

HIGH THROUGHPUT SCREENING CORE FACILITY COMPOUND MANAGEMENT

VANDERBILT UNIVERSITY
MEDICAL CENTER

VANDERBILT INSTITUTE of CHEMICAL BIOLOGY

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Our Mission

Within the High Throughput Screening Core, Vanderbilt houses a cutting edge academic Compound Management facility which provides this critical function to both internal and external partners for a variety of drug discovery efforts at various stages of development. In addition to effectively managing Vanderbilt's HTS plate/tube based libraries, a standard in many HTS facilities for the assistance of early stage hit identification, we also provide a variety of Compound Management services to numerous Hit-to-Lead and Lead Optimization efforts ongoing in the Vanderbilt Community.

Compound Libraries

Library	Size	Description
Vanderbilt Discovery Collection	100,000	Newest collection to be used for full screening or on a per-compound basis. Compounds were selected based on physical properties and diversity.
Chembridge/ ChemDiv (VICB Collection)	160,000	Drug-like, diverse set of small molecules.
Spectrum Collection	2,000	A wide range of biologically active and structurally diverse compounds. 50% drug components, 30% natural products, 20% other bioactive components.
NIH Clinical Collection I and II	730	Small molecules that have history of use in human clinical trials.
Cayman Lipid Library	1,000	Broad variety of bioactive lipids.
Fesik Fragment Library	16,000	Diverse collection of fragment molecules from 8 vendors, rule of 3 compliant, and filtered against non-specific and interfering molecules.
Marnett Collection	215	NSAID derivatives that contain cyclooxygenase inhibitors, PPAR-gamma activators and apoptosis inducers.
Roche Published Protein Kinase Inhibitor Library*	235	Small molecule protein kinase inhibitors disclosed in peer-reviewed scientific publications.
Ion Channel	6,243	A collection from Life Chemicals targeted to ion channels compiled using 2D fingerprint similarity methodology.
Epigenetics Collection	51	A group of small molecule modulators with biological activity for use in epigenetic research.
Enzo Kinase Inhibitor Library	80	The Screen-Well™ Kinase Inhibitor Library contains 80 known kinase inhibitors of well-defined activity.
GSK Published Kinase Inhibitor Library**	349	A set of 349 small molecule kinase inhibitors spanning over 30 chemotypes that have been previously published by GlaxoSmithKline in peer-reviewed scientific journals.

* In collaboration with Roche Pharmaceuticals
** In collaboration with GSK Pharmaceuticals

Instrumentation and Services



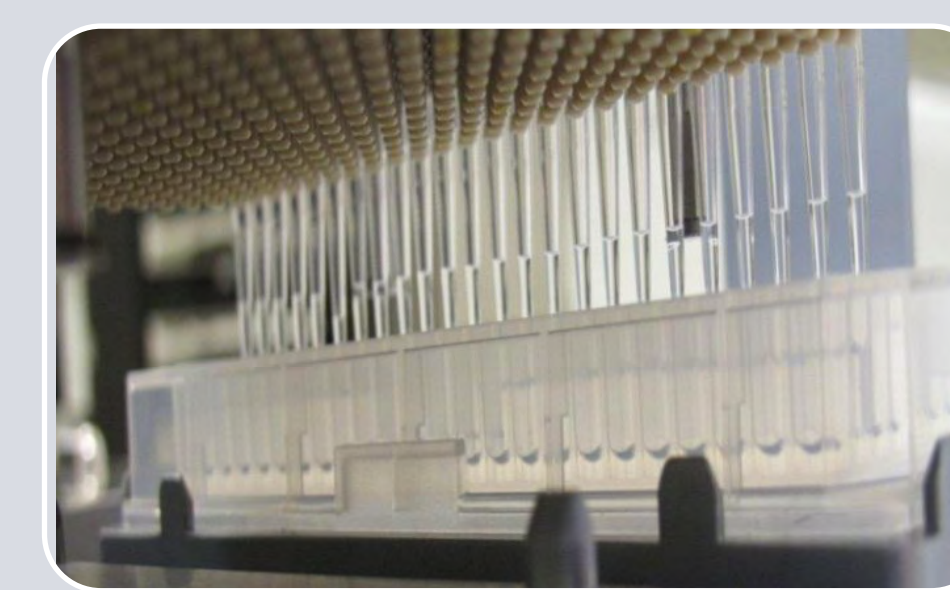
Liquid Handling

- Zinsser Calli Robot (10uL-4 mL, 8 independent probes)
- Agilent Bravo (10 uL-250uL disposable tips)
- Agilent Vprep (10 uL-250 uL disposable tips)
- Labcyte Echo 555 & 555 OMICS Non-contact acoustic dispensers (2.5 nL-1 uL)
- Thermo Combi Liquid Dispensers (uL amounts)



Other Instrumentation

- Brooks Universal Store + Cherry Pick Module
- Brooks X-cap Tube Decapper
- Fluid-X XDC-96-Pro Tube Decapper
- Agilent PlateLoc sealer
- Brooks X-Peel Plate seal remover
- BioMicroLab Volume Check
- Thermo CRS robotics compound management systems
- Barcode Reading/Printing
- Agilent Vspin Automated Centrifuge
- Plate Shakers



Services

- Registration and sample tracking including:
 - New Chemical Entities (NCEs) synthesized at Vanderbilt
 - NCEs synthesized by external pharmaceutical industry collaborators
 - Externally purchased compounds
 - Stock sample preparation of NCEs
 - Compound Library Storage and Maintenance
 - Compound Distribution
 - Compound Reorders

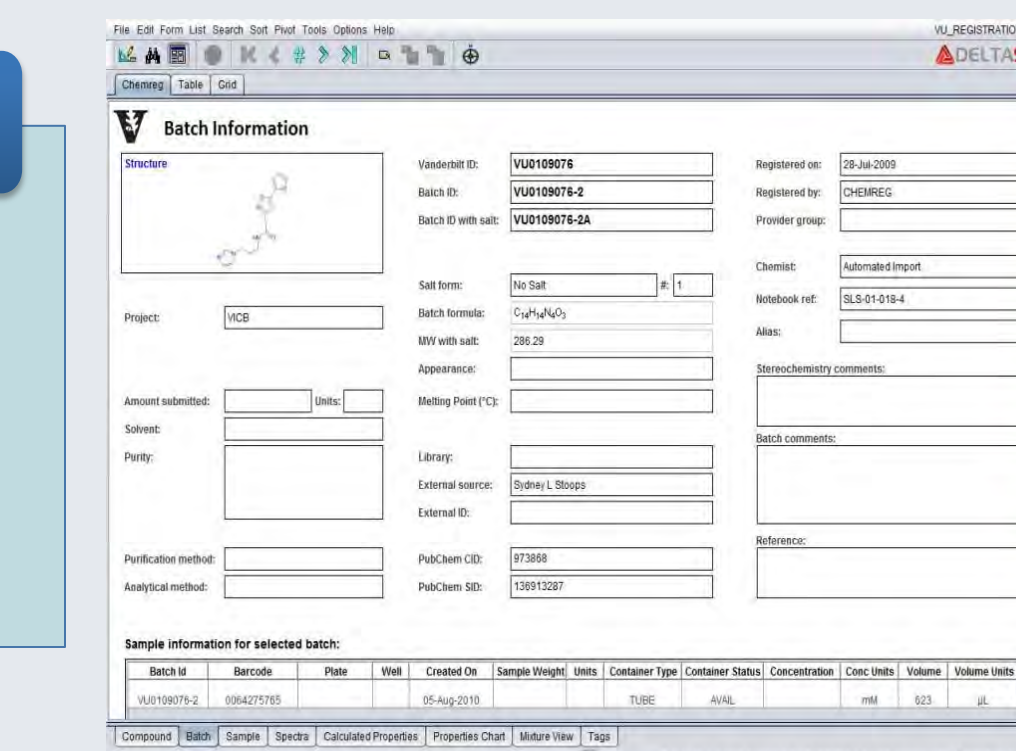
Compound Management Supported Labware for Storage and Distribution

Matrix 96-well 2D Barcoded PP Tubes Septum or Screw Cap	Labcyte PP 384-well plates	Labcyte LDV 384-well plates	Standard 96-well plates
96-well Deep Well Block Plates	1D and 2D barcoded glass vials	Greiner 384-well round bottom plates	Custom formats may also be considered

Informatics Tools and Services

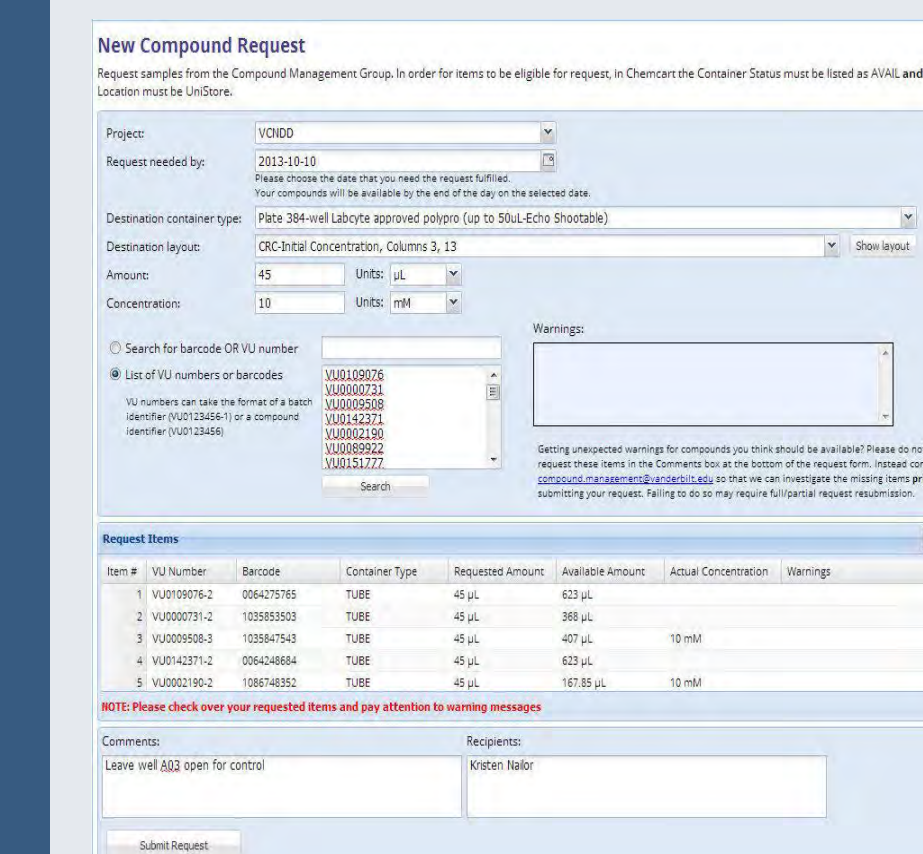
Compound Registration and Sample Tracking

- Custom built Oracle database
- Chemcart User Interface to chemical database
- Custom built Chemcart + Pipeline Pilot based registration system



Compound Requests and Distributions

- Custom built Pipeline Pilot based "LIMS" system including user interface to request compounds, drive liquid handling equipment, create new samples in database and update sample quantity and storage information in real time

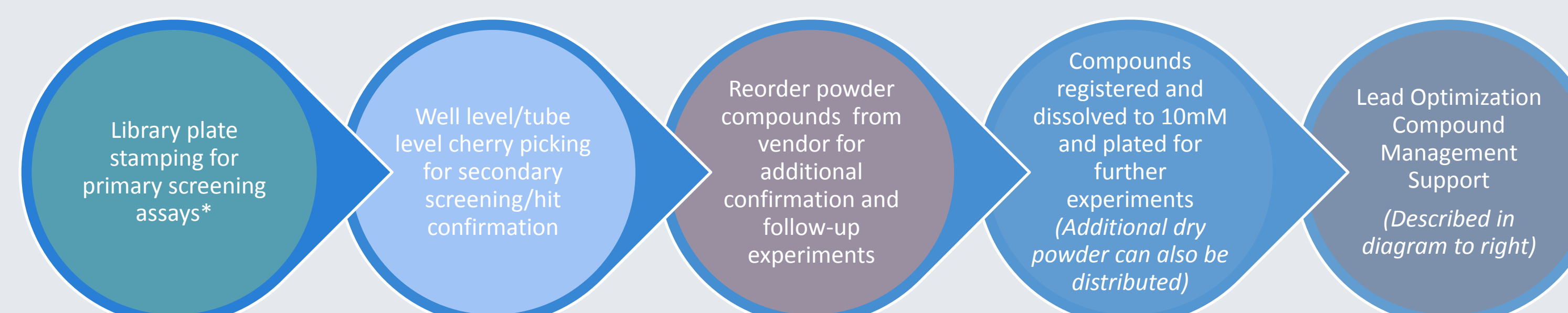


Error Handling Systems and Communications

- Pre-registration user error notifications
- In-registration molecule duplicate checking
- Post-registration Sharepoint based Issue Tracker ticket submission system

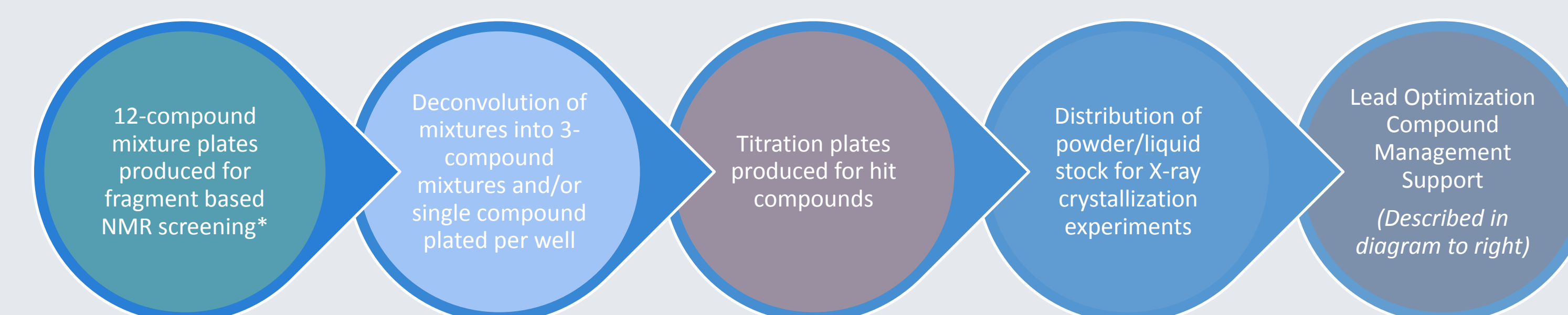
Compound Management Process

High-Throughput Screening Support



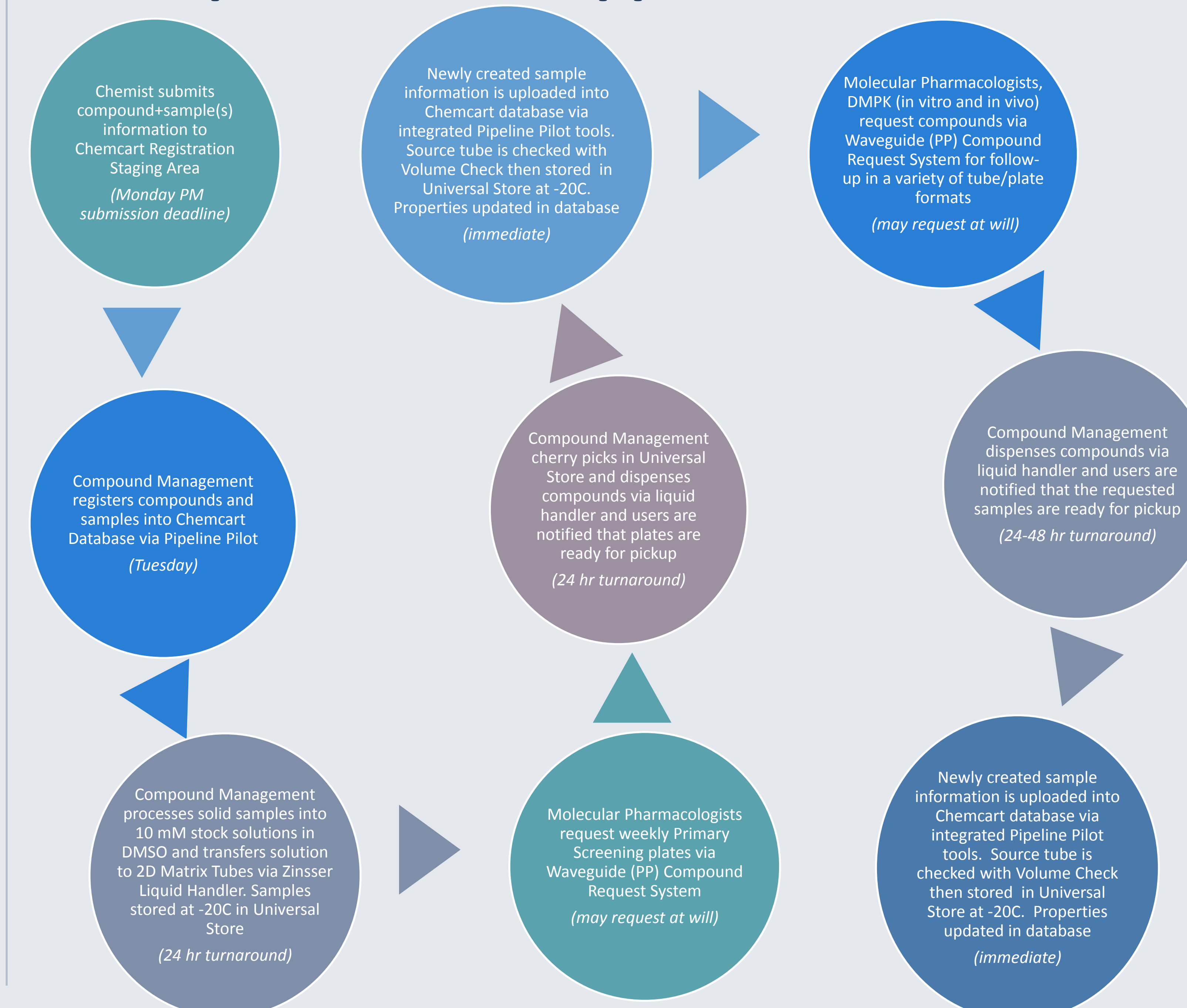
*Most HTS libraries are stored as 10 mM stock solutions in DMSO. Single compounds or small custom compound sets can also be cherry picked and distributed in small volumes.

Fragment Based Screening Support



*Fragment Library is stored as 200 mM stock solutions in d6-DMSO.

Lead Optimization Support

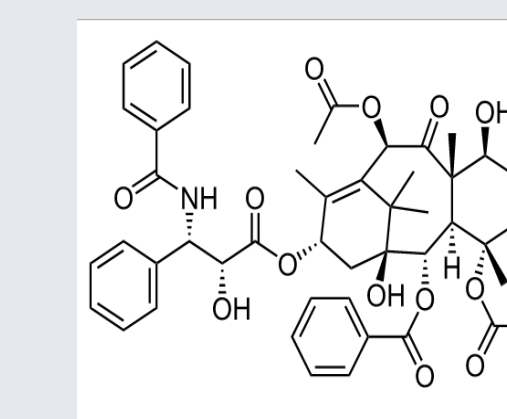


Challenges

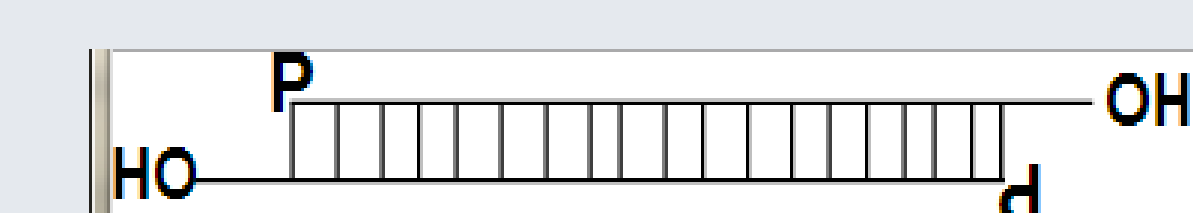
Future Directions

- Mass Spec hit confirmation/QC
- Automated drop visualization (post-acoustic dispensing)
- Automated plate retrieval from Universal Store
- Automated plate sonication for mixing
- Non-standard database registration and sample tracking of compounds with undisclosed chemical structures (e.g. external collaborations)

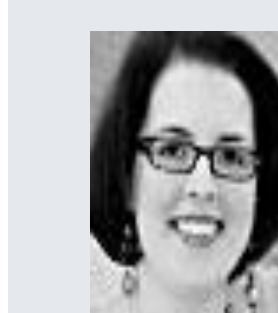
• Natural Products



• siRNA



Vanderbilt Compound Management



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