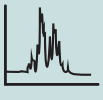
Meeting NIIMBL's Goals

	Industrialization for Existing Products	Manufacturing Platforms for Emerging Products	Standards & Measurement Technologies
Drug Substance 	**Host cell development** • increased productivity and manufacturability • alternatives to CHO **Novel capture and purification methods** • improved chromatographic processes (increased binding capacity, multi-product columns) • optimized resin usage • alternatives processes (precipitation, crystallization, extraction, membrane-based) **Process intensification** • continuous unit operations • process integration • time-matched upstream and downstream operations **Scale-down models** • continuous unit operation models	**Massively parallel small-scale, automated closed manufacturing platform** • scale-out • 100% consistency **Optimized unit operations** • improved selection and separation of target cells • more efficient cell transduction • continuous and integrated processes **Improved gene vector manufacturing** • higher titer, increased % of filled capsid • improved capsid harvest and purification processes	**Reference standards** • MAb standards, including glycosylation pattern • cell-based standards for viability, identity, potency • gene vector capsid standards • gene transduction standards • exosome standards • host cell **Measurement technology** • real-time, in-line analytical methods for CQA • real-time adventitious agent test method • multi-attribute methods • non-invasive analytical methods for evaluation of process parameters • real-time, in-line analytics for massively parallel, closed-system manufacturings
Drug Product 	**Continuous processing** • liquid product • freeze dried product **Link process variation to CQA variation** • freeze dried and liquid • intra- and inter-batch **Develop "standard platform formulations" and processes for products in a given class** • maximize stability • minimize process time • minimize development $ **Improve understanding of protein aggregates** • analytical characterization • relationship of aggregate physicochemical properties to immunogenicity	**Cell therapy product formulations** • improve definition of CQA beyond cell viability • develop innovative final product formulations to maintain cellular function and CQA • improved cryoprotectants • optimized procedures for storage transportation, freezing and thawing **Gene therapy products** • optimized formulations for high titer and activity, minimized aggregation • lyophilization procedures unique to this class of products	**Reference standards** • polysorbates • excipients • aggregates **Measurement technology** • real-time, in-line analytical methods for final product CQA • rapid adventitious agent testing • develop rapid tests for predicting stability in solids • improve in-line and off-line detection and characterization of aggregates
Process Control 	**Real-time, in-line analytics** • novel analytics for CQA glycoprofiling, size, oxidation state, aggregation, impurities, product temperature and mass flux **Integrated process systems engineering and control** • unit operations models • integrated process models • plant-wide models • optimized control strategies	**Real-time, in-line analytics for process control and product release** • novel analytics for identity, potency, purity • vector identity, determination of empty capsid percentage (AAV) • real-time rapid measurement of raw material critical attributes **Closed-loop control of manufacturing process** • unit operations models • integrated process models • plant-wide models • optimized control strategies **Supply chain management** • raw materials, including patient cells/tissue • final product, delivery, activity, formulation	**Regulatory science** • standardized process validation protocols for real-time parametric product release • standards for specific capsid types • test standardized final product; MAb heterogeneity • develop consensus on what constitutes a CQA • develop consensus on the role of first principles modeling in design space definition **Standardizing raw materials** • rapid, non-invasive high-resolution analytical technologies for raw material • industry-wide engagement in method development efforts **Reference standards** • work with industry and NIST to develop reference standards for key quality attributes for important raw materials • tool for comparability (identity potency) • combination manufacturing regimes