2nd Synthetic Therapeutic Peptides Workshop – Regulations, Standards and Quality
November 2-3, 2015
USP Headquarters, Rockville, Maryland, USA

Preliminary Agenda

(As of October 29, 2015 / Subject to Change)

Day One: Monday, November 2, 2015

8:00 a.m.	**Registration & Coffee**
8:30 a.m.	**USP Welcome** Jaap Venema, Ph.D. *Chief Science Officer and Chair of the USP Council of Experts, USP*
8:40 a.m.	**Workshop Overview** Michael De Felippis, Ph.D. *Chair, USP BIO1 – Peptides and Insulins Expert Committee*
8:50 a.m. –10:10 a.m.	**Session I – Raw Materials** Chair: Marion King, Ph.D., *Member, USP BIO1 – Peptides and Insulins Expert Committee*
8:50 a.m.	**Raw materials and Impurities** Kshitij (Kris) Patkar, Ph.D. *U.S. Food and Drug Administration, Center for Drug Evaluation and Research*
9:15 a.m.	**Risk Management on Starting Materials and Its Impact on the Quality of the Final API** Jon Rasmussen, Ph.D., *PolyPeptide Labs*
9:40 a.m.	**Panel Discussion / Q&A (30 min)**
10:10 a.m.	**Morning Break**
10:40 a.m. –12:30 p.m.	**Session II –Analytical Characterization** Chair: Anita Szajek, Ph.D., *USP*
10:40 a.m.	**Modern Analytics for Synthetically Derived Complex Drug Substances: NMR, AFFF-MALS, and MS Tests for Glatiramer Acetate** Sarah Rogstad, Ph.D., *FDA/CDER*
11:05 a.m.	**Analysis of PEGylated Synthetic Therapeutic Peptides Using UHPLC-TOF Mass Spectrometry** Osama Chahrour, Ph.D., *Almac*
11:30 a.m.	**Zwitterionic Chiral Stationary Phases for Amino Acid and Peptide Stereoisomer Separations and as Complementary Tool for Therapeutic Peptide Quality Control** Prof. Wolfgang Lindner *(University of Vienna)* and Prof. Michael Lämmerhofer *(University of Tübingen)*

12:00 a.m.	**Panel Discussion / Q&A (30 min)**
12:30 p.m.	**Lunch**
1:30 p.m. –3:15 p.m.	**Session III – Impurities** Chair: Michael Verlander, Ph.D. *Member, USP BIO1 – Peptides and Insulins Expert Committee*
1:30 p.m.	**USP Recommendations on Peptide Impurities** Aleksander Swietlow, Ph.D. *Member, USP BIO1 – Peptides and Insulins Expert Committee*
1:55 p.m.	**Advantages and Limitation of GC-MS method for Determination of Enantiomeric Purity** Jürgen Gerhardt, Ph.D., *CAT GmbH & Co.*
2:20 p.m.	**Panel Discussion / Q&A (20 min)**
2:40 p.m.	**Afternoon Break I**
3:10 p.m. –5:30 p.m.	**Session IV –Bioassay** Chair: Mike De Felippis, Ph.D. *Chair, USP BIO1 – Peptides and Insulins Expert Committee*
3:10 p.m.	**Bioassay Technique, with Special Emphasis on Method Development/Optimization and Tech Transfer Challenges** Dirk Usener, Ph.D., *Sanofi-Aventis Deutschland GmbH*
3:35 p.m.	**Bioassay Strategy for Therapeutic Peptides** Lone Juhl, Ph.D., *Novo Nordisk A/S*
3:55 p.m.	**Afternoon Break II**
4:10 p.m.	**Insulin: Case Study for Replacing an In-vivo by an In-vitro Assay** Sabrina Rüggeberg, *Sanofi-Aventis Deutschland GmbH*
4:35 p.m.	**Panel Discussion / Q&A (30 min)**
5:05 p.m.	**Networking Reception**
6:05 p.m.	**End Day 1**

Day Two: Tuesday, November 3, 2015

8:00 a.m. **Registration & Coffee**

8:30 a.m. –10:30 a.m. **Session V – Conjugated Peptides**
Chair: Cory Evans, Ph.D
Government Liaison, USP BIO1 – Peptides and Insulins Expert Committee, CVM/FDA

8:30 a.m. **XTEN™ – Protein Polymer - a Biodegradable and Monodisperse PEG Alternative for Half-Life Extension**
Vladimir N. Podust, Ph.D., *Amunix*

8:55 a.m. **Lipid Conjugates for Peptide Drug Delivery**
Jeff Wang, Ph.D., *Western University of Health Sciences*

9:20 a.m. **PEG characterization**
Chris Holmes, Ph.D.

9:45 a.m. **Panel Discussion / Q&A (30 min)**

10:15 a.m. **Morning Break**

10:45 a.m. –12:25 p.m. **Session VI – Peptides in Vaccines**
Chair: Elena Gubina, Ph.D.
U.S. Food and Drug Administration, Center for Biologics Evaluation and Research

10:45 a.m. **FDA Perspective on Development of Peptide-based Therapeutic Vaccines**
Elena Gubina, Ph.D.
U.S. Food and Drug Administration, Center for Biologics Evaluation and Research

11:10 a.m. **Development of Rindopepimut, a Peptide-KLH Conjugate Cancer Vaccine for the Treatment of EGFRvIII-Expressing Glioblastoma Multiforme**
Nicholas Vrolijk, Ph.D., *CellDex Therapeutics*

11:35 a.m. **Considerations When Using Keyhole Limpet Hemocyanin (KLH) as a Carrier Protein or Immune Diagnostic**
Catherine Brisson, Ph.D. and Laura Milbrandt, *Stellar Biotechnologies*

11:55 a.m. **Panel Discussion / Q&A (25 min)**

12:25 p.m. **Lunch**

1:00 p.m. –3:35 p.m. **Session VII – Regulatory**
Chairs: Donna Christner, Ph.D.
Government Liaison, USP BIO1 – Peptides and Insulins Expert Committee, FDA

1:00 p.m. **Brief Tour of FDA Organizational Structure**
Donna Christner, Ph.D., Cory Evans, Ph.D., Elena Gubina, Ph.D. *FDA*

1:25 p.m.	**"Sameness" Considerations for ANDA Peptide Drug Products** Xiaohui (Jeff) Jiang, Ph.D., *OGD/CDER/FDA*
1:50 p.m.	**Building Parity between Brand and Generic Peptide Drug Products** Larisa Wu, Ph.D., *SS/OPQ/CDER/OMPT/FDA*
2:15 p.m.	**Recombinant vs Synthetic Peptides: ANDA or 505(b)(2) Mystery!** Simrat Singh, Ph.D., *AmbioPharm*
2:40 p.m.	**Biological Evaluations and Bioequivalence Considerations for Peptide Drug Products** Xiaohui (Jeff) Jiang, Ph.D., *OGD/CDER/FDA*
3:05 p.m.	**Panel Discussion / Q&A (30 min)**
3:35 p.m.	**Workshop Wrap-up** Mike De Felippis, Ph.D. *Chair, USP BIO1 – Peptides and Insulins Expert Committee*
4:00 p.m.	**Workshop Concludes**

Catherine Brisson, Ph.D.
Chief Operating Officer
Stellar Biotechnologies, Inc.
Port Hueneme, California

Presentation
Session 6
Considerations When Using Keyhole Limpet Hemocyanin (KLH) as a Carrier Protein or Immune Diagnostic
Tuesday, November 3, 2015, 11:35 a.m. – 11:55 a.m.

Selection of an appropriate carrier protein is essential to developing a successful conjugate vaccine. Keyhole Limpet Hemocyanin (KLH) is a well-established immune stimulant, hapten carrier, and immunotherapy vaccine component. KLH is an ideal choice as a carrier protein due to its immunogenic properties and established history of use. KLH is also widely used as a neoantigen in immunotoxicology studies. There are several factors that should be taken into consideration when selecting and using KLH including source, grade, and quality. Parameters including KLH biochemistry and immunogenicity, conjugation techniques and efficiency, and regulatory concerns will be discussed.

About Stellar Biotechnologies: Stellar Biotechnologies, Inc. is a leader in the manufacture of GMP grade Keyhole Limpet Hemocyanin (KLH) protein. KLH is sourced only from the hemolymph of a scarce marine mollusk. Stellar applied decades of specialized aquaculture science to a pharmaceutical industry challenge, and created the only KLH production facility of its kind. Stellar developed the proprietary ability to sustainably produce GMP grade KLH. Our focus is to ensure supply of high quality, traceable KLH for pharmaceutical industry use while protecting its natural source.

Osama Chahrour, Ph.D.
Almac
United Kingdom

Dr. Osama Chahrour interests focuses on drug discovery in several therapeutic areas, especially cancer, and associated analytical services that support this long process form early preclinical testing to patient bedside. He is particularly interested in forging multidisciplinary approaches for drug discovery incorporating mass spectrometry (MS)-based identification and quantitation of molecules in biological matrices. His success has been reflected in published patents, peer reviewed papers and posters.
After receiving his Pharm.D in 2002, Osama spent four years in one of the world leading multi-national pharmaceutical company. As analytical scientist, he helped in implementing mass spectroscopy techniques to serve multiple analytical purposes e.g. quantification of contaminants, peptide sequencing, metabolite identification/quantification, and trace impurity structural elucidation. In 2007, he joined the University of Nottingham as PhD researcher at the School of Pharmacy, one of the top pharmacy school in the United Kingdom. During this time, he developed and applied a broad knowledge to design and implement efficient synthetic routes of novel chemical targets; investigating their SAR, ADME and PK profiles using mass spectroscopy techniques.
Since joining Almac in 2012 as senior mass spectroscopy scientist, Osama has implemented his in-depth protein analysis expertise to meet customer requirements, including characterisation (amino-acid sequence, peptide mapping, disulfide bridges mapping and post-translation modification by broad range of digest strategies followed by LC-MS/MS), physicochemical properties (molecular weight, isoform pattern and spectroscopic profiles) and product related impurity analysis (Truncates and host cell protein determination).

Presentation
Session 2
Analysis of PEGylated Synthetic Therapeutic Peptides Using UHPLC-TOF Mass Spectrometry
Monday, November 2, 2015, 11:05 a.m. – 11:30 a.m.

Donna Christner, Ph.D.
USP Affiliation:
Government Liaison, USP BIO1 – Peptides and Insulins Expert Committee

Branch Chief
U.S. Food and Drug Administration; The Center for Drug Evaluation and Research (CDER)
Silver Spring, Maryland

Session Chair
Session 7
Tuesday, November 3, 2015, 1:00 p.m. – 3:35 p.m.

Presentation
Session 7
Brief Tour of FDA Organizational Structure (co-presented with Cory Evans and Elena Gubina)
Tuesday, November 3, 2015, 1:00 p.m. – 1:25 p.m.

Michael De Felippis, Ph.D.
USP Affiliation:
Chair, USP BIO1 – Peptides and Insulins Expert Committee

Senior Research Fellow
Eli Lilly and Company
Indianapolis, Indiana

Michael R. De Felippis, PhD joined the Lilly Research Laboratories of Eli Lilly and Company in 1990 after completing his doctorate in biochemistry. He is currently a Senior Research Fellow working in the Bioproduct Research and Development division. His work is focused on development of protein and peptide biopharmaceutical products with particular emphasis on characterizing physicochemical properties, defining delivery options, developing control strategies, executing technology transfers and preparing data packages to support worldwide regulatory submissions and post-launch registrations. Dr. De Felippis has published manuscripts, review articles and book chapters on the subjects of protein and peptide structural characterization and formulation design/delivery strategies. He has given numerous presentations on these topics and is a named inventor on several patents related to these areas.

Presentations
Workshop Overview
Monday, November 2, 2015, 8:40 a.m. – 8:50 a.m.

Workshop Wrap-up
Tuesday, November 3, 2015, 3:35 p.m. – 4:00 p.m.

Session Chair
Session 4
Monday, November 2, 2015, 3:10 p.m. – 5:30 p.m.

Cory Evans, Ph.D.
USP Affiliation:
Government Liaison, USP BIO1 – Peptides and Insulins Expert Committee

Chemist
U.S. Food and Drug Administration; Center for Veterinary Medicine (CVM)
Rockville, Maryland

Session Chair
Session 5
Tuesday, November 3, 2015, 8:30 a.m. – 10:30 a.m.

Presentation
Session 7
Brief Tour of FDA Organizational Structure (co-presented with Cory Evans and Donna Christner)
Tuesday, November 3, 2015, 1:00 p.m. – 1:25 p.m.

Jürgen Gerhardt, Ph.D.
CEO
C.A.T. GmbH & Co
Tübingen, Germay

Dr. Juergen Gerhardt is CEO of C.A.T. GmbH & Co, Chromatographie und Analysentechnik KG. Heerweg 10, 72070 Tübingen Germany. In a modern laboratory, chromatographic analysis as a service is offered to the customers, specializing particularly in the analysis of peptides, amino acid derivatives and other chiral substances:
determination of the optical purity via GC-MS, sequencing of peptides and elucidation of byproducts via LC-MS(n),
one of the most efficient amino acid analysis, analysis for product control of fine chemicals (water content, solvent residues, acetate and trifluoro acetate determination). Customers can rely on efficient analysis of samples using validated methods. Validation reports can be issued for specific substances.

Prior to foundation of C.A.T. in 1985 Dr. Gerhardt was a Staff Scientist at the University of Tuebingen. He received his Ph.D. in the Department of Organic Chemistry and Pharmacology in Tuebinegen in 1984 for his work in chiral recognition of hydroxyl carboxylic acids on Chirasil Val and development of a system for automatic derivatization for gas chromatography.

Presentation
Session 3
Monday, November 2, 2015, 1:55 p.m. – 2:20 p.m.

Measurement of the racemate content is an important aspect of the determination of the purity of peptidic products. A technique for quantitation of the racemate content of peptide-bound amino acids is presented, eliminating the contribution of racemization during hydrolysis. Validation shows the capability of the method. Limitation and characteristics for some amino acids will be discussed as well as possible solutions.

Elena Gubina, Ph.D.
Biologist/Expert Regulator
U.S. Food and Drug Administration; Center for Biologics Evaluation and Research (CBER)
Silver Spring, Maryland

Elena Gubina joined FDA in 1997, first in the Division of Monoclonal Antibodies, CDER. She has been working as a full time regulator in the Office of Cellular, Tissue and Gene Therapies for the last eight years.

Session Chair
Session 6
Tuesday, November 3, 2015, 10:45 a.m. – 12:25 a.m.

Presentation
Session 6
Tuesday, November 3, 2015, 10:45 a.m. – 11:10 a.m.

Office of Cellular, Tissue and Gene therapies, CBER, FDA regulates a large number of peptide based therapeutic vaccines. Current challenges, CMC deficiencies, and regulatory considerations for immuno-therapeutic vaccine development will be discussed in this presentation. In addition, a number of case studies will be presented to clarify common misconceptions.

Presentation
Session 7
Brief Tour of FDA Organizational Structure (co-presented with Cory Evans and Donna Christner)
Tuesday, November 3, 2015, 1:00 p.m. – 1:25 p.m.

Chris Holmes, Ph.D.
CMC Consultant
Saratoga, California

BS (Chemistry): 1977-1981 University of California, Irvine
Ph.D. (Chemistry): 1981-1986 University of California, Berkeley. Synthetic organic chemistry, natural product synthesis
Postdoctoral: 1987-1988: Stanford University; bioorganic chemistry
Industrial Experience 1989-2013 Affymax, Inc. (Executive Director, Chemistry), Palo Alto, CA:

- Responsible for the discovery and development of peginesatide, the first PEG-peptide conjugate approved by the FDA; peginesatide is approved for dosing once-monthly for the treatment of anemia.
- Designed process route, oversaw CMOs, developed analytical control strategies for the release/stability of drug substance and drug product lots.
- Developed characterization approach of PEG-peptide conjugates from IND to NDA.
- Wrote significant portions of IND/NDA (NDA received first-pass approval in 2012).
- Interacted with American, Japanese, and European drug agencies on peginesatide IND/NDA/MAA submissions and quality responses to Rapporteurs questions.
- Worked with FDA and corporate partner on recall efforts of peginesatide (CMC and biological investigations, peginesatide was voluntarily recalled in 2013)

Industrial Experience 2014 Regado, Inc. (VP, Chemical and Pharmaceutical Development), Durham, NC:

- Led CMC activities for Revolixys™ Kit a two component anticoagulant comprised of a long acting antithrombotic PEGylated RNA aptamer drug pegnivacogin and its active RNA control agent, anivamersen).
- Developed analytical control and characterization strategies for PEGylated RNA-aptamer
- Wrote IND updates.

Industrial Experience 2014-present, CMC Consulting:

- Consultant to several pharmaceutical companies on CMC issues relating to peptide and small molecules in preclinical through Phase 2 trials.
- CMO oversight, establishing specifications, analytical control strategies, stability protocols, characterization strategies, IND writing, validation exercises.

Presentation
Session 5
Characterization of Peginesatide: Challenges and Lessons Learned
Tuesday, November 3, 2015, 9:20 a.m. – 9:45 a.m.

Xiaohui (Jeff) Jiang, Ph.D.
Chemist
U.S. Food and Drug Administration; The Center for Drug Evaluation and Research (CDER)
Silver Spring, Maryland

Xiaohui (Jeff) Jiang received his Ph.D. in chemistry from University of California at San Diego. Under the guidance of Prof. Murray Goodman, he studied structure activity relationships of bioactive peptides through peptide synthesis and biophysical characterizations. After graduating, Dr. Jiang worked in the private sector and government agencies in the area of drug discovery and development before joining the FDA. At Office of Generic Drugs, Dr. Jiang is a Project Lead for complex drug substances including peptides and played important roles in the development of several product specific recommendations for generic drug products including conjugated estrogens and sevelamer. He has also been managing GDUFA regulatory science projects related to complex drug substances such as analysis of peptide impurities and characterizations of complex mixtures. Dr. Jiang was actively involved in FDA's recent approval of the first generic product of glatiramer acetate injection.

Presentations
Session 7
"Sameness" Considerations for ANDA Peptide Drug Products
Tuesday, November 3, 2015, 1:25 p.m. – 1:50 p.m.

Biological Evaluations and Bioequivalence Considerations for Peptide Drug Products
Tuesday, November 3, 2015, 2:40 p.m. – 3:05 p.m.

Marion King, Ph.D.
USP Affiliation:
Member, USP BIO1 – Peptides and Insulins Expert Committee

Analytical Development Manager
Ipsen Manufacturing Ireland Ltd
Dublin, Ireland

Session Chair
Session 1
Monday, November 2, 2015, 8:50 a.m. – 10:10 a.m.

Wolfgang Lindner, Ph.D.
Professor
University of Vienna
Wien, Austria

Presentation
Session 2
Zwitterionic Chiral Stationary Phases for Amino Acid and Peptide Stereoisomer Separations and as Complementary Tool for Therapeutic Peptide Quality Control
Monday, November 2, 2015, 11:30 a.m. – 12:00 p.m.

Chirality of biomolecules such as proteinogenic receptors, enzymes and transporters results in inequalities of biological activities and in disposition of enantiomers and diastereomers of chiral drugs and drug candidates. It creates a strong quest for chiral technologies in the field of drug discovery, quality control and bioanalysis. This holds for small molecule synthetic drugs and therapeutic peptides likewise. Thus, the quality and safety of therapeutic peptides not only depends on chemical purity but also stereochemical integrity. In general, a multiplicity of peptide drug quality attributes are to be considered and this topic raises increasing concern, in particular not least due to several challenges such as difficulties in separating structurally closely related impurities from the major active pharmaceutical ingredient by common separation principles like reversed-phase chromatography. Since the number of peptide drugs is constantly increasing the quest for new advanced strategies in efficient impurity profiling methods is constantly rising.

In this presentation we wish to report on a complementary liquid chromatographic impurity profiling tools for monitoring therapeutic peptides which have been developed recently for enantiomer separation of amino acids. It takes benefit of a zwitterionic with chiral stationary phase (CSP) derived from quinine or quinidine with sulfohexyl carbamate residue. It is commercially available as CHIRALPAK ZWIX(+) and ZWIX(-) and turned out to be highly selective for various challenging peptide separation problems comprising: i) enantiomer separations of peptides, ii) peptide epimer separations, ii) peptide diastereomer separations, iii) sequence selective peptide separations, iv) resolution of charge-modulating minor structural alterations in peptides such as Asn→Asp, Gln→Glu, NH_2→$NHCOCH_3$ (acetylation), NH_2→NHCOH (formylation), C-terminal COOH→$CONH_2$ exchanges, Asp→isoAsp, v) amino acid residue racemization monitoring in peptides, vi) oxidation detection (e.g. Lys-oxidation, Trp→Kyn), vii) ring-opening detection of cyclic peptides. They further provide viii) complementary peptide separations to RPLC and HILIC, as well as ix) can be used for amino acid absolute configuration detections in hydrolyzed peptide samples. The utility of CHIRALPAK ZWIX as a flexible tool in peptide research will be illustrated by various examples.

Michael Lämmerhofer[1], Wolfgang Lindner[2], Pilar Franco[3], Tong Zhang[3]

[1] *Institute of Pharmaceutical Sciences, University of Tübingen, Auf der Morgenstelle 8, 72076 Tübingen, Germany*
[2] *Department of Analytical Chemistry, University of Vienna, Waehringer Strasse 38, 1090 Vienna, Austria*
[3] *Chiral Technologies Europe, Boulevard Gonthier d'Andernach, 67400 Illkirch-Graffenstaden, France*

Laura Milbrandt, M.S.
Customer Support
Stellar Biotechnologies, Inc.
Ventura, California

Presentation
Session 6
Considerations When Using Keyhole Limpet Hemocyanin (KLH) as a Carrier Protein or Immune Diagnostic
Tuesday, November 3, 2015, 11:35 a.m. – 11:55 a.m.

Selection of an appropriate carrier protein is essential to developing a successful conjugate vaccine. Keyhole Limpet Hemocyanin (KLH) is a well-established immune stimulant, hapten carrier, and immunotherapy vaccine component. KLH is an ideal choice as a carrier protein due to its immunogenic properties and established history of use. KLH is also widely used as a neoantigen in immunotoxicology studies. There are several factors that should be taken into consideration when selecting and using KLH including source, grade, and quality. Parameters including KLH biochemistry and immunogenicity, conjugation techniques and efficiency, and regulatory concerns will be discussed.

About Stellar Biotechnologies: Stellar Biotechnologies, Inc. is a leader in the manufacture of GMP grade Keyhole Limpet Hemocyanin (KLH) protein. KLH is sourced only from the hemolymph of a scarce marine mollusk. Stellar applied decades of specialized aquaculture science to a pharmaceutical industry challenge, and created the only KLH production facility of its kind. Stellar developed the proprietary ability to sustainably produce GMP grade KLH. Our focus is to ensure supply of high quality, traceable KLH for pharmaceutical industry use while protecting its natural source.

Kshitij (Kris) Patkar, Ph.D.
Senior Staff Fellow
U.S. Food and Drug Administration; The Center for Drug Evaluation and Research (CDER)
Silver Spring, Maryland

Kshitij (Kris) Patkar received his Ph.D. in Pharmaceutical Sciences from University of Maryland, Baltimore in 2002 with principle focus on peptide synthesis and analysis. He did post-doctoral work at NIDA, NIH and then worked as a researcher at the University of Kansas and then at Torrey Pines Institute for Molecular Studies. He joined FDA in Oct 2012. Since then he has been involved in review of complex drug products such as enoxaparins, glatiramer acetate and peptides. He is currently Senior Staff Fellow in the Office of Process and Facilities under Office of Pharmaceutical Quality in CDER.

Presentation
Session 1
Therapeutic Peptides: Raw Materials and Impurities
Monday, November 2, 2015, 8:50 a.m. – 9:15 a.m.

Raw Materials: Peptides manufactured by chemical synthesis are assembled typically in solution or on a solid support by coupling amino acid building blocks using coupling reagents. Some of the synthetic processes involve use of amino acid dimers or shorter peptides that are either coupled with other shorter peptides or individual amino acids by a variety of methods such as regular activated amino acid coupling reactions, segment condensations etc. Peptide synthesis can also involve modification of amino acids or incorporation of structures that are not part of natural amino acids using a variety of reagents. Thus an individual amino acid or a short polymer of few amino acids and sometimes organic materials are designated as the “starting materials” for peptide APIs. This presentation will address some of the inconsistencies commonly encountered in designating starting materials used in the peptide synthesis and Agency’s expectations in controlling these starting materials from quality and safety perspectives.

Impurities: One of the major sources of the impurities in peptide APIs is the raw materials (individual amino acids building blocks or small fragments/ intermediates), solvents, reagents, and catalysts. Impurities in the building blocks likely affect the critical quality attributes of the final peptide drug substance as they have potential to get incorporated into the growing peptide chain giving rise to peptide related substances. One of the most significant impurities associated with the amino acid building blocks are the opposite stereoisomers that can affect the safety and efficacy.

Another important source of impurities in peptides is the solvents used in the manufacturing process. Impurities in solvents used in peptides coupling may result in formation of impurities. Furthermore, solvents used in the downstream processes such as final precipitation, concentration, purification, lyophilization could directly affect the quality of the final peptide and impurity levels.

Elemental impurities present in the raw materials could also contribute toward total impurities present in the final peptide.

Control strategy:
This presentation will discuss the controls for starting materials and sources of impurities in peptide drug substances arising from starting materials and control strategy to limit these impurities.

Vladimir Podust, Ph.D.
Director of Analytical Chemistry
Amunix
Mountain View, California

Dr. Podust is a Director of Analytical Chemistry at Amunix and leads company's Protein Analytics and Chemical Conjugation development. Previously he was Senior Scientist at Biomarker Discovery Center, Ciphergen Biosystems, Inc., and Research Assistant Professor at Vanderbilt University. He received a Ph.D. degree in Molecular Biology from Novosibirsk Institute of Bioorganic Chemistry, Russia, and was a postdoctoral fellow at University of Zurich, Switzerland. Dr. Podust has authored 77 publications in peer-reviewed journals and 9 US patents.

Presentation
Session 5
XTEN™ – Protein Polymer - a Biodegradable and Monodisperse PEG Alternative for Half-Life Extension
Tuesday, November 3, 2015, 8:30 a.m. – 8:55 a.m.

XTEN™ is a class of unstructured hydrophilic, biodegradable protein polymers designed to increase the half-lives of therapeutic peptides and proteins. XTEN proteins are typically expressed in E. coli and purified by conventional protein chromatography as monodisperse polypeptides of exact length and sequence. Unstructured XTEN polypeptides have hydrodynamic volumes significantly larger than typical globular proteins of similar mass, thus imparting a bulking effect to the therapeutic payloads attached to them. Since their invention, XTEN polypeptides have been utilized to extend the half-lives of genetically fused therapeutic peptides and proteins. To expand the applications of XTEN technology to half-life extension of synthetic payloads, methods for chemical XTENylation have been developed. Multiple orthogonal chemistries have been shown to be useful to conjugate peptides and small molecules to primary amines and thiols of XTEN polypeptides.

Jon Rasmussen, Ph.D.
PolyPeptide Labs
Copenhagen, Denmark

Presentation
Session 1
Monday, November 2, 2015, 9:15 a.m. – 9:40 a.m.

Sarah Rogstad, Ph.D.
Staff Fellow Chemist
U.S. Food and Drug Administration; The Center for Drug Evaluation and Research (CDER)
Silver Spring, Maryland

Sarah Rogstad received her B.S. in Biology/Chemistry from Harvey Mudd College in 2008. She then received her Ph.D. in Pharmacology from the University of Colorado, Anschutz Medical Campus in 2013. After completing an ORISE post-doctoral fellowship at the US Food and Drug Administration, she joined the agency as a chemist in the Division of Pharmaceutical Analysis. She has a background in mass spectrometry based proteomics and is currently applying this knowledge to the analytical characterization of complex drug products and protein therapeutics.

Presentation
Session 2
Modern Analytics for Synthetically Derived Complex Drug Substances: NMR, AFFF-MALS, and MS Tests for Glatiramer Acetate
Monday, November 2, 2015, 10:40 a.m. – 11:05 a.m.

Glatiramer acetate (GA) is a mixture of synthetic copolymers consisting of four amino acids (glutamic acid, lysine, alanine, and tyrosine) with a labeled molecular weight range of 5000 to 9000 Da. GA is marketed as Copaxone™by Teva for the treatment of multiple sclerosis. The agency evaluated the structure and composition of GA and a commercially available comparator, Copolymer-1. Modern analytical technologies which can characterize these complex mixtures are desirable for analysis of their comparability and structural “sameness.” A molecular fingerprinting approach was taken using mass-accurate mass spectrometry (MS) analysis, nuclear magnetic resonance (NMR) (1D-1H-NMR, 1D-13C-NMR, and 2DNMR), and asymmetric field flow fractionation (AFFF) coupled with multi-angle light scattering (MALS) for an in-depth characterization of three lots of the marketplace drug and a formulated sample of the comparator. Statistical analyses were applied to the MS and AFFF–MALS data to assess these methods’ ability to detect analytical differences in the mixtures. The combination of multiple orthogonal measurements by liquid chromatography coupled with MS (LC–MS), AFFF–MALS, and NMR on the same sample set was found to be fit for the intended purpose of distinguishing analytical differences between these complex mixtures of peptide chains.

Sabrina Rüggeberg,
Head of Laboratory
Sanofi-Aventis Deutschland GmbH
Frankfurt, Germany

In 2001 Sabrina Rüggeberg graduated at the Mannheim University of Applied Sciences, Mannheim / Germany in biotechnological engineering with focus on proteomics. In 2001 she joined the Proteomics Core Facility of Dr. Thomas Franz at the European Molecular Biology Laboratory (EMBL), Heidelberg / Germany. The work was focused on multiple functional and structural proteomic projects, e.g. Moyamoya disease. In 2006, Sabrina Rüggeberg spent time at University of British Columbia, Vancouver / Canada in Prof. Dr. Chris Overvalls research group for metalloproteases as a guest scientist.

More than 7 years she started working in the quality control for biologics at R&D Sanofi Aventis Deutschland GmbH, Frankfurt / Germany. Her team is specialized on developing cell based bioassays into GMP compliance. These assays are then routinely used for release, stability, and characterization tests in a GMP compliant environment, not mainly for small molecules but also for biologics.

Presentation
Session 4
Insulin: Case Study for Replacing an In-vivo by an In-vitro Assay
Monday, November 2, 2015, 4:10 p.m. – 4:35 p.m.

Each Insulin Glargine, Insulin Glulisine, or Insulin Human batch is released for commercial use with an in-vivo bioactivity test, which is required based on United States Pharmacopeia (USP) chapter <121>. In order to save costs and time and because of ethical aspects regarding the in vivo tests, an already available invitro cell based assay was developed and qualified. This cell based assay should substitute the in vivo assay for all batch release and stability testings. It was initially developed in Diabetes Research for screening activities, further developed and qualified in Biopharmaceutical Development and finally transferred to the commercial production site for routine use.

Recently the FDA accepted this cell based assay for the release of Insulin Glargine.

Simrat Singh, Ph.D.
Senior Director
AmbioPharm
North Augusta, South Carolina

Replacing recombinant peptide with a synthetic peptide in the marketed drug leads to a challenge with respect to regulatory filing. Big question on the table is if regulatory pathway should follow ANDA or 505(b)(2) route. Recently, FDA has defined characterization techniques for establishing “sameness” of Glatiramer drug substance which is sold in the market as “Copaxone”. Glatiramer was known as a “difficult to characterize” polypeptide for long time (for which generic version was almost thought to be impossible) until FDA recently provided clarity on establishing sameness for ANDA pathway. We believe that different characteristics described by FDA for establishing “sameness” of Glatiramer for ANDA filing can be also co-related and applied to demonstrate “sameness” of a synthetic peptide with recombinant peptide. Nevertheless, having a guidance from FDA regarding ANDA pathway for replacing recombinant peptide with synthetic peptide will be very helpful.

Presentation
Session 7 - multiple
Recombinant vs Synthetic Peptides: ANDA or 505(b)(2) Mystery!
Tuesday, November 3, 2015, 2:15 p.m. – 2:40 p.m.

Analytical method development and optimization is critical for generic peptide development work, especially when transitioning from a recombinant to synthetic peptide. A tremendous amount of effort is dedicated to developing methods that can separate maximum peaks and optimize the synthetic process to reduce impurities. This is particularly important to demonstrate that synthetic version of a recombinant peptide does not have additional impurities which are absent in the recombinant peptide. Comparing impurity profile of a recombinant peptide with synthetic peptide is very important to demonstrate safety and efficacy of the synthetic peptide. Apart from the impurity profile comparison, detailed characterization of the synthetic peptide is necessary to establish “sameness” between recombinant and synthetic peptide.

Replacing recombinant peptide with a synthetic peptide in the marketed drug leads to a challenge with respect to regulatory filing. Big question on the table is if regulatory pathway should follow ANDA or 505(b)(2) route. Recently, FDA has defined characterization techniques for establishing “sameness” of Glatiramer drug substance which is sold in the market as “Copaxone”. Glatiramer was known as a “difficult to characterize” polypeptide for long time (for which generic version was almost thought to be impossible) until FDA recently provided clarity on establishing sameness for ANDA pathway. We believe that different characteristics described by FDA for establishing “sameness” of Glatiramer for ANDA filing can be also co-related and applied to demonstrate “sameness” of a synthetic peptide with recombinant peptide. Nevertheless, having a guidance from FDA regarding ANDA pathway for replacing recombinant peptide with synthetic peptide will be very helpful.

Aleksander Swietlow, Ph.D.
USP Affiliation:
Member, USP BIO1 – Peptides and Insulins Expert Committee

Global Director, Quality Control
PolyPeptide Group
Torrance, California

Presentation
Session 3
USP Recommendations on Peptide Impurities
Monday, November 2, 2015, 1:30 p.m. – 1:55 p.m.

Anita Szajek, Ph.D.
Principal Scientific Liaison
USP
Rockville, Maryland

Dr. Szajek is currently serving as a Principal Scientific Liaison in Biologics & Biotechnology Department at United States Pharmacopeia (USP). She is the scientific liaison for USP Therapeutic Peptides Expert Panel, USP Unfractionated Heparin Expert Panel, USP Low Molecular Weight Heparins Expert Panel, USP Monographs-B&B 1 Expert Committee as well as other expert panels.

Prior to arriving at USP, Dr. Szajek was a senior scientist in Pharmaceutical Sciences department at Human Genome Sciences Inc. (HGSI), Rockville, Maryland where she worked on purification process development activities, scale-up and analytical assay development from preclinical to Phase III. Prior to her tenure at HGSI, Dr. Szajek was a senior scientist at Antex Biologics Inc., Gaithersburg, Maryland, where she worked on identifying novel vaccine candidates using SELDI (Surface Enhanced Laser Desorption and Ionization) technology.

Dr. Szajek received her Ph.D. degree from the chemistry department at University of Wisconsin in Madison, and her BS in chemistry from the University of Illinois at Urbana-Champaign. Dr. Szajek was postdoctoral fellow at National Institutes of Health and Parke-Davis Pharmaceuticals (later known as Pfizer-Ann Arbor).

Session Chair
Session 2
Monday, November 2, 2015, 10:40 a.m. – 12:30 p.m.

Dirk Usener, Ph.D.
Head Bioassay Cluster
Sanofi-Aventis Deutschland GmbH
Frankfurt, Germany

Dirk Usener studied biology at the Johannes-Gutenberg University in Mainz / Germany and graduated in 2000 at the University Clinics Mannheim in the field of dermato oncology. He prepared his Ph.D. thesis from 2000 to 2003 at the German Cancer Research Center (DKFZ), Heidelberg / Germany. It also covered the field of dermato oncology, in detail the characterization of CTCL specific-tumor-antigens. After a short post-doctoral experience at the German Cancer Research Center in Heidelberg / Germany, Dirk Usener joined the biotech-company Ganymed-Pharmaceuticals in Mainz / Germany as Senior Scientist and Project Manager for nearly 5 years. His work focused on developing effective anti-cancer immune-therapeutics based on ideal targets. This included target discovery and validation, antibody lead selection, functional characterization of monoclonal antibodies, generation of antibody producer clones and preclinical development.

In 2008 Dirk Usener started as head of laboratory at Sanofi Aventis Deutschland GmbH, Frankfurt a.M. / Germany. His team was specialized on release, stability, and characterization tests of biologics in a GMP compliant environment. After promoting to group leadership and head of quality control in 2012, Dirk Usener's group specialized on binding assays - like ELISAs -, cell based bioassays, as well as FACS and Biacore technology. Those assays are developed into GMP compliance and are then routinely used for release, stability, and characterization tests, not only for biologics but also for small molecules.

Presentation
Session 4
Bioassay Technique, with Special Emphasis on Method Development/Optimization and Tech Transfer Challenges
Monday, November 2, 2015, 3:10 p.m. – 3:35 p.m.

Potency tests are mandatory for the characterization of complex peptides and proteins and thus, requested by Health Authorities during different phases of development. Often they are part of the release specification. In-vivo or cell-based bioassays are sensitive and complex biological systems with high variability requiring significant efforts to end up with a robust test. Usually, the development timelines are very long and complex and are therefore frequently on the critical path during CMC development. A chemically synthesized peptide with 44 amino acids is presented as case study to demonstrate assay development, analysis, robustness and transfer parameters.

Michael Verlander, Ph.D.
USP Affiliation:
Member, USP BIO1 – Peptides and Insulins Expert Committee

President
Proactive Quality Compliance
San Diego, California

Session Chair
Session 3
Monday, November 2, 2015, 1:30 p.m. – 3:15 p.m.

Nicholas Vrolijk, Ph.D.
Vice President, Commercial Manufacturing
CellDex Therapeutics
Hampton, New Jersey

Dr. Vrolijk is Vice President of Manufacturing Operations at Celldex Therapeutics. He has been in this position since July 2013 and was brought on board to lead the late stage development and commercialization of rindopepimut. Subsequently he has assumed responsibility for management and oversight of all manufacturing operations at Celldex, including both internal and external manufacturing operations, covering a robust pipeline of therapeutic proteins, therapeutic mAbs, and ADCs.

Previously, Dr. Vrolijk was founder and managing partner of Biopharmaceutical Product Development Services, Inc. Prior to that, he was with Celgene Corp., serving as Vice President of Manufacturing and responsible for supporting the launch of Istodax®, a novel oncology therapy for cutaneous T-cell lymphoma. Prior to Celgene, he was Senior Vice President of Manufacturing Operations at Gloucester Pharmaceuticals where he led all CMC operations for the development of Istodax®, from licensing to NDA filing and approval. He was also responsible for all CMC due diligence activities and played a lead role in supporting the successful acquisition of Gloucester by Celgene. Dr. Vrolijk also had prior consulting experience, having been a founding partner of Pharmaceutical Manufacturing & Compliance Associates and working on projects for more than15 clients over a 3.5-year period, including the successful development of Increlex® on behalf of Tercica, Inc. He previously held management positions in manufacturing operations, quality assurance, and regulatory compliance at Pharmacia Corp. and Sensus Drug Development Corp. in conjunction with the successful development and approval of Somavert®. Prior to this, Dr. Vrolijk was a Regulatory Scientist at Cato Research, a contract research organization (CRO).

Dr. Vrolijk received a BS in Biology and Geology from the University of Rochester, and a Masters and Ph.D. in Marine Biochemistry from the University of Delaware. He performed post-doctoral work at the University of Maryland and the University of Connecticut, which were supported by a National Science Foundation molecular biology training grant and a National Institutes of Health research grant, respectively.

Presentation
Session 6
Development of Rindopepimut, a Peptide-KLH Conjugate Cancer Vaccine for the Treatment of EGFRvIII-Expressing Glioblastoma Multiforme
Tuesday, November 3, 2015, 11:10 a.m. – 11:35 a.m.

Jeffrey Wang, Ph.D.
USP Affiliation:

Associate Professor
Western University of Health Sciences
Pomona, California

Presentation
Session 5
Lipid Conjugates for Peptide Drug Delivery
Tuesday, November 3, 2015, 8:55 a.m. – 9:20 a.m.

Larisa Wu, Ph.D.
Special Assistant to OPQ Directors
U.S. Food and Drug Administration; The Center for Drug Evaluation and Research (CDER)
Silver Spring, Maryland

Larisa Wu, Ph.D., serves as Special Assistant in the Immediate Office (IO) of the Office of Pharmaceutical Quality (OPQ), FDA. Prior to this she was a product quality reviewer on the Peptide Team of the Office of Generic Drugs (OGD)/Office of Pharmaceutical Science (OPS) and a member of the OPS Science and Research Staff, where she performed primary and secondary reviews of applications for products ranging from small molecules to complex drug substances. She contributed significantly to the development of initiatives within OPS that became pivotal to the launch of OPQ, including integrated team-based quality assessment, risk-based review, CMC GDUFA hiring, and ANDA backlog review and management. Her contributions have been recognized in various award ceremonies at the agency, center, and office level. Larisa received her Ph.D. degree in Bioengineering from University of Utah, followed by a postdoctoral fellowship in Pharmaceutical Sciences at University of Maryland, School of Pharmacy. She also holds an M.S. degree in Chemistry and a B.S. degree in Biomedical Engineering.

Presentation
Session 7
Building Parity between Brand and Generic Peptide Drug Products
Tuesday, November 3, 2015, 1:50 p.m. – 2:15 p.m.

In recent years, the number of peptide drug applications submitted to FDA for review and approval has increased considerably. At the same time, challenges related to the evaluation of peptide drug applications have intensified, such as the demand for highly specialized personnel, the drive to better coordinate processes of inspection and review, and the need for consistent application of quality standards to both brand-name and generic drug products. The Office of Pharmaceutical Quality (OPQ) formed in January 2015 strives, not only to meet these challenges, but also to build parity between brand and generic peptide products during product review and approval, as well as over the entire product lifecycle. To properly manage the peptide product lifecycle, OPQ has instituted new tools of team-based integrated quality assessment (IQA), risk management, and knowledge base expansion and deployment. Team-based IQA, a collaborative process within OPQ, evaluates peptide drug applications by integrating review with inspection, surveillance, policy, and research. Team structures exploit the expertise of review staff effectively and leverage knowledge about quality issues, gained from prior peptide product reviews, for the review of generic product applications. Moreover, risk assessments are integrated into the existing drug product knowledge base, which enables reviewers to efficiently resolve routine quality issues, effectively focus on scientific issues that pose particular challenges, and provide patient-focused recommendations. These tools and initiatives will be discussed in the context of peptide drug evaluations, the expanding knowledge base for peptide product review, and regulatory procedures that can be anticipated in peptide drug reviews.

Poster Presenters

(in last name order of presenting author)

National Institute of Neurological Diseases and Stroke: Office of Translational Research
Multiple Authors

Authors:

Chris Boshoff, Ph.D. (presenting author)
Dr. Boshoff is a Scientific Project Manager in the Office of Translational Research. He facilitates translational efforts of the National Institute of Neurological Disorders and Stroke (NINDS) CREATE Bio and legacy translational cooperative agreement programs and intramural innovations.

Linda McGavern, Ph.D.
Dr. Linda McGavern is a Scientific Project Manager in the Office of Translational Research and currently helps administer the National Institute of Neurological Disorders and Stroke (NINDS) CREATE Bio and legacy translational cooperative agreement programs.

Mary Ann Pelleymounter
Dr. Mary Ann Pelleymounter is a Scientific Project Manager for both the Blueprint Neurotherapeutics Network and the IGNITE programs in the Office of Translational Research at the National Institute of Neurological Disorders and Stroke (NINDS).

Christina Vert
Christina Vert, M.S. is a Health Program Specialist in the Office of Translational Research at the National Institute of Neurological Disorders and Stroke (NINDS). Ms. Vert currently assists with the coordination of the CREATE Bio and legacy translational cooperative agreement programs.

Hao Wang, Ph.D.
Dr. Hao Wang is a Program Director in the Office of Translational Research who oversees the National Institute of Neurological Disorders and Stroke (NINDS) CREATE Bio and legacy translational cooperative agreement programs.

Poster Presentation
NINDS Supports Translation of Promising Neurotherapeutic Peptides from Bench to Clinic

Peptide therapeutics are applied in numerous disciplines of medicine such as anti-infection, cardiovascular, renal, pain, dermatology, respiratory, cancer, gastro intestinal, metabolic and neurology. The increasing prevalence of neurological conditions due to an aging population is expected to result in rapid growth of neuropeptide-based therapeutics.

The Office of Translational Research (OTR) at the NIH National Institute of Neurological Disorders and Stroke (NINDS) has recently launched several new translational grant programs to stimulate translational research in biological modalities such as peptides. These include a new early-stage therapy development funding program called IGNITE (Innovation Grants to Nurture Initial Translational Efforts) and CREATE Bio (Cooperative Research to Enable and Advance Translational Enterprises for Biotechnology products and Biologics).

IGNITE is meant to advance innovative projects to later-stage therapy development programs such as CREATE Bio. The first two funding opportunities in the IGNITE program have been released: (1) Assay Development and Therapeutic Agent Identification and Characterization to Support Therapeutic Discovery (R21/R33) (PAR-15-070), which focuses on supporting the development of new in vitro and ex vivo assays and iterative screening efforts to identify and characterize novel therapeutics for neurological disorders, and (2) Pharmacodynamics and In vivo Efficacy Studies for Small Molecules and Biologics/Biotechnology Products (R21/R33) (PAR-15-071), which supports the implementation of pharmacodynamics (PD), pharmacokinetics (PK), and in vivo efficacy studies to demonstrate that proposed therapeutic

agents are appropriately chosen for further development.

The CREATE Bio program is a later stage program and it is designed to support the development of biologics/biotechnology therapeutics from lead optimization through early phase clinical trials. The program is divided into two tracks: the Discovery Track supports lead optimization in order to obtain a candidate appropriate for entering the Development Track, and the Development Track supports IND-enabling studies such as CMC development and may include early-phase clinical trials. For more details, please go to the NINDS CREATE BIO website: http://www.ninds.nih.gov/funding/areas/translational_research/CREATE-Bio.htm

For additional information on NINDS opportunities in translational research, please visit the NINDS Office of Translational Research website.

NINDS Supports Translation of Promising Neurotherapeutic Peptides from Bench to Clinic

Chris H. Boshoff, Linda McGavern, Christina Vert, Mary Ann Pelleymounter, and Hao Wang
Office of Translational Research, NINDS/NIH

Abstract

The Office of Translational Research (OTR) at the NIH National Institute of Neurological Disorders and Stroke (NINDS) has recently launched several new translational grant programs to stimulate translational research in biological modalities such as peptides. These include a new early-stage therapy development funding program called IGNITE (Innovation Grants to Nurture Initial Translational Efforts) and CREATE Bio (Cooperative Research to Enable and Advance Translational Enterprises for Biotechnology products and Biologics).

The CREATE Bio program is a later stage program and it is designed to support the development of biologics/biotechnology therapeutics from lead optimization through early phase clinical trials. The program is divided into two tracks: the Discovery Track supports lead optimization in order to obtain a candidate appropriate for entering the Development Track, and the Development Track supports IND-enabling studies such as CMC development and may include early-phase clinical trials. For more details, please go to the NINDS CREATE BIO website:

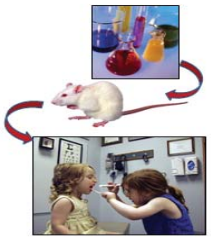
http://www.ninds.nih.gov/funding/areas/translational_research/CREATE-Bio.htm

IGNITE is a feeder program that can support (1) Assay Development and Therapeutic Agent Identification and (2) Pharmacodynamics and In vivo Efficacy Studies.

For additional information on NINDS opportunities in translational research, please visit the NINDS Office of Translational Research website.

Office of Translational Research (OTR)

- **Division of National Institute of Neurological Disease and Stroke (NINDS)**
- **Mission:** *To facilitate the preclinical discovery and development of new therapeutic interventions for neurological disorders*



NINDS/OTR Translational Guiding Principles

- Provide assistance as well as managing risks
- Need to get therapeutics to humans
  - Develop translatable measures of efficacy and target engagement
  - Integrate clinical perspective into discovery process
- Can't do it alone – need partnerships and handoffs
  - De-risk projects for downstream funding
  - Actively facilitate partnership discussions

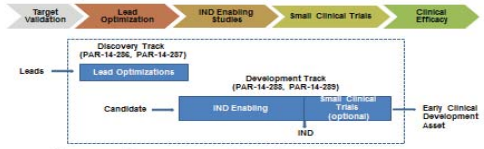
Cooperative Research to Enable and Advance Translational Enterprises Biotechnology Products and Biologics (CREATE BIO)

Modality: Biologics/Biotechnology Products

Purpose:
- Discovery: Optimization of therapeutic leads
- Development: IND-enabling studies/Early phase clinical trials

End Goals:
- Discovery: Characterize and select a lead candidate
- Development: Submit an IND application and conduct phase I trials

CREATE Bio Program Overview



- Cooperative agreement mechanism
- Technical assistance (new):
  - Consultants: statistics, regulatory, CMC
  - Assistance through existing NIH contracts as needed

Budget Guidance

- Non-SBIR: Budget not limited but must reflect the actual needs of the proposed project. Suggestions below:

Suggestions	Discovery Track (U01)	Development Track (UH2/UH3)
Non-SBIR	< $500K/year in direct cost for up to 4 yrs	< $1M/year in direct cost for UH2 for up to 2 yrs < $1.5M/year in direct cost for UH3 Combined UH2+UH3 for up to 5 yrs

- SBIR: Set aside budget

	Discovery Track (U44)	Development Track (U44)
SBIR	< $500K in total cost in Phase I for up to 1 yr <$2M total cost in Phase II for up to 3 yrs	< $1M/year in total cost for Phase I for up to 2 yrs < $1.5M/year in total cost for Phase II for up to 3 yrs

Innovation Grants to Nurture Initial Translational Efforts (IGNITE)

1. Suite of grants that fund early/exploratory drug discovery (small molecule and biologics)
2. PAR-15-070: Establish essential assays to identify and optimize bioactive leads(s)
   a) Characterize therapeutic hits for bioactivity, physicochemical or biophysical properties
3. RFA-TBD: Develop clinically relevant model systems and markers of target engagement to assess efficacy*
4. PAR-15-071: Characterize bioactive lead(s)
   a) In vivo efficacy/target engagement
   b) Pharmacokinetic characteristics

*Anticipated Funding Opportunity Announcement in December, 2015

IGNITE

R21

Planning/Development Phase

PAR-15-070: Assay Development and Validation

PAR-15-071: Further compound characterization including pharmacokinetic studies and planning for in vivo and pharmacodynamic studies

☑ Meet Milestones

R33

Execution Phase

PAR-15-070: Hit identification: screening, physicochemical characterization, in vitro pharmacological characterization

PAR-15-071: Pharmacodynamic, *invivo* characterization of compound(s)

	R21	R33
Budget per year	< $0.25M	< $0.5M
Duration	No more than 2 years	No more than 2 years
Budget total (R21/R33)	<0.75M for Entire 3 Year Period	

Next Application Date: February 16, 2016

Advice for Preparing an Application

- **Read the Funding Opportunity Announcements (these are not typical NIH applications)**
- **Contact NIH staff**
  - Confirm which program and entry stage is best fit
  - Discuss appropriate activities
  - Applications $500K+ in any given year must be preapproved
- **Ask your questions early**
- **Feedback and suggestions are welcome**

Renata Varga, Ph.D.
Scientist
Teva Pharmaceuticals Inc.
West Chester, Pennsylvania

Renata Varga graduated as a Chemist working with solid phase peptide synthesis and enzymatic reactions. She obtained a PhD in Hungary in analytical chemistry by analyzing surface water samples for pharmaceutical residues with LC-MS/MS after solid phase extraction. She started to work in Teva Pharmaceuticals as a Researcher Analyst in the Sterile R&D, Godollo, Hungary. She has expertise in the development of sterile infusions, injections, eye-drops and lyophilized powders, furthermore in the development of therapeutic peptides. She was involved in the analytical development of several small-molecule and peptide-based therapeutics, but also supported the regulatory work by submitting files and answering regulatory questions all over the world. She was heavily involved in the ANDA submissions of peptide-based injection therapeutics recently. Now she is working as a Characterization Scientist in CMC Biologics, West Chester, PA, USA. She is supporting the development of generic peptide therapeutics by providing with CQA assessment, characterization and comparability plans and executing analytical testing. She is also involved in the development and characterization of innovative biomolecules, such as monoclonal antibodies and fusion proteins.

Poster Presenter
From Critical Quality Attribute Assessment to Specification and Characterization