

BiomekFX Enhanced Automated Sample Titration (BEAST): A Fully Automated Method of Titrating Compound for Counterscreen Assays

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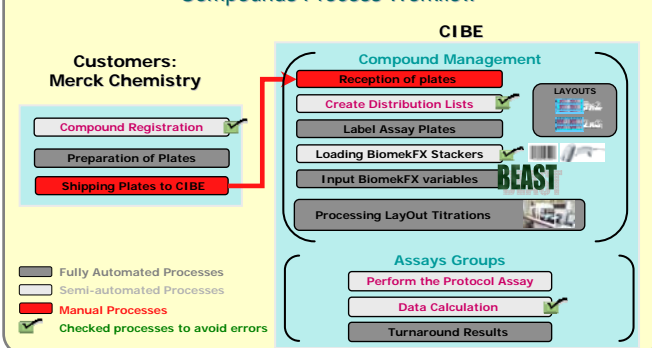
Introduction

➤ The overall objective regarding Laboratory Automation that Pharmaceutical Industries face is to achieve full automation of the main laboratory processes. This goal strives to reduce as much as possible the human manual steps (and human error) while increasing the capacity and turn around time of current workflow processes.

➤ One of the missions at CIBE is the centralization of a number of counterscreens used to assess potential toxicity and drug-drug interaction issues of chemical leads in a diverse range of therapeutic areas.

➤ In the following compound workflow, BEAST supports the full automation of the counterscreen sample processing: from the initiation of BiomekFX variables to performing the final LayOut Titrations

Compounds Process Workflow



Before BEAST

- More than 10 different complex BiomekFX methods → Additional source of errors and an extra time
- A long time and big efforts for including new titration Layouts in the system
- Many incomplete final titration assay plates.
- Many manual steps without checking errors: Up 20 different assay conditions; Manual input of a high number of method variables; Manual replacement of labware and several manual pipetting steps

What is BEAST?

It is a complex system of several integrated tools driven by a Visual Basic (VB) application, able to connect the CIBE LIMS with BiomekFX LiHa Robotic system without additional interface.

Materials & Methods

➤ BiomekFX robotic station (Fig. 1) with the worktable configuration (Fig. 2)



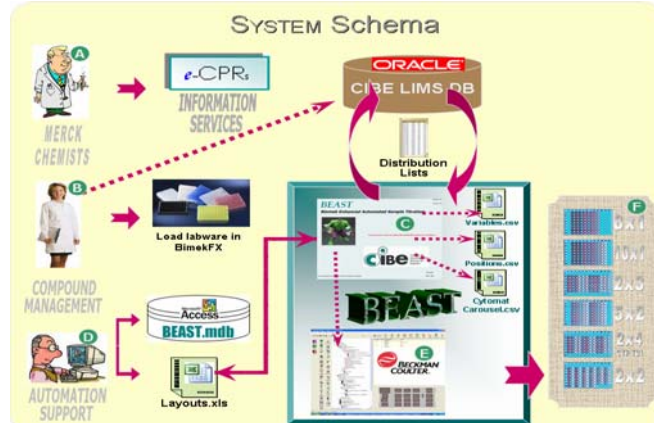
Fig. 1: BECKMAN-COULTER BiomekFX Dual-Arm LiHa with KENDRO Cytomat Carousel (capacity for 28 tip boxes and 70 DW plates)



Fig. 2: BiomekFX workstation configuration: Tip Loader on TL1; Barcode reader on OFF1; Recirculating reservoir on P5; Orbital Shaker on P6; Reservoirs for solvents on P9 and Tip Trashes on TR1 and TR2

- A simple and user friendly VB front-end Application (BEAST.vb)
- One unique but complex BiomekFX method used as Titration LayOut template (BEAST.bmf).
- One VB dynamic linked library (eCPR.dll) to connect with an ORACLE db in order to retrieve the compound data registered by our Merck Chemistry clients.
- One local MS Access database (BEAST.mdb) storing the BiomekFX specific variables and parameters.
- An Excel file with the precise information about the different titration LayOuts (Layouts.xls)

Results & Discussion



- Chemist clients registered their compounds in CIBE Web Site.
- Compound Management people create the distribution lists, load labware in BiomekFX Stackers and start BEAST.vb.
- BEAST.vb capture data from Access db and Layout.xls (updated by Automation Support Dpt.), generates 3 csv files and connect with BEAST.bmf that retrieves data of these 3 source files and initiates the compound titration process.
- At the end of the process BiomekFX creates the final dilution plates with the titration LayOut pattern ready to be tested in different counterscreen assays.

BEAST.vb

- Designed to be used with a minimum # of possible user-clicks: 2 clicks and 2 barcode reads for processing an unlimited # of assay plates (Fig. 3)
- Connect with Merck LIMS to retrieve data about:
 - Distribution Lists (working orders, assays, etc.)
 - Titration Layout (dilutions x replicates)
 - Titration parameters (compound cc., serial dil., etc.)
 - Final required titration volume of the dilution plate
- Capture data from BEAST.mdb:
 - Type of Labware (Source, Titration and aliquot plates)
 - Solvents information: Type (MeOH, DMSO, etc.),
 - Other: # of aliquots, volumes, shaking parameters.

Fig. 3: BEAST VB main form running a process

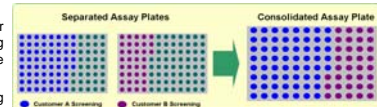
- Consolidate positions in titration plates.
- Calculation of each pipetting step position depending on the layout chosen (aspirate and dispense positions).
- Remote control of BiomekFX Workstation using ActiveX component without displaying the BiomekFX software interface
- Allow users to change predefined parameters (Fig. 4)
- Allow users to review and print assay conditions.
- Disable barcode check for QC processes.



Fig. 4: BEAST VB parameter form.

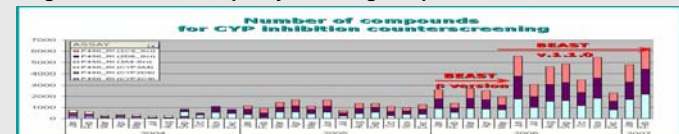
BEAST.bmf

- Is a BiomekFX template method able to process any type of Titration LayOut in 96-well plate format.
- Almost all the parameters are local variables or imported from csv files (labware, pipetting techniques, solvents, aspirate and dispense positions, washing and shaking parameters)
- Allows consolidation of titration plates by using compounds from different source plates.

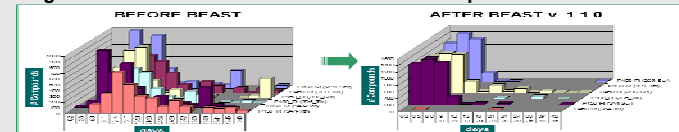


Conclusions

High Increase in the capacity of testing compounds



Reduce the turnaround times on results for compounds sent to CIBE using the BEAST version 1.1.0 with consolidation option



Dramatic reduction of user induced errors by introducing variables and/or parameters for the BiomekFX daily use

Only 5 minutes for creating a new titration layout and 1 working-day in its validation