Short Course: Antibody-Drug Conjugates, Oligonucleotides, Peptides, and Other Complex Drug Modalities Characterization and Quantification by Mass Spectrometry

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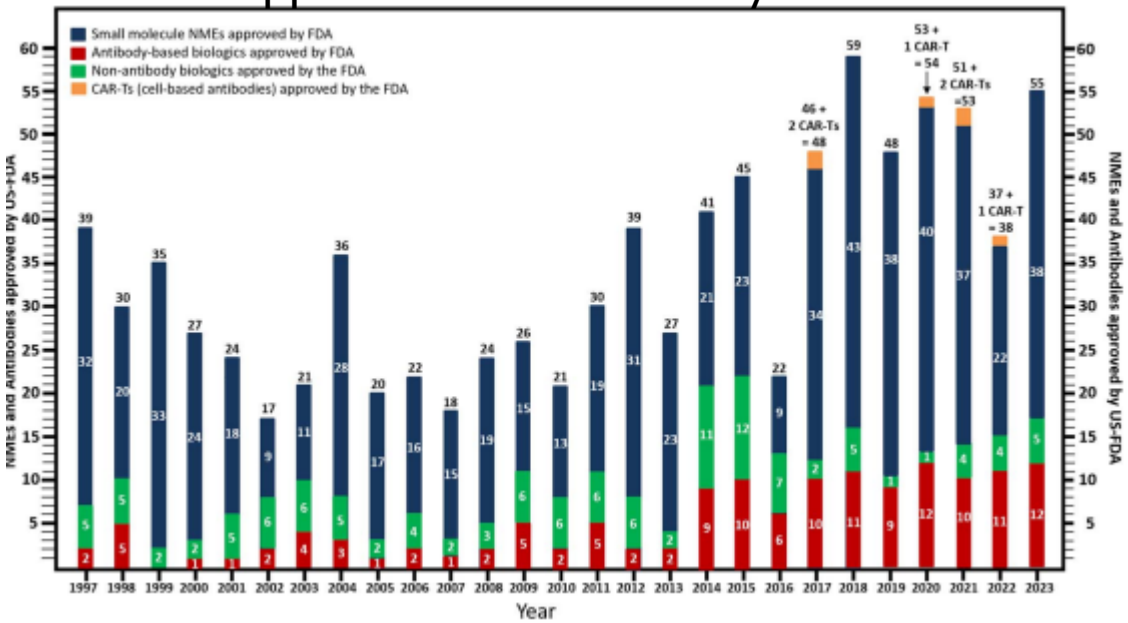
Topics Covered in this Short course

- Complex pathway of pharmaceutical R&D
- Bioanalysis of Peptides
- Bioanalysis of Oligonucleotides
- Bioanalysis of ADCs
- Bioanalysis of therapeutic proteins and biomarkers
- Integrating qualitative (Qual) and quantitative (Quant) Bioanalysis
- HRMS and QQQ applications to quantitative and qualitative workflows
- Various HRMS scan types available for Qual/Quant: TOF-MS, TOF-MS with IDA, SWATH (DIA) and MRM^{HR}
- Application of Qual/Quant for ADC bioanalysis
- DMPK studies for small molecules vs complex drug modalities
- Relevant regulatory guidance for complex drug modalities
- Metabolites in safety testing (MIST)
- Radiolabeled studies
- New technologies to improve sensitivity, speed and coverage for complex drug modalities

Complex Drug Modalities Added to Treat Complex Diseases

FDA approvals in the last 27 years



Number of small molecules, antibody-based biologics, non-antibody biologics, and chimeric antigen receptor T cells (CAR-Ts) approved on an annual basis from 1997 to 2023.

Figure from: Strohl, W. R. Structure and function of therapeutic antibodies approved by the US FDA in 2023 Antibody Therapeutics, 2024, Vol. 7, No. 2 132–156

Year	Total Number of Drugs (NCEs + Biologics) Approved By the U.S. FDA	Biologics Approved By the U.S. FDA	% Biologics Approved
2015	45	13	28.8
2016	22	7	31.8
2017	46	13	28.2
2018	59	17	28.8
2019	48	12	25.0
2020	53	15	28.3
2021	50	14	28.0
2022	37	15	40.5
2023	55	12	21.8
2024	50	17	34.0
2025	>34	>7	>21.0

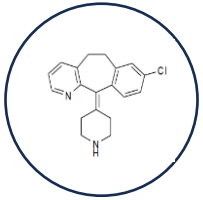
FDA=Food and Drug Administration;

- Over the last 27 years, the number of small-molecule drugs still dominates the disease treatment landscape.
- Antibody-and antibody-drug conjugates contribute to major components of the biologic drugs (20-40%) approved.

Complex Modalities Result in Complex Drug Discovery and Development

Structural Complexity/ Molecular Weight

Small Molecules



LC-MS, LC-HRMS, HDX-HRMS, NMR, AMS,

TIDES (Peptides (Oligonucleotides)

LC-MS, LC-HRMS, hybrid-LC-MS, HDX-HRMS, NMR, Ligand binding, qPCR, Laser-induced fluorescence, capillary gel electrophoresis

Monoclonal Antibodies (mAbs)

LC-MS, LC-HRMS, NMR, X-ray crystallography, cryo-electron microscopy, Ligand binding,

Therapeutic Conjugates

LC-MS, LC-HRMS, hybrid-LC-MS, NMR, Ligand binding, RT-PCR, Capillary gel electrophoresis, Forster resonance energy transfer

Analytical Techniques/Assay Complexity

Delivery & Manufacturing Complexities

DMPK Liabilities

AMS = Accelerator Mass Spectrometry,
DMPK = Drug Metabolism & Pharmacokinetics
FRET = Forster Resonance energy transfer,
HDX = Hydrogen Deuterium Exchange
LC-MS = Liquid Chromatography-Mass Spectrometry,
LC-HRMS= Liquid Chromatography-High Resolution Mass Spectrometry,
mAbs = Monoclonal Antibodies,
NMR = Nuclear Magnetic Resonance
qPCR = Quantitative Polymerase Chain Reaction,
RT-PCR = Reverse Transcription Polymerase Chain Reaction