters–Dosage Forms Expert Committee*
9:15 – 9:45 a.m.	**Overview on the Project for Solubility Evaluation for Veterinary Drug Products** Marilyn Martinez, Ph.D., *Government Liaison, USP Solubility Criteria for Veterinary Products Expert Panel*
9:45 – 10:15 a.m.	**Break**
10:15 – 10:45 a.m.	**Solubility Evaluation versus Dissolution Testing** Marilyn Martinez, Ph.D., *Government Liaison, USP Solubility Criteria for Veterinary Products Expert Panel*
10:45 – 11:30 a.m.	**Challenges When Working with Different Animal Species** Steven Sutton, Ph.D., *University of New England*
11:30 a.m. – 12:30 p.m.	**Lunch**
12:30 – 1:00 p.m.	**Assessment and Interpretation of Solubility for Canine Oral Drug Products** Mark Papich, DVM, MS, *Member, USP Solubility Criteria for Veterinary Products Expert Panel*
1:00 – 1:30 p.m.	**Solubility evaluation – Cattle** Vivek Fellner, Ph.D., *North Carolina State University*
1:30 – 2:00 p.m.	**Feline Gastrointestinal Physiology** Andrea Fascetti, Ph.D., *University of California, Davis*
2:00 – 2:30 p.m.	**Solubility Evaluation – Pigs** Jérôme Del Castillo, m.v., M.Sc., Ph.D., *University of Montreal, Canada*
2:30 – 3:00 p.m.	**Break**

3:00 – 3:30	**Solubility Evaluation – Horses** Jane Owens, DVM, Ph.D., *Elanco Animal Health*
3:30 – 4:00 p.m.	**Solubility Evaluation – Poultry** Jeff Buhr, Ph.D., *US National Poultry Research Center, U.S. Department of Agriculture*
4:00 – 4:45 p.m.	**Panel Discussion & Next Steps**
4:45 – 5:45 p.m.	**Networking Reception & Adjourn**

DAY TWO: Tuesday, March 15, 2016

8:00 – 8:30 a.m.	**Registration & Coffee**
8:30 – 9:15 a.m.	**Overview on Dissolution Testing** Mansoor Khan, Ph.D., *Texas A&M Health Science Center, College of Pharmacy*
9:15 – 9:45 a.m.	**Use of USP Apparatus 4** Sunil Potdar
9:45 – 10:15 a.m.	**Dissolution of Medicated Feeds** Danna Mattocks, *Tergus Pharma*
10:15 – 10:45 a.m.	**Break**
10:45 – 11:15 a.m.	**Development and Validation of an *in vitro* Drug Exchange Method – A Case Study from Industry** Timothy Priddy, Ph.D., *Boehringer Ingelheim Vetmedica, Inc.*
11:15 a.m. – 12:00 p.m.	**Panel Discussion**
12:00 – 1:00 p.m.	**Lunch**
1:00 – 1:30 p.m.	**Tablets: Definitions and Characteristics** Elizabeth Pollina Cormier, Ph.D., *Center for Veterinary Medicine, FDA*
1:30 – 2:00 p.m.	**Development of Chewable Dosage Forms** Julie Lorenz, Ph.D., *Zoetis*
2:00 – 2:30 p.m.	**Dissolution of Chewable Formulations and Spray-dried Dispersions** Kevin White, *Elanco Animal Health*
2:30 – 3:00 p.m.	**Break**
3:00 – 3:30 p.m.	**Palatabilily Testing** Ann Stohlman, VMD, *Center for Veterinary Medicine, FDA*
3:30 – 4:15 p.m.	**Panel Discussion**

4:15 – 4:45 p.m.	**Potential Topics for Webinars and Next Workshops** Margareth Marques, Ph.D., *USP Principal Scientific Liaison, General Chapters*
4:45 – 5:00 p.m.	**Workshop Report / Closing Remarks** Margareth Marques, Ph.D., *USP Principal Scientific Liaison, General Chapters*

SPEAKER BIOGRAPHIES & ABSTRACTS
(listed alphabetically)

Jeff Buhr, Ph.D.
Research Animal Physiologist
U.S. National Poultry Research Center, U.S. Department of Agriculture
Athens, Georgia

Buhr has served as a Research Physiologist in the Poultry Microbiological Safety and Processing Research Unit at the US National Poultry Research Center's Russell Research Center since 1997, and holds an Adjunct Faculty appointment in the Department of Poultry Science at the University of Georgia. He earned a Ph.D. in Veterinary Anatomy from the University of California-Davis and he conducts research that is focused in the area of poultry food safety specifically on *Salmonella* and *Campylobacter* detection, recovery, and decontamination during the rearing of table egg laying hens, broiler breeders, and broilers, and during the slaughter and processing of broilers.

His research evaluating processing mechanical factors (electrical stunning voltage, electrocution, decapitation, application of electrical stimulation, and feed withdrawal duration) on evisceration efficiency demonstrated that the crop and intestines rupture during processing mainly because of greater adhesion, not because of weakness. His research was among the first to introduce molt diets for the molting of laying hens as a replacement to feed removal and revealed the associated suppression of the horizontal transmission of *Salmonella* during the molt. His recent research has evaluated alternative housing systems for table egg laying hens and the incorporation of probiotics or prebiotics into broiler feed or water to reduce the colonization and persistence of *Salmonella* and *Campylobacter* during growout through feed withdrawal, cooping, transport, and the sequential steps for processing broilers.

Buhr has served as the course instructor for lectures and laboratories at the University of California-Davis in Avian Microanatomy, Comparative Anatomy, Musculoskeletal Anatomy, Thoracic and Abdominal Anatomy; and at the University of Georgia in Avian Anatomy and Physiology, Avian Reproductive Physiology, and Poultry Processing Technology.

Buhr's research collaborations have resulted in 160 manuscripts, 275 abstracts, and 50 proceeding paper presentations. Forty-nine of these manuscripts were first-authored by undergraduate, M.S., Ph.D., or postdoctoral students, and for many was their very first manuscript. Buhr has valued the experiences mentoring students in the classroom and research projects in several disciplines. He is the recipient of the Poultry Science Association National Chicken Council Broiler Research Award in 2009 and the Frank Perdue Food Safety Award in 2012.

Presentation
Solubility Evaluation – Poultry
Monday, March 14, 20016, 3:30 p.m. – 4:00 p.m.

The chicken alimentary track differs in several ways from most other domestic food production animals. Chickens are considered monogastric omnivores although their stomach consists of two adjacent segments; the chemical proventriculus followed by the mechanical ventriculus (gizzard). The names used for the segments of the chicken small and large intestines are not consistently used in the literature and the boundary landmarks between adjacent segments varies or are not provided. The small intestine consists of three segments (duodenum, jejunum, and ileum) but the demarcation between the jejunum and ileum is frequently arbitrary and not based on morphology or function. The large intestine consists of the paired long cecum and a short colon, and the absence of a rectum (that portion of the colon within the pelvic canal) due to non-fusion of the pubic bones and the termination of the tract into the cloaca in the chicken.

Chickens can only swallow their feed whole with no chewing since they have no teeth, but an adult can quickly swallow a whole mouse or discarded sparkplug. The chicken's alimentary tract

is short in length and the ingested feed also has a short passage time compared to other domestic animals. The frequent occurrence of antiperistaltic contractions (ingesta reflux) moves the ingesta back-and-forth among several alimentary tract segments (duodenum to crop, gizzard to mouth, and cloaca to ceca) providing repeated opportunity for further digestion and adsorption of nutrients. The anatomical placement of the pancreatic and bile ducts entrances into the distal duodenum, just before transitioning to the jejunum, utilizes these antiperistaltic waves to neutralize the ingesta pH from 2 as it leaves the gizzard to a near neutral pH of 6 within the duodenum.

A clear understanding of the relationship between small intestine luminal villi morphology and function is, to a large extent, lacking for poultry. It is frequently stated and assumed that an increased small intestine villus height is an indication of improved absorptive function. However, experiments by Yamauchi et al. (2010) where they resected the proximal jejunum (50% removal), clearly demonstrated that ileal villi lengthening was a consequence of the dysfunctional resected jejunum. The small intestines of the chicken appear to have compensating ability to modify luminal morphology among segments to meet the physiological demand for absorptive surface area and maintain growth performance.

Chickens are provided precisely formulated feeds designed specifically to optimize growth in broilers or egg production in laying hens. Pelleting of broiler feed (compared to feed in mash form) can increase feed consumption in broilers by 10 to 20% resulting in an elevated ventriculus-gizzard pH and shorter feed passage times. Broilers reared under continuous light will eat every 20 to 30 minutes, those raised on less than 8 hours light will eat every 20 to 30 minutes in both the light and dark periods, and those subjected to 20 hours light and 4 hours dark daily will fill their crop to capacity within the last hour that proceeds the onset of the dark period.

Elizabeth Pollina Cormier, Ph.D.
Chemist
Center for Veterinary Medicine, U.S. Food and Drug Administration
Rockville, Maryland

Elizabeth Pollina Cormier, Ph.D. is a chemist for the US Food and Drug Administration's Center for Veterinary Medicine where she focuses on the evaluation of the various quality aspects of drug manufacturing. Prior to joining the FDA, Dr. Cormier received her bachelor's degree with honors in chemistry from Dartmouth College, during which time she conducted research at SUNY Stony Brook and Merck Research Laboratories and was a Howard Hughes Medical Institute Undergraduate Fellow. She received her Ph.D. in organic chemistry from the University of Pennsylvania, where she developed novel synthetic methods using samarium(II) iodide. Dr. Cormier is recognized as an expert in the regulation of active pharmaceutical ingredients, and has served on several FDA-wide committees involved in the development of Agency policies for Good Manufacturing Practices, contract manufacturing, and drug substances. With over ten years at FDA, she has received numerous awards, including the FDA Centennial Honor Award, for her contributions to FDA and the public health.

Presentation
Tablets: Definitions and Characteristics
Tuesday, March 15, 2016, 1:00 p.m. – 1:30 p.m.

Challenges must be overcome when developing novel dosage forms for veterinary products. Tablets, although a seemingly simple dosage form, present unique difficulties to drug manufacturers, not the least of which is consistency of definitions and usage of terms. Tablets may be categorized by route of administration, release, and method of manufacture. For veterinary products, chewable tablets do not need to be chewed to be effective and may be manufactured in several ways. Various control strategies and regulatory considerations are also discussed.

Jérôme del Castillo, M.V., M.Sc., Ph.D.
Associate Professor
University of Montreal
Montreal, Canada

Biography forthcoming.

Presentation
Solubility Evaluation – Pigs
Monday, March 14, 2016, 2:00 p.m. – 2:30 p.m.

Abstract forthcoming.

Andrea Fascetti, VMD, Ph.D.
Professor
University of California, Davis
Davis, California

Andrea Fascetti graduated from the University of Pennsylvania, School of Veterinary Medicine. Following graduation she completed an internship and medicine residency at The Animal Medical Center in New York City. She holds a doctoral degree in nutrition from the University of California, Davis. She is a Diplomate of both the American College of Veterinary Internal Medicine and the American College of Veterinary Nutrition. Andrea is currently a Professor of Nutrition at the University of California, Davis. She is the service chief for the Nutrition Support Service in the Veterinary Medical Teaching Hospital, as well as the Scientific Director of the Feline Nutrition and Pet Care Center, the Feline Research Laboratory and the Amino Acid Laboratory.

She has authored over 50 peer-reviewed original research publications. She also co-edited a textbook entitled, “Applied Veterinary Clinical Nutrition.” Andrea has served as the Secretary/Treasurer of the American College of Veterinary Nutrition and as a member at large on the executive board.

Her current research interests are trace mineral and amino acid metabolism in dogs and cats, obesity, carnivore nutrition, improvement of pet foods and clinical nutrition.

Presentation
Feline Gastrointestinal Physiology
Monday, March 14, 2016, 1:30 p.m. – 2:00 p.m.

The disciplines of nutrition and gastroenterology are intimately related by virtue of the primary role of the gastrointestinal tract in the assimilation of food. For all animals the digestive process is one that involves the combination of sequential mechanical, chemical and microbial activities. One way to think about the intestinal tract is that it is a continuous tube separated into regions by not only structure, but also function. As a result food is broken down, digested, absorbed and ultimately utilized by the animal. In mammals, fish and birds the processes of digestion and absorption are similar; but when looked at from an anatomical lens, the gastrointestinal tracts can differ significantly between these groups.

Mammals evolved to have even more significant variation on an anatomical basis. The major distinction is between ruminants (i.e. sheep and cattle), and simple stomached animals such as dogs, cats, pigs and humans. However, even amongst simple stomached animals there exist significant differences. When it comes to this subcategory, other species are often compared to the dog as the quintessential example of this anatomical type. Dogs and cats are members of the order Carnivora. Scientific observation supports differences in their anatomy, metabolism and nutritional requirements correlating with the evolution of these species. Nutritionally and metabolically, dogs and other members of Cannidea are generally considered omnivores, whereas cats and other members of the family Felidea are regarded as carnivores. While the gastrointestinal tract of the dog and cat are similar, there are some characteristic differences. The canine gastric mucosa has two distinct regions, whereas the cat has a uniform gastric mucosa. The dog has a distinct cecum but the cat only possess a vestigial appendix. The high surface area to bodyweight ratio is associated with a carnivorous diet. While the dog and cat have a very similar surface area per cm of intestinal length, the cat has a greater potential absorptive capacity than the dog. This presentation will review the response to a meal integrating the mechanical, chemical and microbial aspects of the digestive process through the cephalic, oral, esophageal, gastric, duodenal, small intestinal and large intestinal phases in the cat.

Vivek Fellner, Ph.D.
Professor
North Carolina State University
Raleigh, North Carolina

Dr. Fellner currently serves as full professor in the department of animal science at North Carolina State University. He received his PhD in animal science and biochemistry from the University of Missouri, Columbia. He pursued a post-doc at McGill University, Montreal, Canada and then joined a team of scientists at Agriculture and Agri-Food Canada in Ottawa where he worked as a Rumen Biochemist in the area of lipid chemistry. His main area of expertise is ruminant nutrition. Over the years, he has focused primarily on microbial ecology and energetics of microbial fermentation. Much of his research includes improving efficiency of nutrient use by gut microbes to enhance animal performance and minimize waste. He has spent more than 25 years looking at microbial requirements for growth and metabolism. He has used rumen microbes as a model for studying microbial physiology and to compare gut microbial ecology across various species of animals. His work has highlighted microbial transactions in the gut that mitigate production of greenhouse gas (GHG) emissions and optimize energy capture.

Presentation
Solubility Evaluation – Cattle
Monday, March 14, 2016, 1:00 – 1:30 p.m.

Oral administration of drugs in animals is a challenge due primarily to differences in their anatomy and physiology. Ruminants are pre-gastric digesters with a large fermentation chamber that harbors a complex and highly diverse microbial ecology. Bacteria are the most abundant rumen microbes present in concentrations as high as 10^{12} per mL of rumen fluid. Anaerobiosis and near basic pH (6.5) are two critical pre-requisites for microbial survival and optimal rumen fermentation. Ruminants rely on microbial enzymes to degrade plant material into methane, short chain fatty acids (SCFA) and microbial mass. Acetate, propionate and butyrate are the major SCFA that meet nearly 70 % of the animals energy needs. Actual production of SCFA is difficult to quantitate due to limited understanding of the complex metabolic processes and fluxes of SCFA within the rumen. Nevertheless, SCFA comprise the largest fraction among the end products of fermentation and they can have the greatest clinical consequence. It's commonly accepted that the bulk of SCFA are absorbed in their non-ionized (protonated; HSCFA) form. Others have argued the presence of specific transport systems for uptake of dissociated SCFA ($SCFA^-$). Production of SCFA also releases a large amount of protons that lower pH with a detrimental impact on rumen microbes. Several mechanisms exist that buffer the acid production and ameliorate rumen pH. Differential rates of passage for solid and liquid fractions has an impact on diffusion gradient across the rumen and plasma. Solids move at a slower rate compared to liquids. Soluble material moves faster but is more rapidly degraded by the microbes. In contrast, particulate matter has a reduced rate of fermentation but the increased retention allows more time for microbial attack. Attachment to particulate matter is a pre-requisite for the initiation of microbial digestion. This may likely interfere with the ability of drugs to exert their influence since several drugs are known to rapidly and extensively adsorb to solids in the rumen. The highly reduced environment in the rumen may also be another impediment to orally administered drugs. If drugs are designed to be absorbed post-ruminally they would have to remain intact and survive rumen conditions. If drugs are to be absorbed within the rumen they would need to rapidly solubilize, escape microbial attack and compete with SCFA absorptive processes. Rumen thermodynamics are important considerations in the pharmacokinetics of drugs administered orally to ruminants. The rate and extent of drug absorption depends on the degree of ionization, lipophilicity, and molecular weight. Antimicrobials and non-steroidal anti-inflammatory drugs (NSAID) are the two most prescribed class of drugs for cattle. Antimicrobials, in general, target specific microorganisms and alter

cellular mechanisms and membrane permeability. In comparison, NSAID are non-specific weak acids and occur mainly in non-ionized form in the acidic environment. There is considerable research on the mechanism of antimicrobials however very little is known about the fate of NSAID within the rumen. Both drugs however have to be delivered in a manner to minimize inactivation in the rumen either by physiological conditions or microbial metabolism.

Mansoor Khan, Ph.D.
Texas A&M Health Science Center, College of Pharmacy
College Station, Texas

Biography forthcoming.

Presentation
Overview on Dissolution Testing
Tuesday, March 15, 2016, 8:30 a.m. – 9:15 a.m.

Abstract forthcoming.

Julie Lorenz, Ph.D.
Director
Zoetis
Kalamazoo, Michigan

Julie Lorenz is currently Director of Analytical Sciences at Zoetis, Inc. Since obtaining her PhD in Physical Chemistry from The University of Wisconsin – Madison, she has worked in analytical, product development and pharmacokinetic/bio-analytical functions in the chemical, food and pharmaceutical industries. Her industry experience has allowed her to work on teams developing food and oral, chewable pharmaceuticals for humans and companion animals. For the last several years she has led a team responsible for chewable dosage form research and development across multiple species and active ingredients.

Presentation
Development of Chewable Dosage Forms
Tuesday, March 15, 2016, 1:30 p.m. – 2:00 p.m.

Chewable formulations are quickly becoming one of the most common oral dosage forms in companion animal health. The forms vary from soft and malleable to hard and crunchy, and each has its unique, positive attributes. This talk will provide an overview of the development of different chewable dosage forms and manufacturing processes. It will also include discussion on palatability, bioequivalence/ pharmacokinetics and physical properties testing.

Margareth Marques, M.Sc., Ph.D.
Principal Scientific Liaison, General Chapters; Workshop Moderator
USP
Rockville, Maryland

Biography forthcoming.

Presentations

Welcome
Monday, March 14, 2016, 8:30 a.m.

Potential Topics for Webinars and Next Workshops
Tuesday, March 15, 2016, 4:15 p.m. – 4:45 p.m.

Workshop Report / Closing Remarks
Tuesday, March 15, 2016, 4:45 p.m. – 5:00 p.m.

Marilyn Martinez, Ph.D.
Senior Research Scientist
Center for Veterinary Medicine, U.S. Food and Drug Administration
Rockville, Maryland

USP Affiliation:
Government Liaison, USP Solubility Criteria for Veterinary Products Expert Panel

Biography forthcoming.

Presentations

Overview on the Project for Solubility Evaluation for Veterinary Drug Products
Monday, March 14, 2016, 9:15 a.m. – 9:45 a.m.

Solubility Evaluation versus Dissolution Testing
Monday, March 14, 2016, 10:15 a.m. – 10:45 a.m.

Danna Mattocks
Senior Manager Analytical R&D/IVRT
Tergus Pharma, LLC
Durham, North Carolina

Biography forthcoming.

Presentation
Dissolution of Medicated Feeds
Tuesday, March 15, 2016, 9:45 a.m. – 10:15 a.m.

Abstract forthcoming.

John Mauger, M.S., Ph.D.
Associate Vice President for Health Services and Professor
University of Utah
Salt Lake City, Utah

USP Affiliation:
Member, USP General Chapters–Dosage Forms Expert Committee

John Mauger is currently professor of pharmaceutics and pharmaceutical chemistry at the University of Utah where he also serves as Associate Vice President for Health Sciences. His educational background includes a B.S. degree in pharmacy (Union University, Albany College of Pharmacy) and M.S. and Ph.D. degrees in pharmaceutics (University of Rhode Island). John's association with USP includes membership on expert committees and service as a member of the USP Board of Trustees where he also served as chair. His research interests include solubility properties pharmaceutical active ingredients and the application of physicochemical hydrodynamic principles to standards related to dissolution testing. He is an elected fellow of the American Association for the Advancement of Science.

Presentation
USP Revision Process
Monday, March 14, 2016, 8:30 – 9:45 a.m.

Overview of the USP standards setting revision process will be given, focusing on the work of the USP General Chapters–Dosage Forms Expert Committee.

Jane Owens, DVM, Ph.D.
Director
Elanco Animal Health
Greenfield, Indiana

Dr. Owens received a B.S. in Animal Science from the University of Kentucky and her DVM from Tuskegee University, School of Veterinary Medicine. She completed her Doctoral training in Equine Pharmacology at the Department of Veterinary Physiology, Pharmacology and Toxicology at Louisiana State University. She completed a Post-Doctoral Fellowship at the Chemical Industry Institute of Toxicology, Research Triangle Park, North Carolina. Dr. Owens has worked in the Animal Health Pharmaceutical industry for over 20 years to discover, develop and register new drugs for all veterinary species. While at Pfizer Animal Health, she was responsible for a team of scientists dedicated to understanding the pharmacokinetics, drug metabolism and food animal drug residues of new animal health products. At ELANCO Animal Health she has led teams to develop novel drugs for companion animals, equine and most recently, food animals. Dr. Owens is board certified by the American College of Veterinary Clinical Pharmacology and is the Past President of the American Academy of Veterinary Pharmacology and Therapeutics. She also serves as President and founding member of the Veterinary Pharmacology Research Foundation. Dr. Owens is an active participant on American Veterinary Medical Association committees and is the past chair of the Council on Biologic and Therapeutic Agents.

Presentation
Solubility Evaluation – Horses
Monday, March 14, 2016, 3:00 p.m. – 3:30 p.m.

Abstract forthcoming.

Mark Papich, DVM, MS
Professor of Clinical Pharmacology
North Carolina State University
Raleigh, North Carolina

USP Affiliation:
Member, USP Solubility Criteria for Veterinary Products Expert Panel

Dr. Mark G. Papich is a Professor of Clinical Pharmacology, and Supervisor of the Clinical Pharmacology Laboratory in the College of Veterinary Medicine at North Carolina State University. He is a diplomate in the American College of Veterinary Clinical Pharmacology (ACVCP), and has served as president of ACVCP. He is also a Fellow in the American Academy of Veterinary Pharmacology and Therapeutics. He has served on the Council of Experts and Chairman for the Veterinary Drugs Expert Committee for the United States Pharmacopeia (USP) and a member and current Chairholder of the Clinical Laboratory Standards Institute (CLSI) Veterinary Antimicrobial Susceptibility Testing subcommittee (VAST). He has taught veterinary pharmacology for over 25 years. He has authored/edited seven books on veterinary pharmacology and is one of the editors of the 9th and 10th editions of Veterinary Pharmacology and Therapeutics. He is author or co-author of 200 research papers published in refereed journals and has authored over 105 book chapters, and review papers. He has also delivered hundreds of presentations on veterinary pharmacology at national and international veterinary meetings, conferences and symposia.

Presentation
Assessment and Interpretation of Solubility for Canine Oral Drug Products
Monday, March 14, 2016, 12:30 p.m. – 1:30 p.m.

Oral drug delivery is a major route of drug administration in dogs, just as it is for humans. Therefore, it is important to consider how the physiological characteristics of the dog may influence the considerations that go into the classification of drug solubility. A recent assessment [1] used the Biopharmaceutical Classification System (BCS) criteria to classify oral medications administered to dogs as either low solubility or high solubility. In this analysis, there was uncertainty of the volume parameter to use for calculation of the Dose Number (Do) for dogs. A drug substance for people is considered *highly soluble* when the highest dose strength is soluble in 250 ml or less of aqueous media over the pH range of 1-7.5. The volume estimate of 250 ml is derived from typical bioequivalence study protocols that prescribe administration of a drug product to fasting human volunteers with a glass (about 8 ounces) of water. The *Dose Number* can be used to evaluate the solubility of the drug according to this formula: Do = (M/V)/C, where Do is the *Dose Number,* M is the *dose strength* of the tablet/capsule, V is the *volume administered* (defined as 250 mL in people), and C is the *drug's solubility* (mg/mL). A *Dose Number* ≥ 1 has been used to define a drug as a *low solubility drug*, whereas a *Dose Number* ≤ 1 has defined a drug as *high solubility drug*.
However, there is uncertainty in how to calculate this value for dogs. There is a lack of understanding of the residual volume of fluid in the canine gastrointestinal (GI) tract, and uncertainty regarding how much water (if any) is administered simultaneously with an oral dose form. The full capacity of a dog's stomach has been estimated, but this somewhat old reference[2] listed the stomach capacity in dogs is 100-250 mL per kg, with a range of 0.5 to 8 liters per dog. It is unreasonable to expect that a dog's stomach would contain this capacity each time an oral drug is administered. In the analysis of oral absorption of medications in dogs[1], there was little difference in the calculation of Do above 1.0 or less than 1.0 when using a value of 6 mL (conservative estimate for residual volume in canine GI tract) or a value of 35 mL (extrapolated from the value of 250 mL used in people). Furthermore, an analysis of oral absorption of medications in dogs found no relationship between drug solubility and oral absorption (F, fraction absorbed). It was concluded that other factors, besides solubility play a role in oral absorption of medications in dogs. Factors such as GI pH differences, GI transit

time, intestinal transporters, and intestinal metabolism all contribute to the complexity of predicting oral absorption of medications in dogs based on physical/chemical properties of the drug.

1. Papich MG, Martinez MN. Applying Biopharmaceutical Classification System (BCS) Criteria to Predict Oral Absorption of Drugs in Dogs: Challenges and Pitfalls. AAPS Journal. 2015 Apr 29.

2. Ellenberger W. & Baum H. Handbuch der vergleichenden Anatomie der Haustiere. 18th Ed. Berlin, Springer. 1943.

Sunil Potdar

Mr. Sunil Potdar is currently the Associate Director, Drug Development at Medefil, Inc. Mr. Potdar has expertise in formulation & analytical method development and validation for various pharmaceutical dosage forms.Mr. Potdar is leading a team of formulation and analytical scientists for parenterals drug development for ANDA and NDA applications. He provides formulation and analytical chemistry expertise to Medefil drug development programs.

Mr. Potdar received a Bachelor of Science in Chemical Engineering from UDCT, Mumbai, India and a Master of Science in Biomedical Engineering from University of Arkansas, Fayetteville, AR and is a PMP certified project management professional.

Before joining Medefil, Mr. Potdar worked as the Manager of Formulation Development at SGS life sciences where he was in charge of liquid and lyophilized formulation development and in vitro release method development using various apparatus such as USP APP-1, APP-2, APP-4, and APP-5. He successfully developed and validated multiple in vitro release methods for various dosage forms such as suspensions, lipophilic drugs, and capsules.

Presentation
Use of USP Apparatus 4
Tuesday, March 15, 2016, 9:15 a.m. – 9:45 a.m.

Abstract forthcoming.

Timothy Priddy, Ph.D.
Senior Scientist
Boehringer Ingelheim Vetmedica, Inc.
Saint Joseph, Missouri

Dr. Priddy has served BI in various roles for nearly nine years. He currently manages a small team in Vaccine R&D. They are tasked to develop, validate, and transfer analytical methods for both in-process and finished product testing for vaccines marketed in the USA and Europe. Previously, as Senior Manager of the Preformulations Laboratory in Ingelheim, Germany, Tim also managed a team responsible for developing, manufacturing, and testing small molecule pharmaceutical formulations used in global proof of concept studies for BI Vetmedica GmbH. Before transferring to Germany, he was responsible for small molecule formulation development for products manufactured at BIVI's Saint Joseph site. During the summer of 2011 came the challenge to develop and validate the *in vitro* Drug Exchange method that is the subject of this workshop. At that time, Tim was able to take the project from proof of concept at the BI facilities, through screening and validation in partnership with the contract laboratory that was evaluated and selected in collaboration with his colleagues. Dr Priddy earned his Ph.D. from the University of Missouri – Kansas City in the Department of Molecular Biology and Biochemistry. Prior to returning to industry, Tim performed his post-doctoral studies at the Macromolecule and Vaccine Stabilization Center on the Lawrence Campus of the University of Kansas in the Department of Pharmaceutical Chemistry.

Presentation
Development and Validation of an *in vitro* Drug Exchange Method – A Case Study from Industry
Tuesday, March 15, 2016, 10:45 a.m. – 11:15 a.m.

The release or exchange profile of an active pharmaceutical ingredient (API) from its carrier is an important characteristic of a drug product, especially a long-acting or modified release formulation. The ability to measure this phenomenon *in vitro* assures the product is manufactured using the intended quality of raw materials, including API and excipients, and that control of the overall compounding process is maintained. Developing and validating an *in vitro* drug exchange (IVDE) method that is capable to reproducibly demonstrate quality requires addressing some fundamental challenges. Primarily, identifying a suitable medium to extract the API over a reasonable amount of time to generate a release profile, while also ensuring the API is not degraded by this medium during the exchange interval and brief storage, prior to being assayed. Secondarily, design of a system and processes that can be used in a quality control (QC) laboratory setting to enable extraction, sampling, and quantitative measurement of the API exchanged from one medium (phase) into another. The final challenge is the ability to differentiate high-quality drug product from others containing the same API in what could be a lesser quality, or perhaps even a completely different formulation. To meet the third objective, the development strategy at Boehringer Ingelheim included comparison of the release profiles of the developmental product against numerous other formulations. These included a commercial product containing the same API in a different matrix, lab-scale batches containing the same API and excipients at variable concentrations, lab-scale batches containing similar or related excipients, and lab-scale batches containing degraded excipients. Statistical criteria were set to demonstrate the method was capable of discriminating the IVDE profiles of the developmental formulation from all others. QC testing at release and at real-time stability intervals assures the quality of the product throughout the intended shelf-life of the drug in the marketplace.

Ann Stohlman, VMD
Veterinary Medical Officer
Center for Veterinary Medicine, U.S. Food and Drug Administration
Rockville, Maryland

Ann Stohlman, VMD is a veterinary reviewer at the US Food and Drug Administration's Center for Veterinary Medicine (CVM) in the Office of New Animal Drug Evaluation. Dr. Stohlman's areas of focus include evaluation of endocrine and antiparasitic drugs for dogs and cats as well as labeling for companion animal drugs. Dr. Stohlman graduated from the University of Pennsylvania, School of Veterinary Medicine, in 1984. A native Washingtonian, she returned to the DC area to practice small animal medicine. After 14 years in private practice, Dr. Stohlman joined CVM as a veterinary reviewer in the Division of Therapeutic Drugs for Non-Food Animals.

Presentation
Palatabilily Testing
Tuesday, March 15, 2016, 3:00 – 3:30 p.m.

This talk will present an overview of considerations for clinical evaluation of palatability of oral dosage forms.

Steev Sutton, Ph.D.
Associate Professor and Chair
Department of Pharmaceutical Sciences, The University of New England
Portland, Maine

Steven (Steev) C. Sutton, BS Pharmacy, Ph.D, University of New England: Portland, ME
Dr. Sutton is Associate Professor and Chair of Pharmaceutics, College of Pharmacy, University of New England in Portland, Maine. He received his B.S. in Pharmacy from Massachusetts College of Pharmacy and a Ph.D. in Pharmaceutical Sciences from the State University of New York at Buffalo, New York. Dr Sutton began his career in the pharmaceutical industry working for CIBA-Geigy in Ardsley, NY (now Novartis), for INTERx in Lawrence, KS (then a part of Merck), and for Pfizer in Groton, CT, before embarking in a second career – that of academia – at the University of New England College of Pharmacy in Portland in 2009. Dr. Sutton founded the AAPS Oral Absorption Focus Group and in 2003, he became a Fellow of the AAPS. His research interests include predicting active pharmaceutical ingredient concentration-time profile in human after oral administration from chemical structure, modeling and simulation of oral absorption of low permeability and/or low aqueous soluble compounds, in vitro – in vivo correlation of orally administered controlled release dosage forms, species differences in GI physiology and transport of nanoparticles across the GI epithelium. Dr. Sutton has authored or co-authored over 120 book chapters, abstracts of work in progress, invited presentations and patents.

Presentation
Challenges When Working with Different Animal Species
Monday, March 14, 2016, 10:45 a.m. – 11:30 a.m.

Abstract forthcoming.

Kevin White
Research Scientist
Elanco Animal Health
Greenfield, Indiana

Kevin White, B.S. (Elanco), received a Bachelor of Science degree in biochemistry from Indiana University in 1987, and joined Eli Lilly and Company as an associate analytical chemist in 1990. In his 25 years with Lilly, Mr. White has led analytical control strategy development for multiple projects throughout the drug development process. His experience spans early pre-clinical development through to product registration as well as manufacturing and includes solid oral formulations, parenterals and oral pediatrics. In 2009 he joined a drug product performance team responsible for dissolution development strategies including method and control strategy development, application of biowaiver and post approval guidances as well as IVIVC/IVIVR strategies. He joined Elanco in 2014 as a research scientist in companion animal product development focusing on analytical control strategy development and dissolution strategies.

Presentation
Dissolution of Chewable Formulations and Spray-dried Dispersions
Tuesday, March 15, 2016, 2:00 p.m. – 2:30 p.m.

Developing a dissolution method for chewable companion animal dosage forms with multiple actives can be challenging. The dosage forms can increase in size due to dosing requirements and may contain problematic excipients designed for animal products or modified active ingredients (Spray-dried dispersions). In addition, dissolution development challenges are compounded when a large concentration difference exists between actives. For our presentation, we outline some general considerations when developing dissolution methods for such dosage forms. We examine how to approach solubility differences, precipitation issues and disintegration differences (erosion vs classical disintegration). We also relate these activities to the overall control strategy for dissolution of such dosage forms.