INTRODUCTION

Modern drug discovery involves high throughput screening processes on large numbers of microplates that produce "hits" or "leads". These hits are the important precursors to potential drug candidates. Since the screening process generally involves testing large numbers of compounds from a library, the generation of hits is a mostly random process. Any given microplate may have a few hits, many hits, or even no hits. To efficiently continue the development process, it is necessary to consolidate the hits from the various source plates into destination plates to simplify further analysis and development. This is called "hit consolidation", "cherry picking", or "hit picking".

It is desirable to automate the hit picking process, as with any other drug discovery process. This has proven to be difficult because of the random nature of the hits and the variability in automation capability of the various instruments required. These factors, combined with the vital importance of the hit compounds, have resulted in many labs performing this process manually. However, this is labor-intensive and prone to errors.

Automated Hit Picking from Hudson is a proven solution for automation of the hit picking process. When combined with a liquid handler, bar code reader, and Hudson PlateCrane or PlateSilo, it provides an easy to use, flexible, and reliable hit picking automation solution.
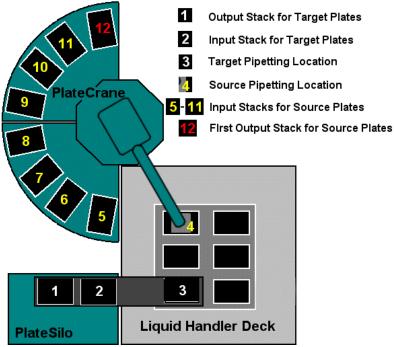
SYSTEM REQUIREMENTS

- **Hudson Control Group Automated Hit Picking** software to oversee the hit picking process. Based on Hudson's Total Control for Windows software.

- **Liquid Handler Workstation** for pipetting of hits from source to destination plates. The liquid handler can be configured with either a single tip pipettor or a multichannel pipettor with independent z-axis control of each tip. This capability can be used to speed up the hit picking process because fewer trips to the source plate are required. Beckman Coulter, CCS Packard, Tecan, and others offer this capability with 4 or 8 tips.

- **Database software** to send and receive hit information. Any structure/format is compatible.

- **Hudson Control Group PlateCrane** Pick and Place System to supply microplates from stacks and/or move microplates. Source plates and/or destination plates can be supplied by the PlateCrane. (Optional)

- **Hudson Control Group PlateSilo Stacker** to supply microplates to the liquid handler. The PlateSilo can be used to provide a supply of destination plates. (Optional).

- **Bar Code Reader** for identification of source plates.

- **Pentium Computer** to run Automated Hit Picking software. The computer will require one serial port for each module in the workstation. Standard PC's are easily configured with additional serial ports.

OPERATION

The Automated Hit Picking software provides supervisory control of the system modules and convert's the hit database into commands for the Liquid Handler's aspirating and dispensing functions. An easy to use graphical user interface is used to set up, program, and operate the system.

A typical hit picking system would include a Liquid Handler, a PlateCrane to deliver source
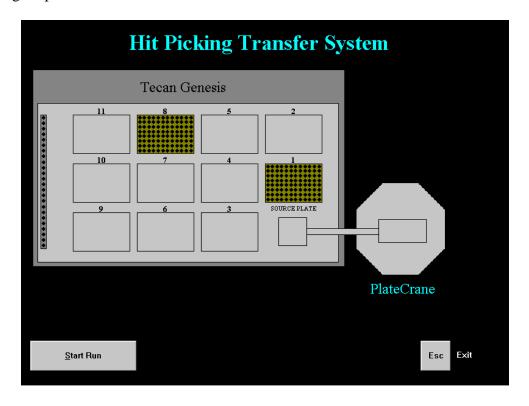
(hit) plates, and PlateSilo to supply fresh destination plates, and a bar code reader.

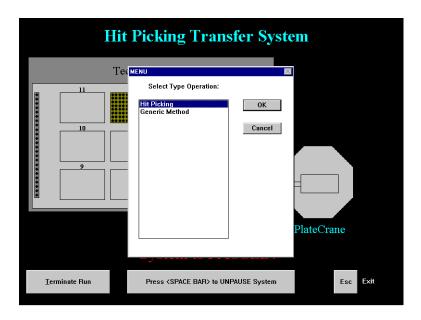|	
1	Output Stack for Target Plates
2	Input Stack for Target Plates
3	Target Pipetting Location
4	Source Pipetting Location
5-**11**	Input Stacks for Source Plates
12	First Output Stack for Source Plates

The hit picking operation follows these steps:

- The PlateCrane moves a bar-coded source plate onto the liquid handler's deck in the Load position, scanning the barcode as the plate moves there.

- The PlateSilo dispenses and positions a clean "target" or consolidation plate on the liquid handler deck at the beginning of each run, and continues to supply target plates as they are filled.

- Using the scanned barcode, the software searches the database for prior assay hits from that source plate.

- The hit data is consolidated and converted into pipetting commands for the liquid handler.

- The liquid handler transfers the correct amount of compound from each hit well into the designated well on the target plate. (If the liquid handler is configured with independent multichannel pipetting capability, it will aspirate multiple wells from one trip to the source plate to speed up operations).

- The software monitors the liquid handler and provides live status graphics for the user, while recording completed transfers in a results file as they occur.
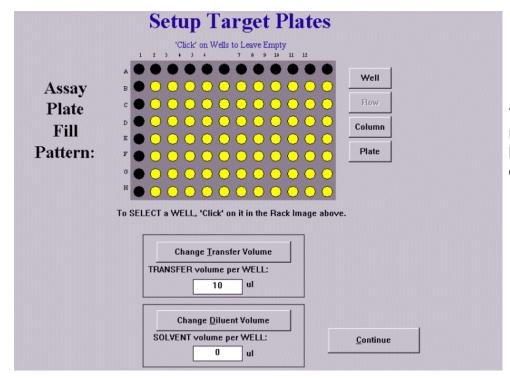
After loading the PlateCrane and PlateSilo with source and destination plates, the operation of the system is initiated by selecting "Run Method" from the Main Menu. The Status Screen is brought up as shown below.
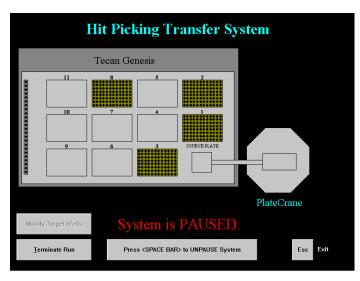

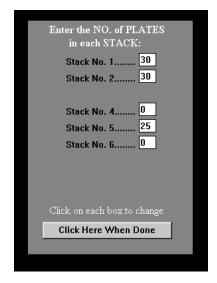Selecting Start Run allows the user to select the Hitpicking Application.

The user can easily set up the Target Plates through a graphical point and click interface. Wells can be excluded for future use as standards or controls either individually, or by rows and columns. The user also specifies the volume to be transferred, and a volume of diluent to be added, if required.
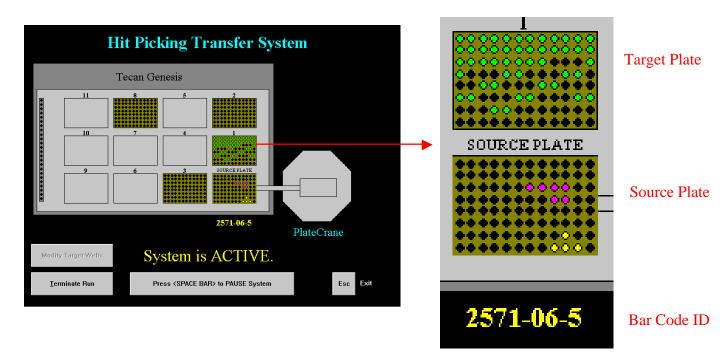

YELLOW wells receive samples, BLACK wells are excluded.

The system will begin in "Paused" mode and prompt the user to load the stacks with source plates.
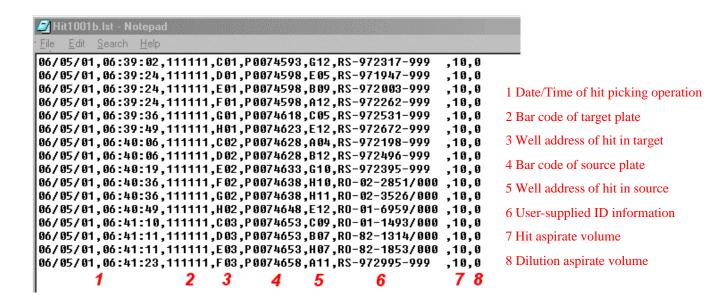
Target Plate

Source Plate

Bar Code ID

The Status screen provides a live update of system operation with an easy to follow color scheme. On the Source Plate, the Hit wells are shown in YELLOW, and the non-hits are BLACK. As each source well is aspirated, it becomes MAGENTA. When it is dispensed into the Target Plate, it turns LIGHT GREY and the Target Plate well turns GREEN.

The software uses a copy of the supplied worklist file for the hit picking operations. A "Hit" file is also generated in comma-delimited text format, as shown below. All pertinent hit picking information is automatically stored for traceability.

1 Date/Time of hit picking operation

2 Bar code of target plate

3 Well address of hit in target

4 Bar code of source plate

5 Well address of hit in source

6 User-supplied ID information

7 Hit aspirate volume

8 Dilution aspirate volume

CONCLUSION

Hudson's Automated Hit Picking software provides a reliable and easy to use solution for the automation of hit consolidation. Hudson's ability to integrate with any available liquid handler means that any laboratory can quickly implement an automated solution for hitpicking that will be specific to their needs.