Andrew Alliance

APPLICATION NOTE
No. 4 – 20160118 v5

Versatile Interfaces for Integrating the Liquid Handling Robot Andrew into Automated Lab Workflow

Manual pipetting for handling liquids is a common mundane task in many lab processes, ranging from standardized chemistry to diverse and complex biological experiments in clinical testing, diagnostics, and research. This tedious routine not only poses significant risk of repetitive strain injury to bench workers but also is subject to human variability and errors, leading to degraded data quality. The affordable bench-top pipetting robot Andrew addresses these problems by its labor- and time-saving automatic pipetting operation with high accuracy and reproducibility, using the conventional manual pipettes. Bench workers interface with Andrew via ***Andrew Lab*** – the intuitive graphical user-friendly software for designing pipetting protocols. Andrew OS – the commander of Andrew via *Andrew Lab,* completes the trio as a compact, mobile, and stand-alone automatic liquid handler for low- to medium-throughput lab processes.

However, liquid dispensing and mixing is rarely an independent operation. It is rather often an integral task of multiplexed procedures spanning an array of other activities involving diverse lab equipment and instruments, such as fluorometric/spectrophotometric reading, bar code scanning, colony picking, plate handling, incubation, centrifugation, washing, etc., all of which are in the trend of automatization. A comprehensive automated lab workflow increases productivity, improves data quality, achieves timely progress, and frees up user's time for value-added activities such as designing experiments and interpreting results.

Tailored to the growing need of integrating the pipetting robot Andrew into other lab automated systems, the newly launched ***XML/API toolkits*** of Andrew Alliance provide an advanced user interface for customized solutions to integration challenges. Following the lauded easy and friendly *Andrew Lab* software, this advanced versatile tool now empowers users with even greater flexibility to design and control complex experimental procedures, incorporate seamlessly into lab informatics platforms such as LIMS, ELNs, and SiLA, as well as accommodates specific and diverse user needs for future expansion and innovation.

ANDREW LAB – THE BEAUTY OF SIMPLICITY

Andrew executes the manual liquid handling protocols designed by users using the software *Andrew Lab.* Requiring neither computer programming skills nor complicated training, this intuitive graphical interface simplifies the design of pipetting protocols, from repetitive procedures to the more error-prone calculation-based schemes such as normalization, cross-reaction matrix, serial dilution, and cherry picking. An example of cherry picking made simple by *Andrew Lab* is illustrated below for selecting and transferring the primers, the concentration of which falls below 20nM, from a 96-well plate to another 96-well plate or to separate microtubes.

- In the Excel primer list: (a) **multiple-select** the ones with values less than 20, (b) **copy and paste this selection** in Excel to generate the cherry-picked primer list, and (c) **copy this new list (Fig. 1)**:

Multiple selection of cherry-picked primers

Excel

Source Position	Source ID	Source Concentration
A1	Primer_1	41.7
A2	Primer_2	19.3
A3	Primer_3	92.4
A4	Primer_4	38.9
A5	Primer_5	20.7
A6	Primer_6	11.3
A7	Primer_7	15.4
A8	Primer_8	31.9
A9	Primer_9	36.9
A10	Primer_10	29.3
A11	Primer_11	57
A12	Prime	
B1	Prime	
B2	Prime	
B3	Prime	
B4	Prime	
B5	Prime	
B6	Prime	
B7	Primer_19	45
B8	Primer_20	76.4
B9	Primer_21	32.9
B10	Primer_22	29.3
B11	Primer_23	41.7
B12	Primer_24	14.9

New cherry-picked list

Excel

Cherry-picked Source	Picked Source ID	Picked Source Conc.
A2	Primer_2	19.3
A6	Primer_6	11.3
A7	Primer_7	15.4
B4	Primer_16	13.3
B12	Primer_24	14.9

Figure 1: Generation of a cherry-picked list in Excel

- In *Andrew Lab* interface (**Fig. 2**):
  - > To transfer the cherry-picked list into a 96-well plate: (a) **drag and drop** the "Microplate 96" icon from the consumable dock into the virtual lab bench, then under the pull-down menu of this icon, choose "**Import stock solutions**"; (b) in the pop-up window, verify the list and click on "**Fill microplate**"; (c) the 96-well plate is now filled with the cherry-picked primers.
  - > To transfer the cherry-picked list into separate microtubes: (d) from "**Import/Export**" in the menu bar, "**Import stock solutions**"; (e) in the pop-up window, verify the list and click on "**Create x consumables**"; (f) x microtubes of the cherry-picked primers now appear in the virtual lab bench.

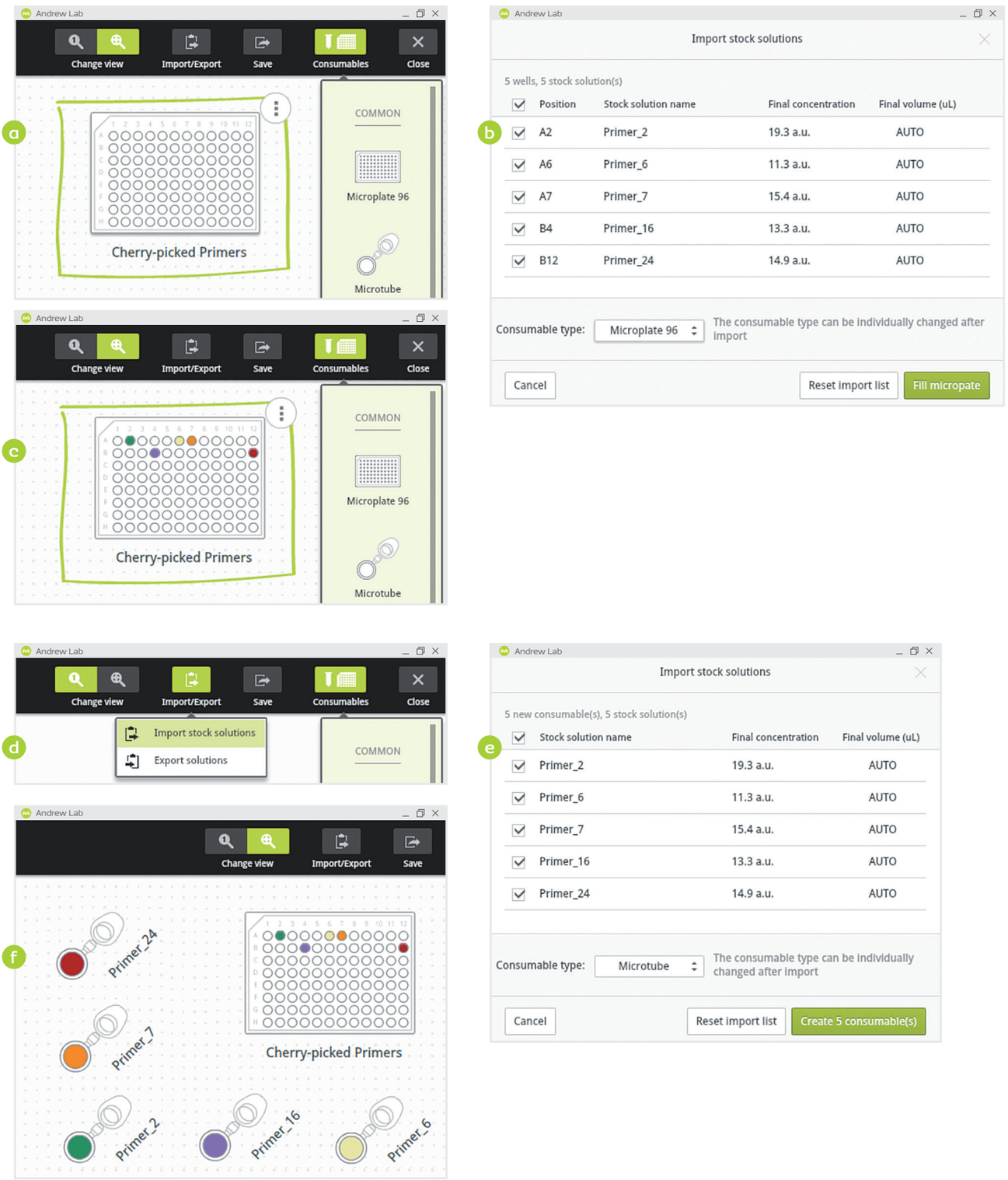


Figure 2: Import cherry-picked list in *Andrew Lab*

More information on protocol design in *Andrew Lab* is at **https://www.labtube.tv/channel/saroler**

XML PROTOCOL – THE FLEXIBILITY AND SCALABILITY OF PROTOCOL DESIGN

The ease of use of *Andrew Lab*, though well serving for most small-scale experiments, does not always extend to larger-scale and more complex processes; for instance, daily liquid handling protocols that need frequent modifications or scaling up of various parameters, multiple Andrews simultaneously executing different protocols, or Andrew integrated with other lab instruments and equipment controlled by different software. Designing such advanced protocols is not feasible with *Andrew Lab*; instead, the Andrew *XML Protocol* made this possible.

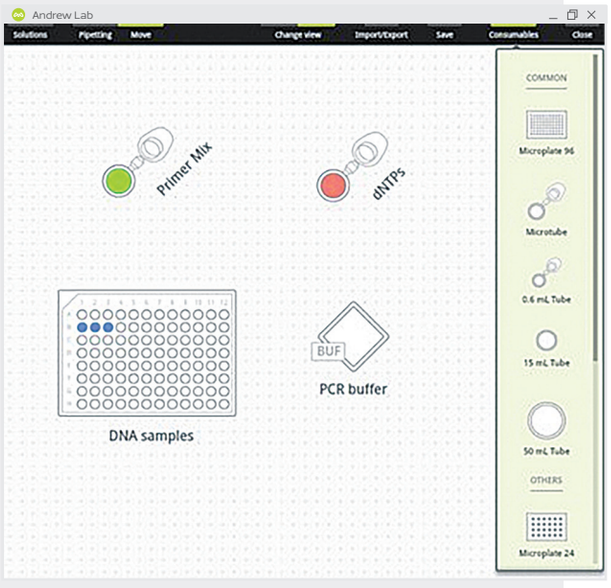
Written in the XML language widely-accepted for lab automation, *XML Protocol* is the textual description of all requisite information of an experiment performed by Andrew, with **components** corresponding to the graphical representations in *Andrew Lab*, as explained below:

```
<?xml version="1.0"?>
<protocol version="1.3.0">
   <properties />           → Information about the protocol file
   <stock_solutions />      → Stock solutions required for the experiment
   <consumables />          → Consumables as liquid vessels
   <set />                  → Pipette sets
   <actions />              → Different types of actions  such as pipetting, incubation, serial
                              dilution, cross reaction, notification, user action
</protocol>
```

Each **component** is an expandable module defined and modified by users according to the specific experimental process. In the following streamlined example, the **consumables** component includes:

- one microtube containing 500 µL of Primer Mix
- another microtube containing 60 µL of dNTPs
- one microplate96 where each of the three wells in columns 1, 2, and 3 of row B contains 4 µL of DNA samples
- one custom consumable labeled as PCR buffer but empty (as defined by volume="-1").

```
<consumables>
    <consumable type="microtube">
         <label> <![CDATA[Primer Mix]]> </label>
         <stock_solution volume="500" color="green"/>
    </consumable>

    <consumable type="microtube">
         <label><![CDATA[dNTPs]]></label>
         <stock_solution volume="60" color="red"/>
    </consumable>

    <consumable type="microplate96">
         <label><![CDATA[DNA samples]]></label>
         <wells>
              <well column="1" row="B">
              <stock_solution volume="4"
                              color="blue"/>
              </well>

              <well column="2" row="B">
              <stock_solution volume="4"
                              color="blue"/>
              </well>

              <well column="3" row="B">
              <stock_solution volume="4"
                              color="blue"/>
              </well>
          </wells>
     </consumable>

     <consumable type="custom">
          <label><![CDATA[PCR buffer]]></label>
          <stock_solution volume="-1"/>
     </consumable>
</consumables>
```



Furthermore, an *XML Protocol* can easily be altered and expanded in the text format, exported in encrypted format for protection, or even dropped into *Andrew Lab* to be converted into a graphical interface protocol, and executed by Andrew.

ANDREW OS API – THE MASTER CONTROL FOR INTEGRATION AND EXPANSION

Simple and routine liquid handling protocols can easily be handled by Andrew operated via Andrew OS and *Andrew Lab*. However, when more advanced processes encoded by the *XML Protocol* or different software are essential, such as integration and synchronization of Andrew/multiple Andrews with other hardware, users can bypass *Andrew Lab* altogether. Instead, Andrew OS can communicate with Andrew(s) as well as other lab instruments and equipment via the *Application Programming Interface (API)* (**Fig. 3**). This sophisticated toolkit enable users to take Andrew(s) to a higher level as a valuable and seamlessly integral partner of the entire lab automation process. For example, the *Andrew OS API* can integrate Andrews in the following molecular diagnostic workflow for detecting diverse types of viruses in a group of patients: (1) aliquot each patient plasma sample from large vials into specific wells of multiple microplates in various volumes according to the LIMS, (2) dispense and mix specific reagents to the exact wells of different microplates for specific virus tests, (3) add and discard wash buffers to and from test microplates which have been moved to incubators, shakers, or wash stations, (4) cherry-pick the positive hits of the test results for further characterization. Heavily manual labor of many lab staffs in such a workflow can be automatized with excellent traceability at every steps by the API remotely controlled through the following different functionalities:

- **Andrew :** To run actions or get any information from Andrew.
- **Protocol:** To deploy a protocol or obtain the current protocol. Usually called during the initialization and preparation steps.
- **Domino:** To get or set any information or allocations related to the blocks or dominos in the workbench. Usually called during the preparation step.
- **Experiment:** To start, pause, resume, and stop an experiment. Usually called while an experiment is running.
- **Error:** To get any errors occurred during any actions or calls. Can be used at any time during the initialization, preparation or as an experiment is running.
- **Status:** To get the status of any step (initialization, preparation, experiment). Each status should be used in its corresponding step.

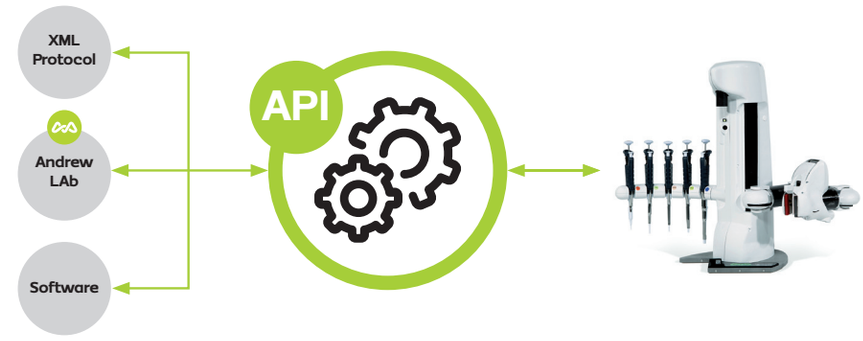


Figure 3: *Andrew OS API* interface between Andrew and other software

SUMMARY

Designed and developed with the end users in mind, the suite of versatile interfaces for Andrew delivers flexible and beneficial solutions for substituting manual lab operation and processes of liquid handling: ***Andrew Lab*** for standardized automatization, and ***XML/API toolkits*** for sophisticated synchronization with other software and hardware. Last but not least, the versatility and scalability of the toolkits ensures fulfillment of future evolving needs for adjustment and expansion, enhancing efficiency and productivity of automated lab workflows.

For more information about how *Andrew Lab* and the *XML/API toolkits* can address your lab automation needs, contact us at

andrewalliance.com or +41 22 518 03 57
+1 781 761 0119

21 Chemin Grenet ▪ 1214 Vernier, Switzerland
185 Dartmouth St. ▪ 02116 Boston, USA

Giorgio Horak
Director R&D - Andrew Alliance
giorgio.horak@andrewalliance.com

Quy A. Ngo
Senior Application Scientist - Andrew Alliance
quy.ngo@andrewalliance.com