Liquid handling in Chemical Synthesis- The Celltech approach

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Liquid handling - why?

- Not for speed
- Economies of scale
  - >10 reactions
- Accuracy
- Boredom!

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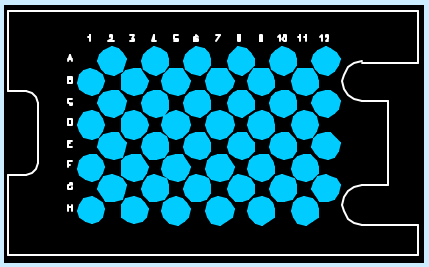
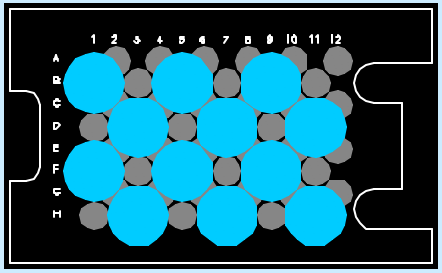
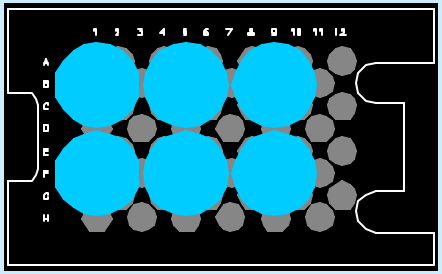
What's different about Chemistry?

- Variety of organic solvents
  - Viscosity
  - Vapour pressure
  - Material suitability
- 'Hard to handle' reagents
- Biphasic mixtures
  - Liquid-liquid
  - Solid-liquid
- Flexibility







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The Tools

- Tecan Genesis ChemSystem
- (Zinsser Calli)

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Tecan features

- Chemically Inert fittings
- 6 Independent solvent lines via switching valve
- Co-axial septum piercing tips (8)
- Flexible software
- Good deck capacity (150cm, 200cm)
- Good Z-clearance

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Programming the Tecan

- Button-driven, drag & drop, cut & paste
- Sub-routines pre-defined for;
  - Aspirate, dispense, mix, replicates, copy, serial diln., merge
- Ability to program loops, variables, system fluid changes, waste switching, time delays
- Other features
  - Cherry picking
  - liquid class selection
  - Turn inerting on/off
  - Control of 3rd party devices (reaction block)

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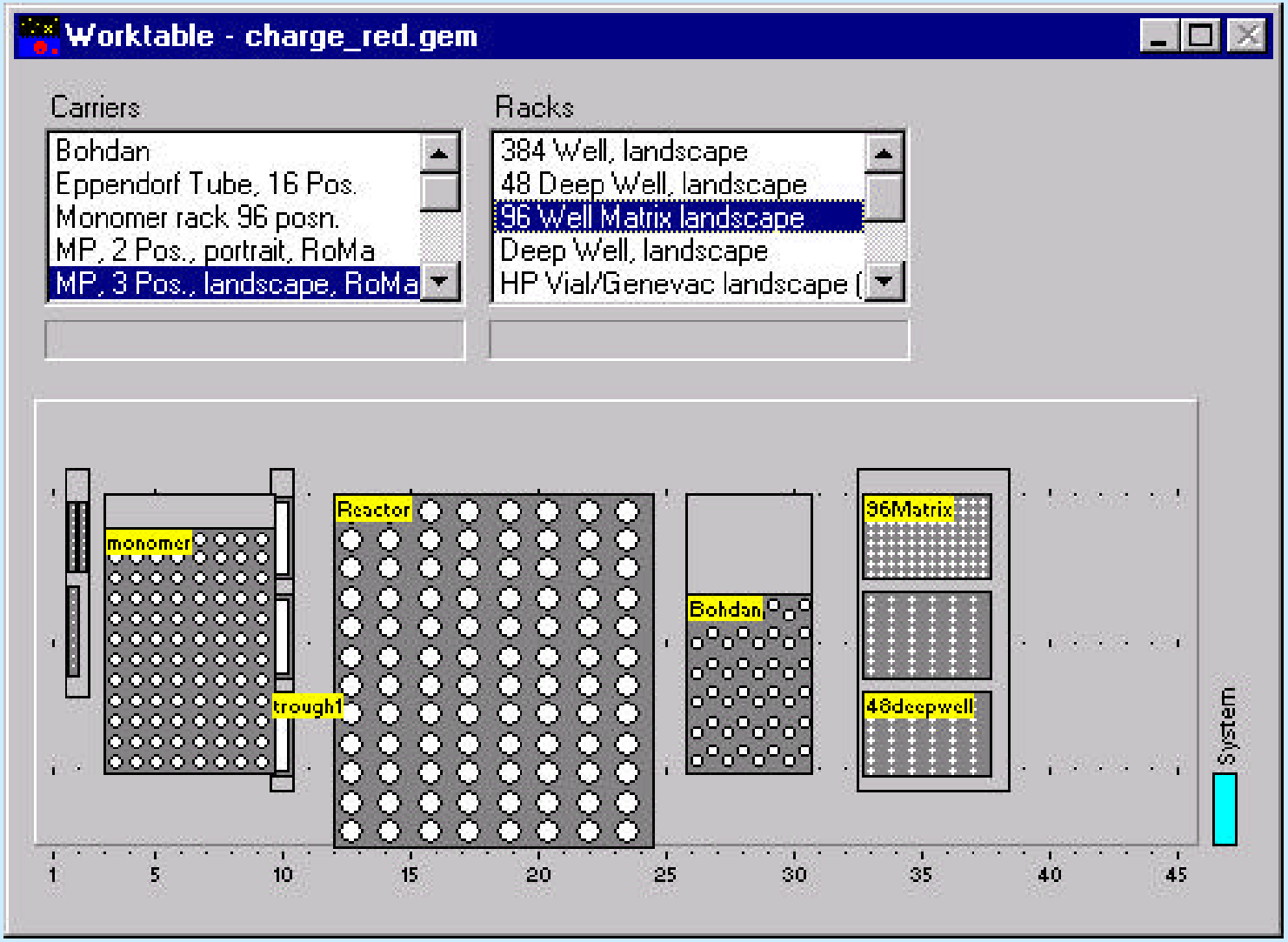
Worktable



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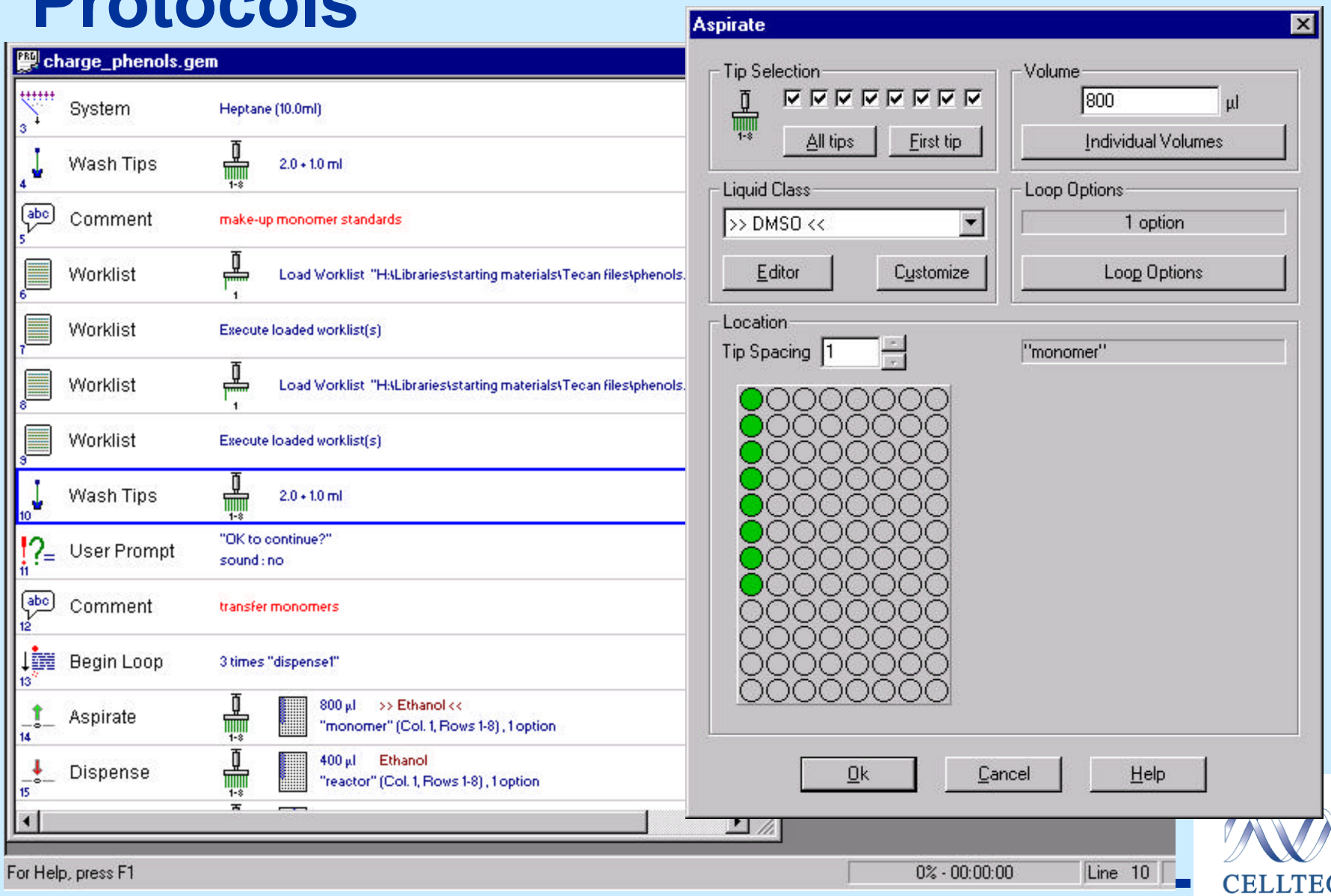
Protocols



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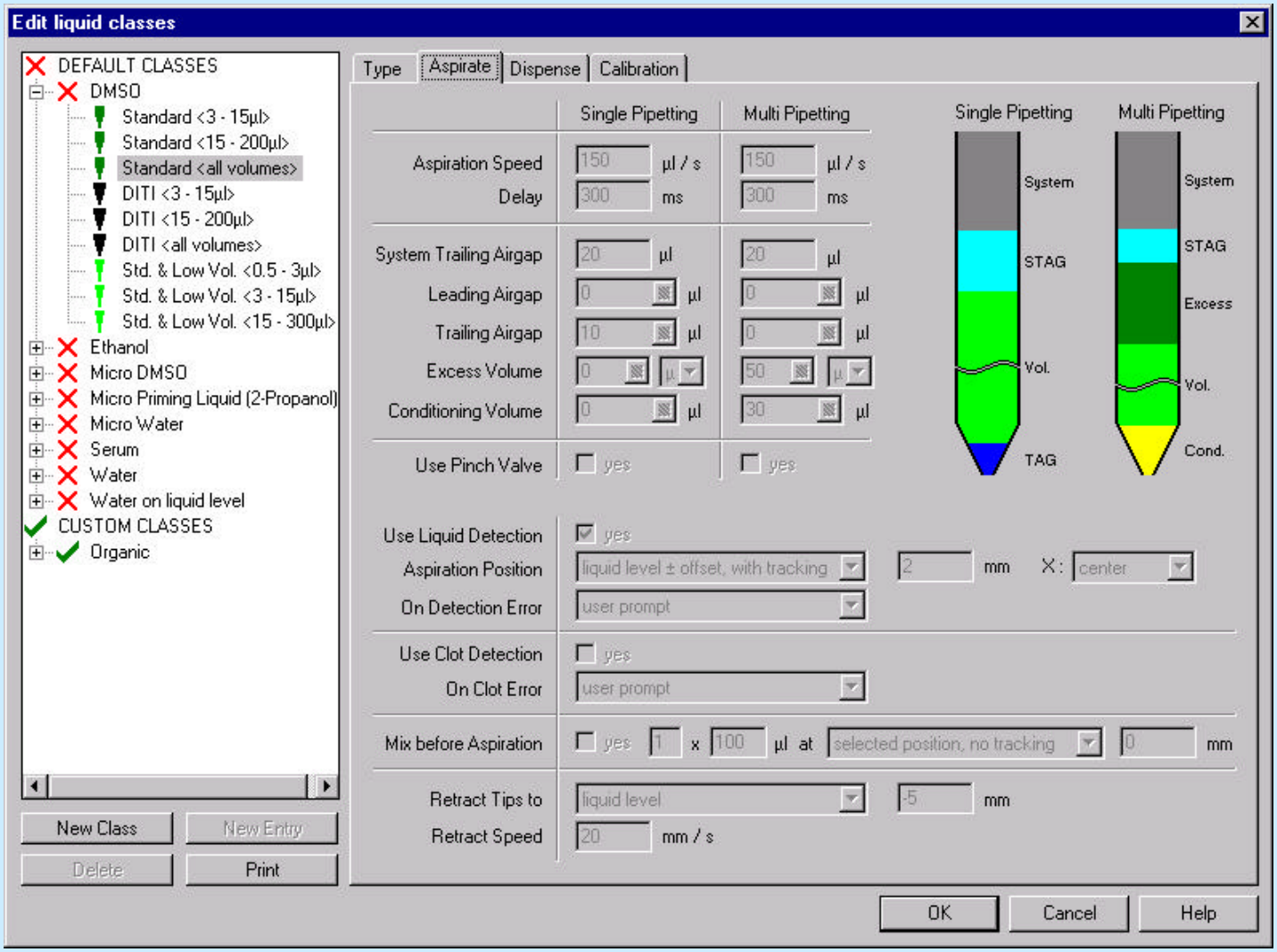
Liquid classes



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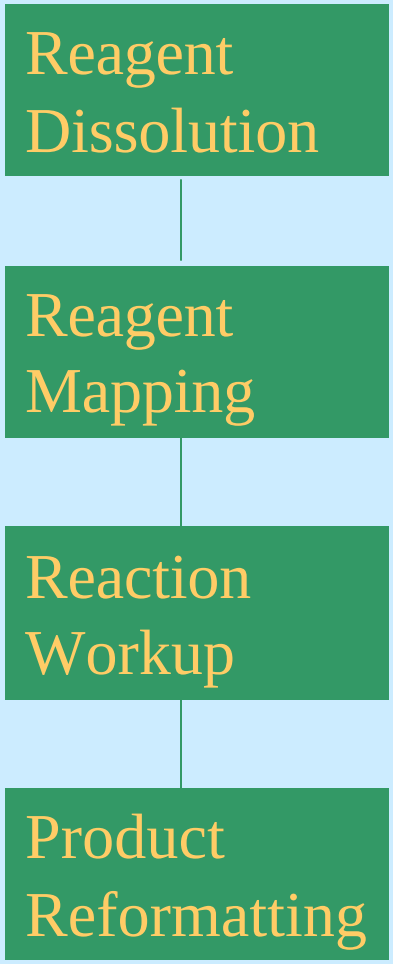
The Chemical Synthesis Process



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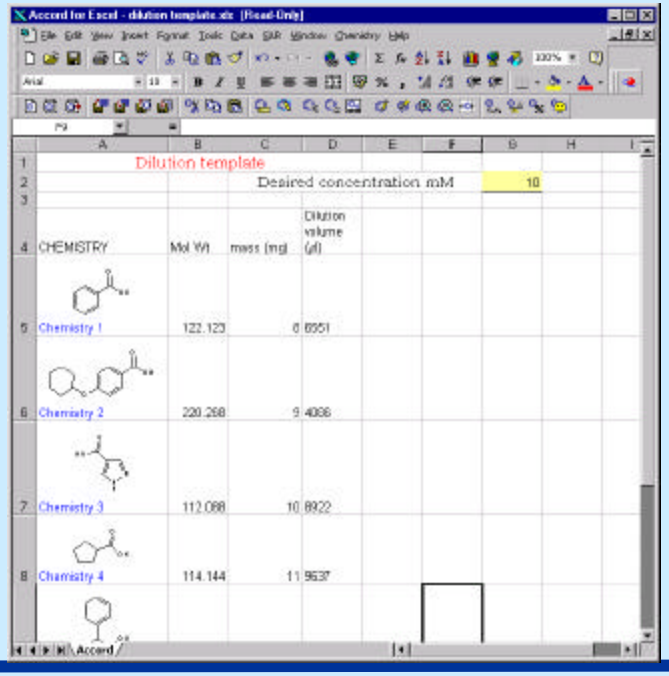
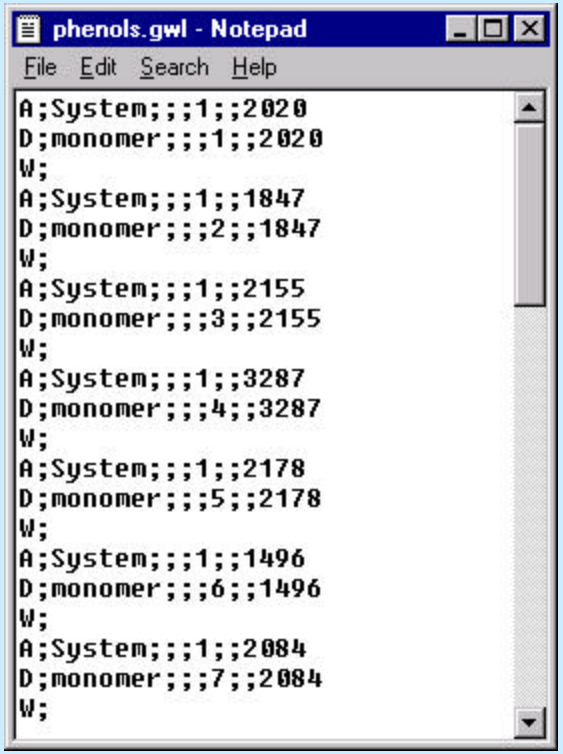
Reagent Dissolution

- Preparation of equimolar solutions
- Link to weighing station
- Max/Min permissible volumes
- Air-sensitive reagents





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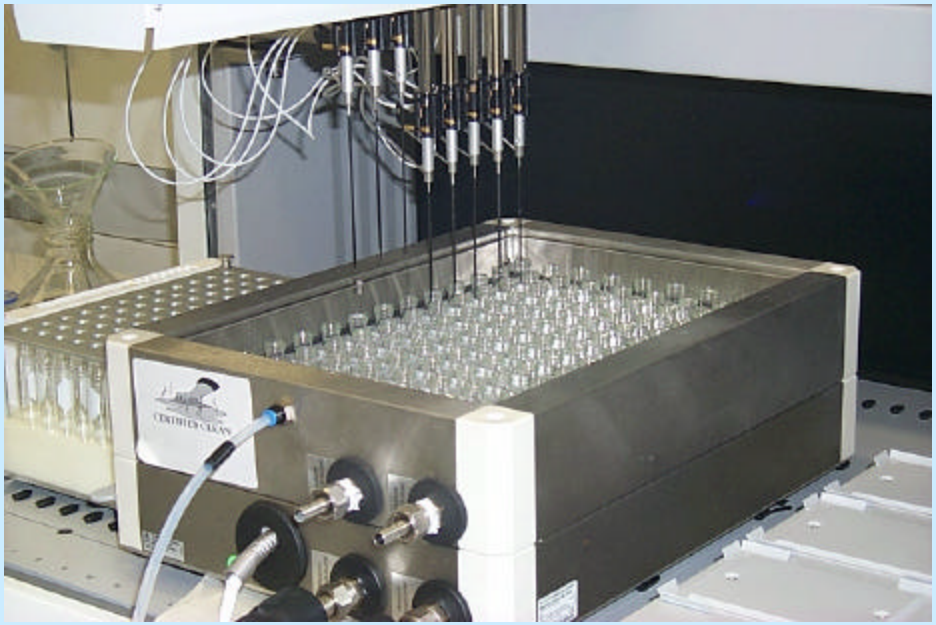
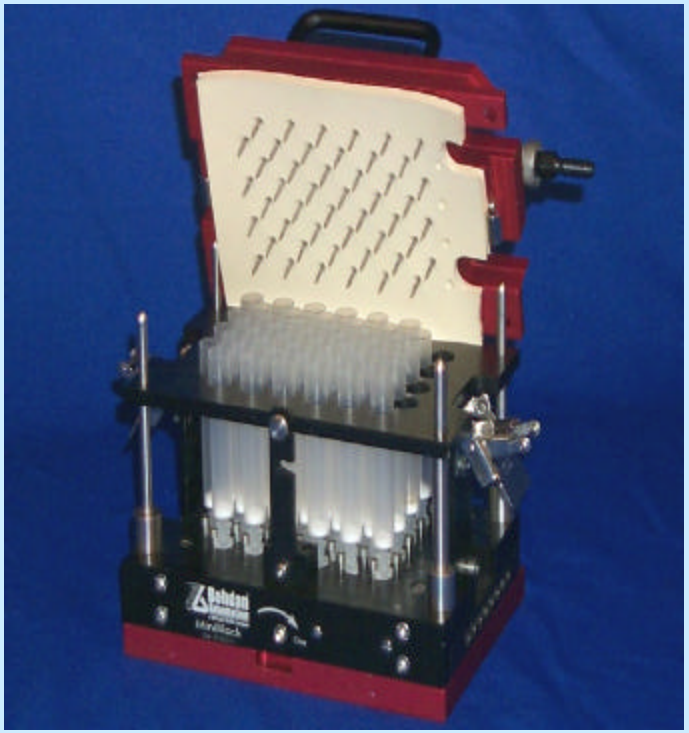
Reagent Mapping

- What goes where?
- Variety of block designs/layouts
- Variety of reaction protocols
- Tracking via Excel





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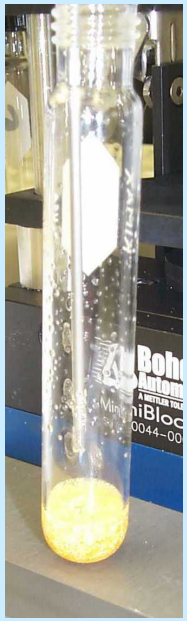
Reaction work-up and product isolation

- Reaction quench with aqueous acid
- Separation of layers
- Separation of solids (resins)
- Distribution to analysis/purification plates



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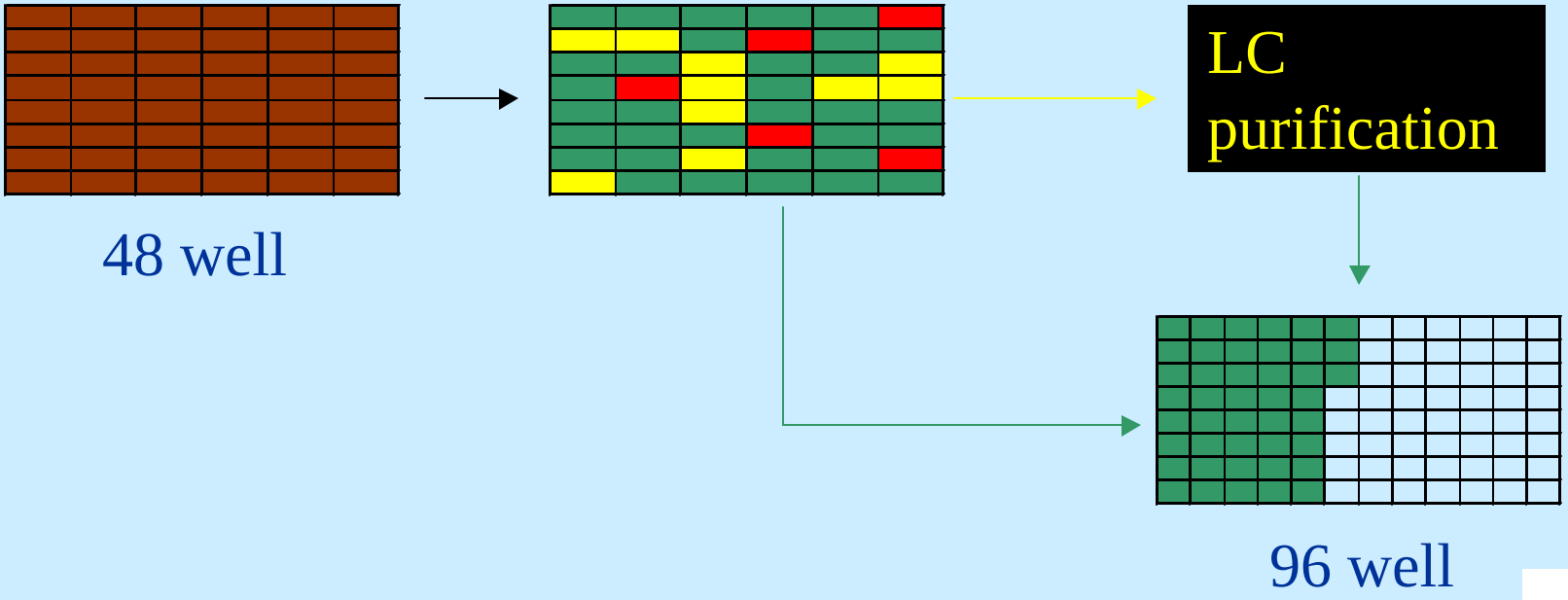
Product Reformatting

- Re-uniting purified/non-purified samples
- Reconstitution to standard molarity
- Replating



Summary

- A liquid handler for chemistry must:
  - Be chemically robust
  - Be flexible
    - Deck
    - Programming
  - Allow the use of multiple solvents
  - Use a common interface (Excel)
- Optionally it should:
  - Allow septum-piercing
  - Allow inerting
  - Be multi-tipped

Tecan was our choice, but there are other machines available……...

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