CE 2797 IVD

Instructions for Use

IdentiClone® Dx Software

The IdentiClone Dx *IGH* Software is required for use with the IdentiClone Dx *IGH* Assay (REF 91010101) to analyze data of raw FSA files from the ABI 3500xL Dx and ABI 3500xL Genetic Analyzer instruments.

IVD For *in vitro* diagnostic use.

Catalog Number	Description	Version	UDI
REF 91010111	IdentiClone Dx *IGH* Software Package	1.2.x.IVD	00810022732694

Product Compatibility

The IdentiClone Dx *IGH* Software (REF 91010111) was developed specifically for and is compatible with **only** the following Invivoscribe assay:

Catalog Number	Description	UDI
REF 91010101	IdentiClone Dx *IGH* Assay	00810022732502

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1. Intended Use

The IdentiClone Dx *IGH* Software is required for use with the IdentiClone Dx *IGH* Assay (REF 91010101) to analyze data of raw FSA files from the ABI 3500xL Dx and ABI 3500xL Genetic Analyzer instruments.

2. Glossary and Abbreviations

2.1. Glossary

Table 1. Glossary Terms

Term	Definition
Amplicon	A DNA fragment created during the replication of genetic material.
Assay	IdentiClone Dx *IGH* Assay
Clonal	The aggregate of genetically identical cells or organisms produced from a single progenitor cell. • A *Sample ID* result (final call) in which Clonality is detected. • A *Sample Name* result (for a master mix) in which a Significant Peak is detected in the valid size range.
Final Call / Final Clonality Call	The final *Sample ID* clonality result, determined from the *Sample Name* results.
Indeterminate	A *Sample ID* result in which all three master mix (or *Sample Name*) results generate indeterminate results; alternatively, a master mix (or *Sample Name*) result in which the presence or absence of clonality cannot be determined (i.e., ambiguous result)
Injection	Set of up to 24 samples simultaneously analyzed on the ABI 3500xL Dx or ABI 3500xL Genetic Analyzer instrument. These may include run controls from one or more PCR runs.
Intermediate Results	This term is used interchangeably with *Individual Master Mix Results, Sample Name Results,* or *Run Results,* referring to the clonality result determined for an individual master mix product from a valid run.
Invalid	A sample result in which one (of 3) master mix generated an Invalid result; or a sample master mix result does not meet the validity criteria. (see Figure 23)
Master Mix	Amplification reagent with primers to amplify specifically targeted region; this assay has three MM: A, B and C.
Master Mix Product	Amplicons generated from the amplification of *IGH* Tube A (FR1) MM, *IGH* Tube B (FR2) MM, or *IGH* Tube C (FR3) MM; *Sample Name* is the unique identifier for each master mix product and ties to the *Sample ID* for the clonality result.
Negative Control	A buffer solution containing polyclonal DNA; this control is expected to generate a Non-Clonal result with each master mix.
Non-Clonal	A *Sample ID* result in which clonality is not detected; or a *Sample Name* (or master mix) result in which a significant peak is not detected within the valid size range.
Platemap / Plate Map	Visual representation of a detection plate which is imported to the ABI Genetic Analyzer. It provides a 96-well plate layout containing associated run information, including *Run designation, Sample Name*, *Sample Type*, and *Master Mix* for each well location.
Positive Control	A buffer solution containing DNA used to assess assay validity; this control is expected to generate a Clonal result with each master mix.
Run	A group of samples processed together with a set of run controls (Positive Control, Negative Control, NTC) through amplification and detection, using the same master mix.
Sample ID	A user-assigned identification associated with a patient sample. Each Sample ID will be tested at least once with each master mix (MMA, MMB and MMC) using a Sample Name. Therefore, a Sample ID should be unique for each patient and will have at least three associated Intermediate Results. See Figure 1 for an example.

Table 1. Glossary Terms

Term	Definition
Sample Name	A user-assigned identification associated with a patient sample (identified by Sample ID), tested with a specific master mix. See Figure 1 for an example.
Semantic Versioning	A software version scheme consisting of three numbers (Major.Minor.Patch), aligned with the risk factor of the update.
Software	IdentiClone Dx *IGH* Software
SQ Error	The calculated similarity between the fragment pattern of the specific size standard dye and the observed distribution of size standard peaks in a sample did not pass the predetermined threshold.
System	The whole package of software, hardware, and assay (as applicable) that make up the medical device.

2.2. Abbreviations

Table 2. Abbreviations defined

Abbreviation	Definitions
ABI	Applied Biosystems Instruments, a Life Technologies brand of Thermo Fisher Scientific
CE	Capillary electrophoresis; an electrokinetic method used to separate amplicons by size.
Dx	Diagnostics
DNA	Deoxyribonucleic Acid
EULA	End User License Agreement
FNC	File naming convention
FSA	Fragment analysis data file created by the capillary electrophoresis instrument.
IFU	Instructions for use
IGH	Immunoglobulin heavy chain gene
IVD	*In Vitro* Diagnostics
LIVS	A file format that gets generated while annotating a plate. Also known as an annotated plate map file.
MM	Master mix
NTC	No template control
OS	Operating system
PCR	Polymerase chain reaction
PDF	Portable document format
QC	Quality Control
SQ	Size quality
UI	User Interface

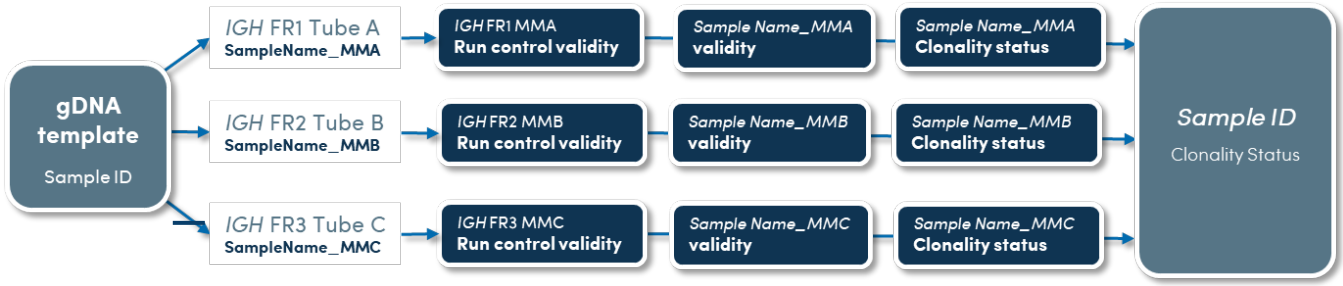
3. Principles of the Procedure

During ontogeny in B lymphocytes, antigen receptor genes undergo rearrangements that increase genetic diversity, generating approximately 10^{12} unique DNA sequences.[1,2] When polymerase chain reaction (PCR) is applied to these gene rearrangements, products that are unique in length and sequence are generated.[2,4,7] Thus, this methodology can be applied to identify lymphocyte populations derived from a single cell by identifying the unique V-J gene rearrangements present within these antigen receptor loci.[3,4,6,7] The IdentiClone Dx *IGH* Assay amplified the immunoglobulin heavy chain (*IGH*) gene using fluorescently labeled primers, followed by capillary electrophoresis-mediated fractionation and result interpretation with the IdentiClone Dx *IGH* Software. This DNA-based test is used to detect the vast majority of clonal B-cell populations; presence or absence of clonality can support the differential diagnosis of reactive lesions and B-cell malignancies.[5,8,9,10,11]

Software interpretation includes assessment of the raw data files generated by the differential fluorescence detection while referencing a configured plate map for sample traceability. Since this assay requires three master mixes to determine the clonality status, a naming hierarchy is used to correlate the master mix results, identified by a *Sample Name*, to the patient sample, which is identified by a *Sample ID* (see Figure 1). Each master mix test set, including samples, a positive control, a negative control, and a no template control, is considered a "run," can be configured individually using the Software Plate Setup function and loaded onto the same plate containing additional runs. After detection is complete, the data files are uploaded to the Software, which proceeds with analysis, referencing the plate map to complete the intermediate analysis for that master mix. If runs for all three master mixes are determined to be valid, the data is processed to generate intermediate results, depicted by *Sample Names*, which are displayed for the user to choose and generate the clonality status for each *Sample ID*.

Figure 1: Sample naming convention

- Results from three *Sample Names* are combined to determine the final clonality result for the *Sample ID*.
- The final clonality result requires an *Intermediate Result* from one valid run generated from each master mix (MMA, MMB and MMC). These results must be from a valid run and can include Invalid and Indeterminate results.
- The *Sample Name* assigned for each master mix are tied to the *Sample ID*.



4. Minimum System Requirements

- **Hard Drive:** At least 50 GB of free disk space is required; 250 GB recommended.
- **RAM:** 8 GB required; 16 GB or more recommended.
- **Operating System:** Windows (64-bit) 11 is required.
- **Export Capability:** The computer containing the installed Software needs the ability to export and import files to and from the ABI 3500 Genetic Analyzer instruments; e.g., via USB.
- A **PDF reader** to visualize data reports generated by the IdentiClone Dx *IGH* Software.
- An **internet connection** for obtaining the software package.

Note: An internet connection is not required for installation or usage of the software.

5. Warnings and Precautions

5.1. System font

5.1.1. User interface is designed to use the default system font settings on a Windows computer.

5.2. Compatible files

5.2.1. IdentiClone Dx *IGH* Software is compatible with FSA files generated by the ABI 3500xL Dx and ABI 3500xL Genetic Analyzers.

5.3. Characters in pathname and file name

5.3.1. It is important that the filenames only contain the following characters (A-Z, a-z, 0-9, ., _ (underscore), - (hyphen)). If the Software encounters a character not within this set, it may fail.

5.4. End-user and in-use environment

5.4.1. The Software is for professional use only in a clinical laboratory setting. Use of this product must be limited to trained personnel.

5.5. Security

5.5.1. Use of endpoint protection software is highly recommended to protect the computer running the Software.

5.5.1.1. Ensure no unauthorized devices are plugged into the workstation on which the Software is running, physically block all USB and other communication ports when not in use.

5.5.1.2. Endpoint protection software installed on the workstation containing the Software should be monitored for alerts so that action can be taken when the endpoint is compromised.

5.5.1.3. Verify Windows and other installed software applications are always updated to the latest available security patches.

5.5.2. This software has been validated to work with the following endpoint protection software:

5.5.2.1. ESET Endpoint Security 11.0.2044.0

5.5.2.2. Symantec Endpoint Protection 14 (14.3 MP1) build 1169 (14.3.1169.0100)

5.5.2.3. Trellix Endpoint Security 10.7.0.6809

5.5.3. When a cybersecurity incident is suspected on a computer running the Software, follow these steps:

5.5.3.1. Turn off the computer.

5.5.3.2. Notify an IT professional

5.5.3.3. Once it has been determined to be safe, re-start the software to verify that all results are still available.

5.5.3.3.1.1. If there is suspicion that the software may have been accessed by unauthorized parties, use the audit log to determine what actions were taken.

5.5.3.3.1.2. If result data was deleted or is no longer accessible, examine the backup location for results.

5.6. Network settings

5.6.1. This software does not communicate over a network and no software specific firewall settings are needed.

5.6.1.1. Ensure the operating system firewall is turned on and that any network ports not needed for the functioning of the workstation are closed.

5.6.1.2. If the workstation containing the software is connected to a network, ensure all appropriate network security safeguards are in place, e.g., ensuring the workstation cannot be reached directly from the internet.

5.7. Access controls

5.7.1. This Software supports account-based access controls. Passwords and account information must not be shared amongst users. If more users need to use the software, new accounts can be created.

5.7.1.1. Do not provide regular Software users administrator rights on the workstation, following the principle of least privilege. This Software does not require administrator rights to run.

5.7.1.2. Each Software user on the workstation must have the minimal access rights needed to perform their assigned tasks following the principle of least privilege.

5.7.1.3. When a new user account is created in the Windows OS, the password associated with the account must be changed before the account is used.

5.8. Updates

5.8.1. When software updates are made, including but not limited to security updates, Invivoscribe, Inc. will send a notification via email that will include details pertaining to the purpose of the update and the applicable instructions for installation.

5.9. Patient information

5.9.1. This software does not require any personal information about the patient from which a sample was derived to function.

5.9.1.1. However, if the user chooses to do so, it is possible to enter this type of information into the software.

5.9.1.2. It is strongly recommended to avoid entering directly identifiable personal information into the software.

5.10. Backup precautions

5.10.1. The software has functionality to save a backup of the generated results to a pre-specified directory (see section 13.9).

5.10.2. This directory should be backed-up as part of the normal backup procedure as used by the implementing organization.

5.10.3. Back-up the workstation in its entirety so it can be quickly restored in case of an emergency.

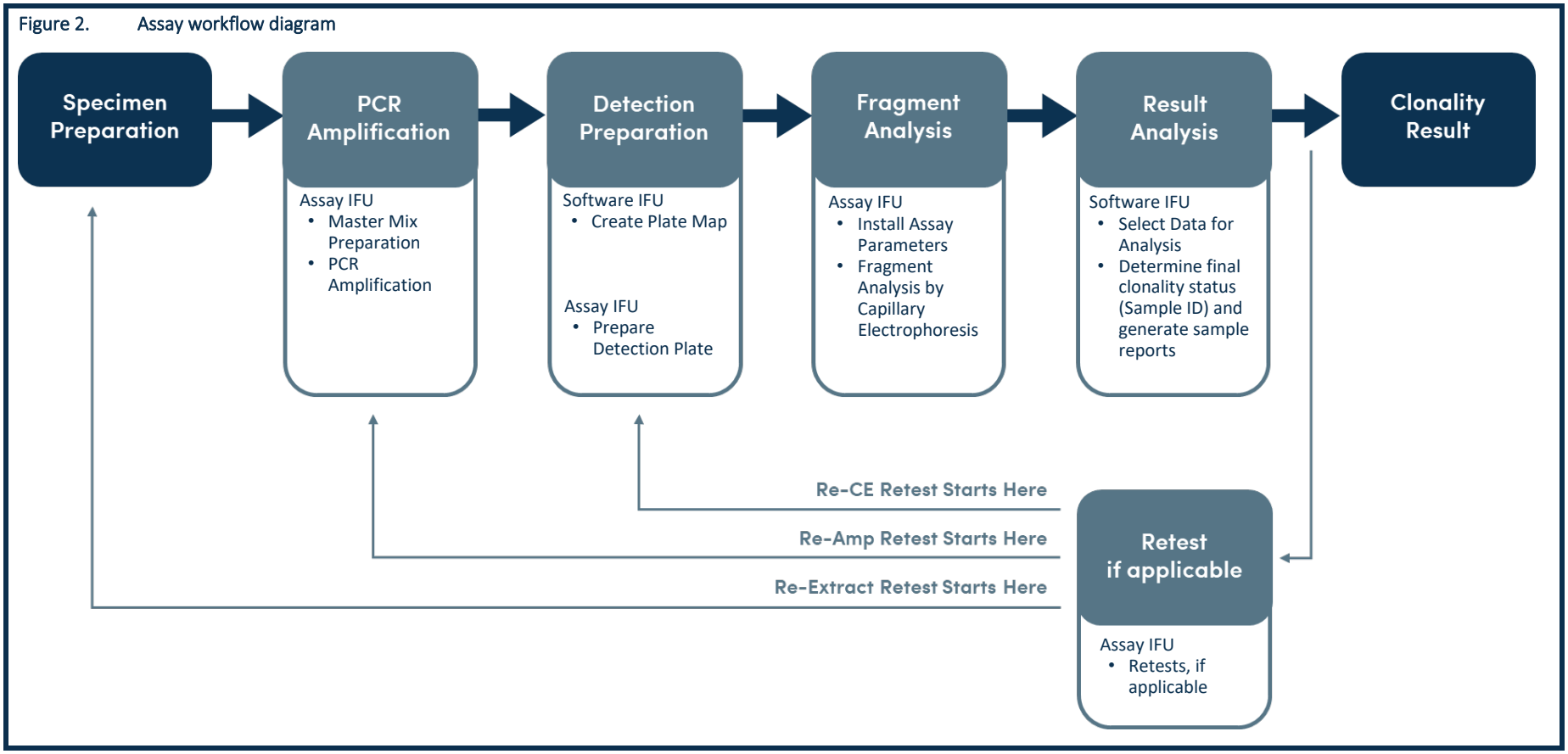
IMPORTANT! **Do NOT change or alter any files generated by the Software.**

- **Editing the Plate map files generated by the Software using ABI Genetic Analyzer software will lead to file corruption and an inability to perform analysis.**

6. Software Procedure

Note: The Software requires utilizing this document in conjunction with the IdentiClone Dx *IGH* Assay IFU.

Figure 2. Assay workflow diagram



6.1. Download the Software Package

6.1.1. Using any web browser, navigate to the Invivoscribe Software Portal (https://catalog.invivoscribe.com/softwareportal/) and follow the instructions.

6.1.2. Contents of the downloaded ZIP file include:

6.1.2.1. *IdentiClone-Dx-IGH-Software-1.2.x.IVD.msi* – the software application

6.1.2.2. *IGH_FNC.xml* – the file name convention settings, see section 8.4 in the Assay IFU

6.1.2.3. *IGH_IP.xml* – the instrument parameters, see section 8.4 in the Assay IFU

6.1.2.4. *IGH_RG.xml* – the results group parameters, see section 8.4 in the Assay IFU

6.2. Administrative Configuration

6.2.1. Create the Admin user account. (Figure 3)

- The first time using the IdentiClone Dx *IGH* Software, a prompt will appear to create the first Admin user.
- The first Admin user is required to create subsequent users.

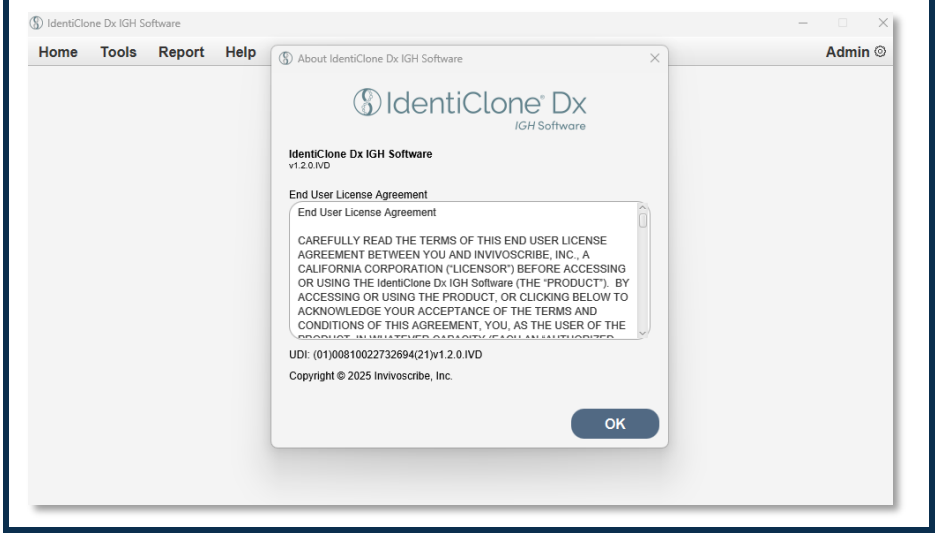
Note: If the Admin password needs to be reset, please contact Invivoscribe Customer Support at support@invivoscribe.com.

Figure 3: IdentiClone Dx *IGH* Software Create First Admin User window

6.2.1.1. During the first successful login, the Software End User License Agreement (EULA) will be displayed. (Figure 4)

- The software EULA must be accepted in order to continue to the main application.

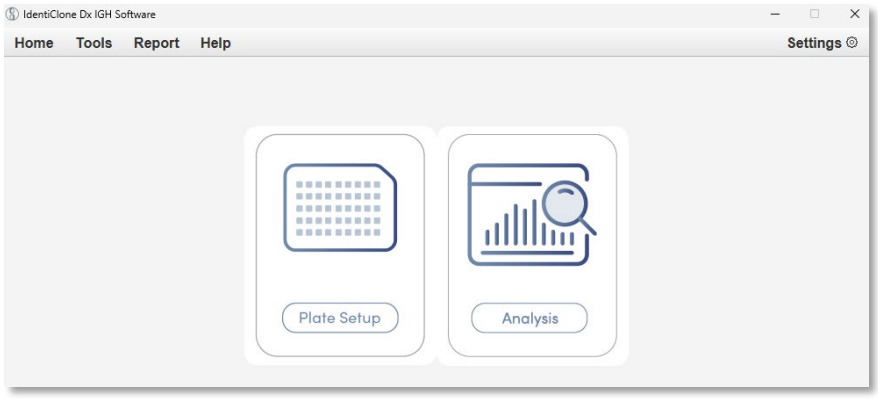
Figure 4: End User License Agreement (EULA) window



6.2.1.2. The IdentiClone Dx *IGH* Software will always open to the home page after the EULA is accepted. (Figure 5)

- The home page can be used to navigate to the key features of the application, such as *Plate Setup*, *Analysis*, and *Set PDF Password* (available only for administrator).

Figure 5: IdentiClone Dx *IGH* Software home user interface

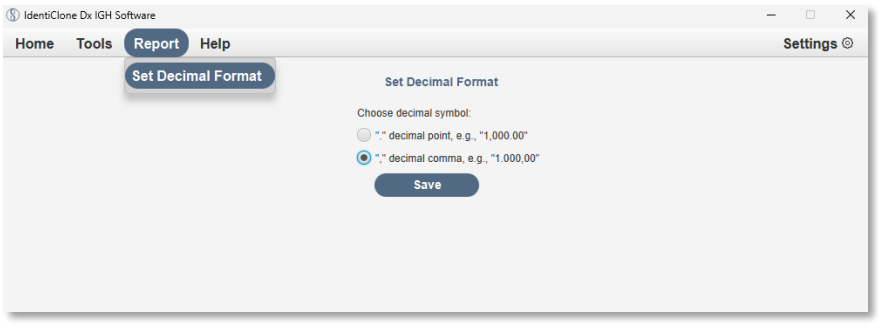


6.2.2. Enter login credentials and click **Login**. (Figure 6)

Figure 6: IdentiClone Dx *IGH* Software login window

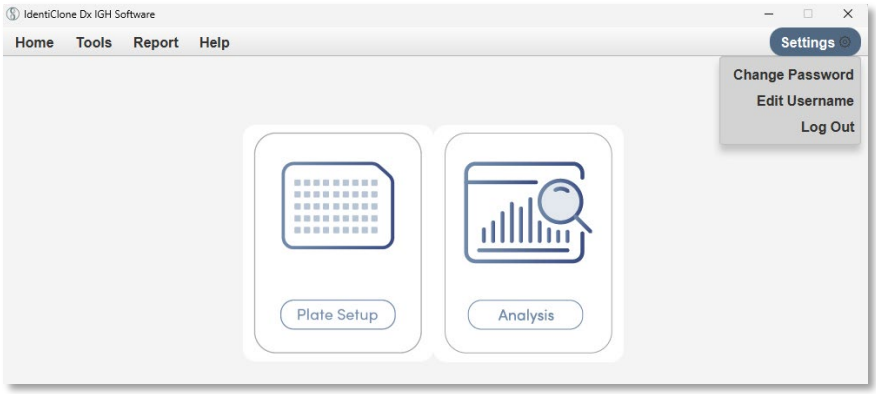
6.2.2.1. Verify the report settings align with the data output decimal format; the default setting is decimal comma format. (Figure 7)

Figure 7: IdentiClone Dx *IGH* Software user *Report* dropdown menu confirms decimal format



6.2.2.2. Click **Log Out** to logout from the application; the Software will automatically logout any user after 5 minutes of inactivity. (Figure 8)

Figure 8: IdentiClone Dx *IGH* Software user Settings dropdown menu



6.3. Create Plate map

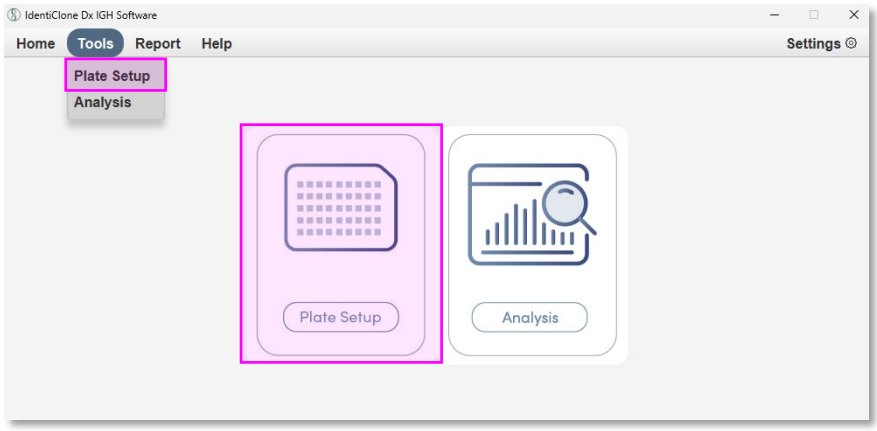
Note: To create a new plate map with the Software, go to section 6.3.1. To create a plate map using a previously saved plate map (and make modifications), go to section 6.3.4.

6.3.1. Create a plate map using the *Plate Setup* function

6.3.1.1. Click **Plate Setup** from the home user interface. (Figure 9)

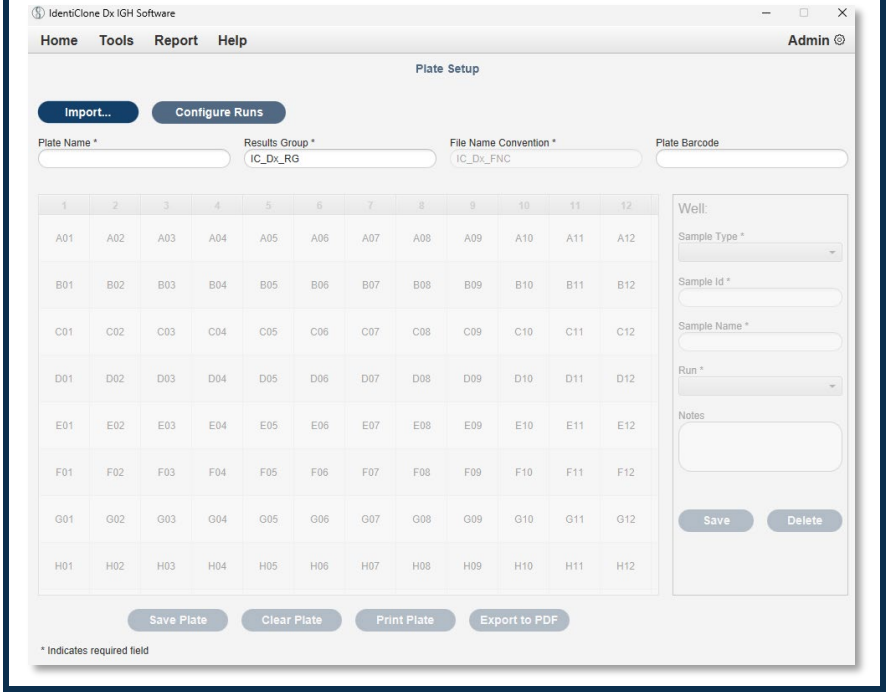
6.3.1.2. Alternatively, *Plate Setup* can be accessed by navigating to **Tools** → **Plate Setup**.

Figure 9: IdentiClone Dx *IGH* Software Plate Setup



6.3.1.2.1. By default, the *Plate setup* window is disabled for annotation and enabled only after configuring a run or by importing an ABI formatted CSV file. (Figure 10)

Figure 10: IdentiClone Dx *IGH* Software Plate setup window



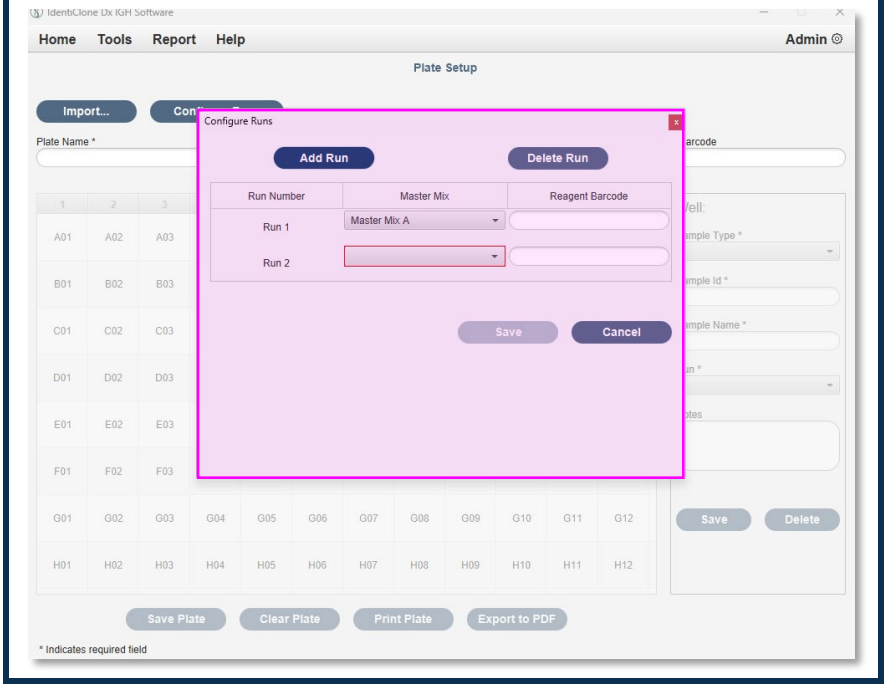
6.3.1.3. Click **Configure Runs**, then click **Add Run.**

Note: Include a set of controls in each run. Up to 24 runs can be configured.

6.3.1.3.1. For each run, select the master mix from the dropdown box. (Figure 11)

- Runs must be configured before annotating the plate.
- Up to 24 runs can be added per plate.
- The same master mix can be used to configure multiple runs on the same plate.

Figure 11: IdentiClone Dx *IGH* Software Plate Setup ⇨ Configure Runs



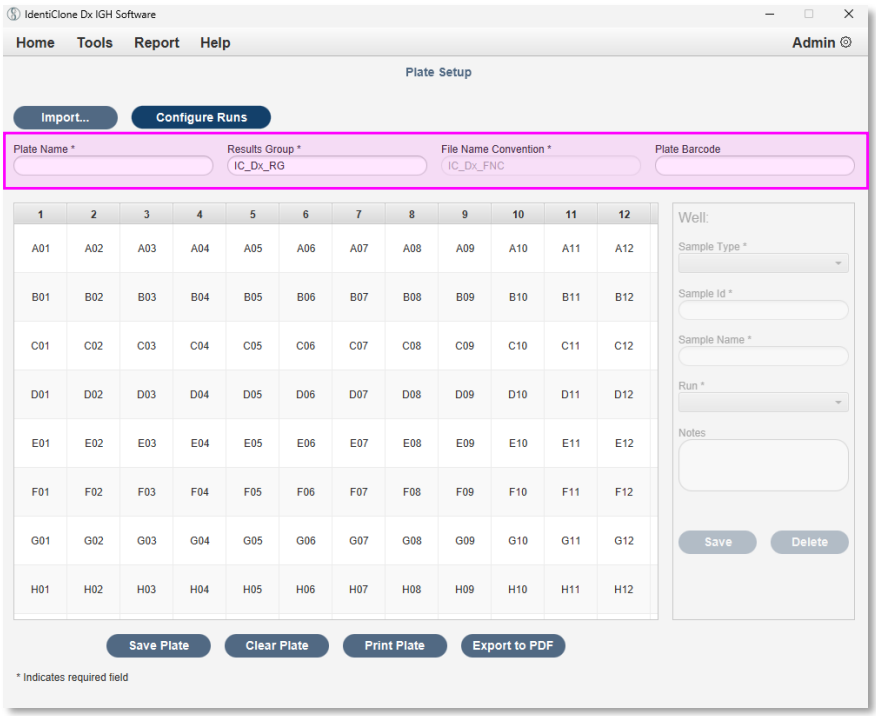
6.3.1.3.2. (Optional) Scan or manually enter the associated assay kit UDI barcode(s), then click **Save**.
- This information allows traceability of the testing reagents used.
- The barcode follows a format that contains the device identifier, expiry date and lot number, e.g., (01)12345678901234(17)501231(10)A1234567
- (01) indicates the 14-digit device Identifier
- (17) indicates the 6-digit expiry date, formatted YYMMDD
- (10) indicates the 8-digit reagent lot number used for the run

6.3.1.4. To remove a run, click **Delete Run**.
- By default, the most recent run created will be deleted first; a run can be deleted only if there are no wells assigned to the run.

6.3.2. Configure and save a new plate.

6.3.2.1. Navigate to *Plate Setup* and enter information into the *Plate Name* field located above the plate map. (Figure 12)
- These fields are limited to 50 characters or less and may only include letters (A-Z, a-z), numbers (0-9), hyphen (-) and underscore (_). No spaces or special characters (other than specified) will be accepted.

Figure 12: IdentiClone Dx *IGH* Software Plate Setup interface



6.3.2.1.1. *Plate Name* refers to user designated plate name and must be populated before proceeding to the next step.

6.3.2.1.2. *Results Group* indicates the FSA file save location and is automatically populated by the software; verify ***IC_Dx_RG*** is indicated.

6.3.2.1.3. *File Name Convention* defines the FSA file naming convention and is automatically populated by the software.

6.3.2.1.4. *Plate Barcode* may be left blank since information entered here will not be traced.

6.3.2.1.5. *Results Group* and *File Name Convention* entries must match the names of the corresponding entries on the ABI 3500xL Dx or ABI 3500xL Genetic Analyzer.

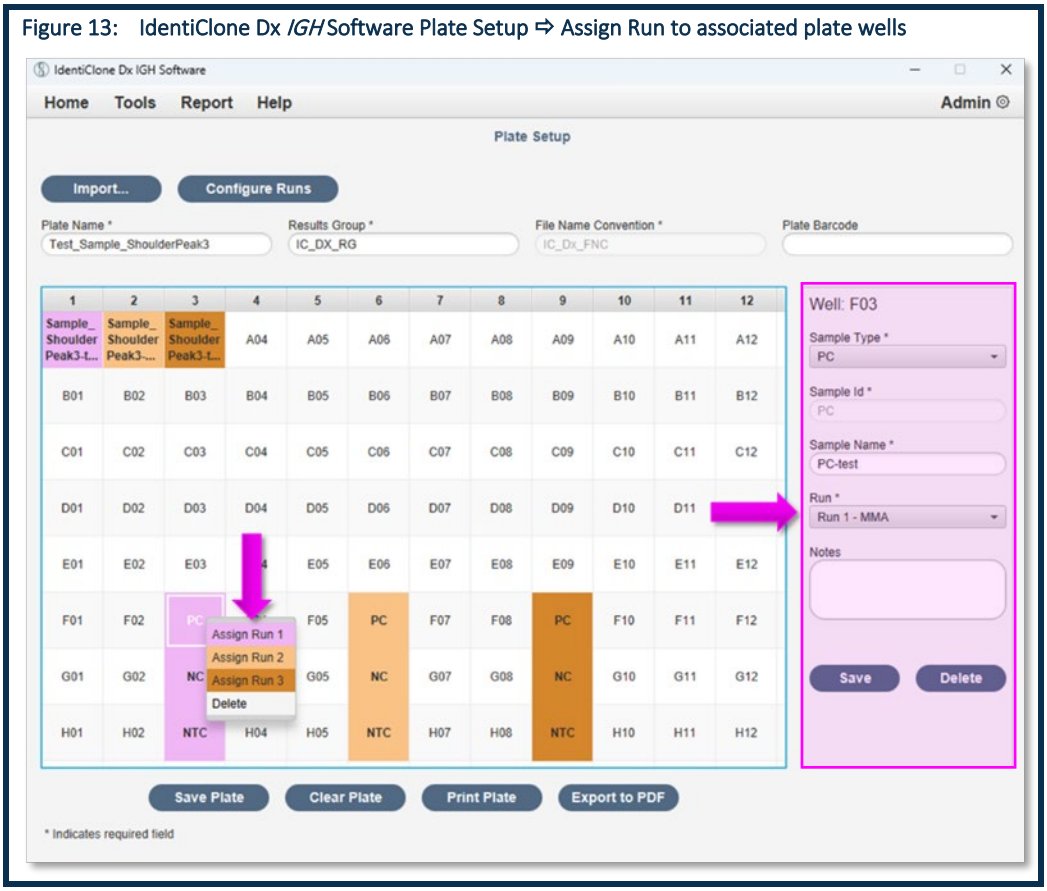
6.3.2.1.5.1. Refer to the Assay IFU section: *Install Assay Parameters*.

6.3.3. Select the well(s) to be used (i.e., to be loaded with diluted amplicon).
- **Shift+Click**: selection of multiple adjacent cells;
- **Ctrl + Click**: selection of multiple individual cells.

6.3.3.1.1. **Right-click** over the well selection to prompt the run assignment window, then assign a run.
- The run can be assigned by individual wells or by selecting a group of wells.

6.3.3.2. Select each well assigned to a run and enter required information on the right side of the window. (Figure 13)

Figure 13: IdentiClone Dx *IGH* Software Plate Setup ⇨ Assign Run to associated plate wells



6.3.3.3. Select the appropriate *Sample Type* from the designated dropdown box: PC, NC, NTC or Sample.

6.3.3.3.1. If *Sample* is selected for the *Sample Type*:

6.3.3.3.1.1. Enter the *Sample ID*, a unique identification associated with a patient sample. See Figure 1 for an example.

6.3.3.3.1.2. Enter *Sample Name*, a unique identification associated with a patient sample (identified by Sample ID), tested with a specific master mix. See Figure 1 for an example.

6.3.3.3.2. Confirm that *Run* is assigned the correct master mix.

6.3.3.3.2.1. (Optional) Enter *Notes*.

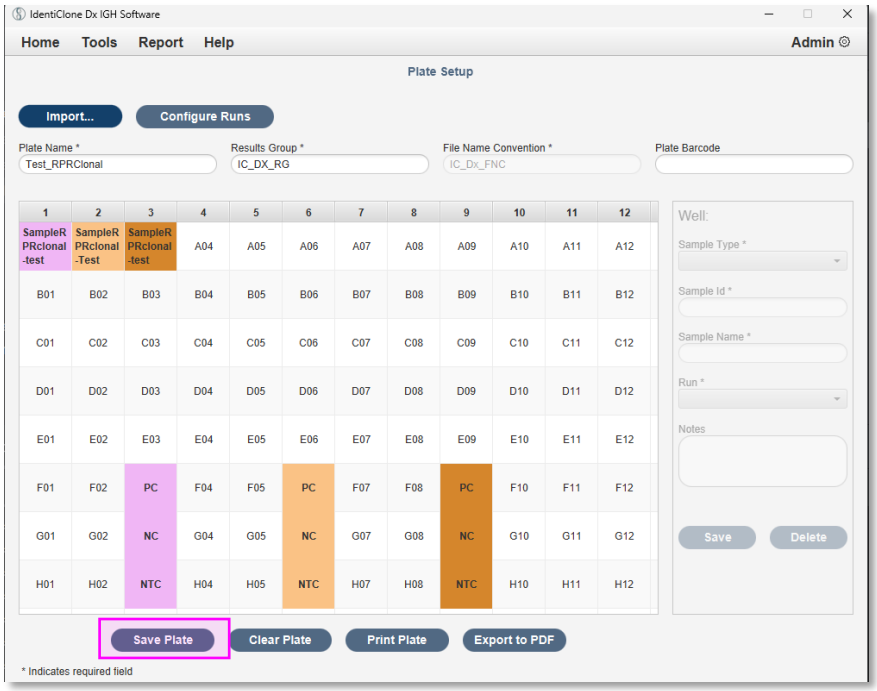
6.3.3.3.3. Click **Save** to complete configuration of the well; repeat step 6.3.3 for each assigned well on the plate.

Plate map rules:
- Each run must include a Positive, Negative and No Template Control; these controls will be indicated on the plate map as *PC* (positive control), *NC* (negative control), and *NTC* (no template control)
- Fields marked with asterisk (*) are required to save a well.
- The fields *Sample ID*, *Sample Name* and *Notes* may only contain 50 characters or less.
- *Sample ID* and *Sample Name* can only include letters (A-Z, a-z), numbers (0-9), hyphens (-) and underscores (_). No spaces or special characters (other than specified) are allowed.
- The highlighted well position in the Plate Setup will become bold once all parameters are defined and saved for a particular sample or control.

6.3.3.4. After all samples and controls are defined and saved for all runs within a plate, click **Save Plate.** (Figure 14)

- Different runs will be highlighted and displayed in an assortment of colors on the plate map.

Figure 14: IdentiClone Dx *IGH* Software Plate Setup ⇨ Save Plate



6.3.3.5. Select the directory file path for the output files.

6.3.3.5.1. Once the plate map is saved, a paired set of output files will be generated, as CSV and LIVS file formats.

6.3.3.5.2. The CSV file contains plate map information and will be imported to the ABI 3500xL Dx or ABI 3500xL Genetic Analyzer.

6.3.3.5.3. The LIVS file contains plate map specific data required for analysis and will be used in conjunction with the respective to ABI 3500xL Dx or ABI 3500xL result files (i.e., FSA file).

IMPORTANT! **Do NOT alter CSV and LIVS. If modifications are made, return to section 6.3.2 and generate a new plate map, which will generate a new set of paired CSV and LIVS output files.**

6.3.4. Create a plate map using a previously saved plate map file.

- Using a previously used plate map will not replace existing results; every saved plate map possesses a unique identifier and is paired with unique LIVS file.

IMPORTANT! **Only use this option to re-use a previously configured plate map, with (or without) small number of modification(s).**

6.3.4.1. Manually setup the plate using a spreadsheet application, then import the resulting CSV file using the **Import** button. (Figure 15)

6.3.4.1.1. Follow the CSV format and plate map rules defined above; the CSV format and columns mapping includes:

6.3.4.1.2. User Defined Field 1 => *Sample Type*, which can include SAMPLE, PC, NC or NTC

6.3.4.1.3. User Defined Field 2 => *Run Number* requires a value from Run 1 to Run 24

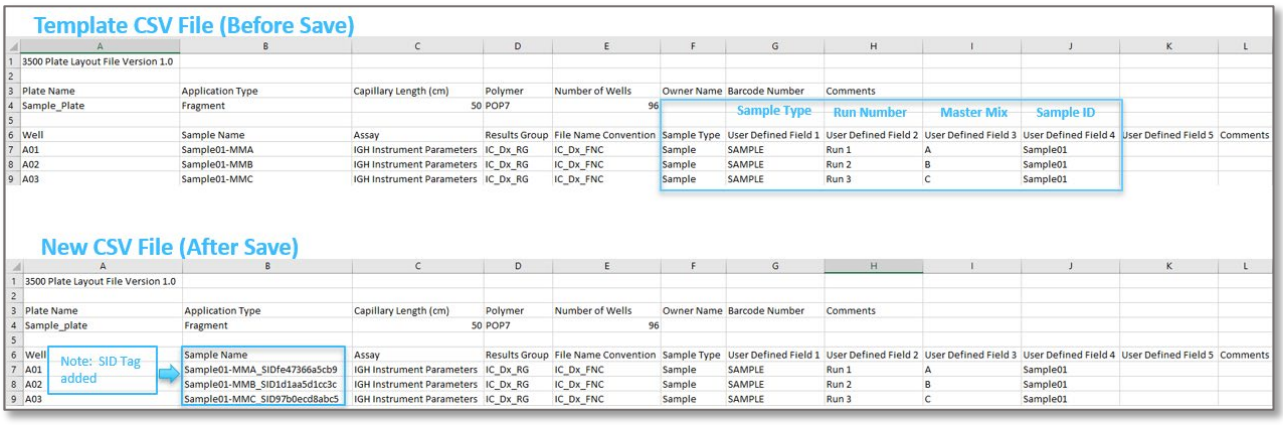
6.3.4.1.4. User Defined Field 3 => *Master Mix* is identified as A (FR1),B (FR2) or C (FR3)

6.3.4.1.5. User Defined Field 4 => *Sample ID*

6.3.4.1.6. If a *Sample Name* is provided in the CSV file, values for the user defined fields (mentioned above) are required.

Figure 15: Example CSV file layout

- ***Template CSV File*** **indicates the file prior to modification. Once the file is updated and saved, new, unique SID number will be assigned to the end of the** ***Sample Name*** **(column B) in the newly generated CSV file.**
- ***New CSV File*** **indicates the file after modification and saving.**



6.3.4.1.7. Click **Import**, then select the corresponding CSV file.

6.3.4.1.8. Verify the correct CSV file populates the *File name* box, then click **Open**.

6.3.4.2. Confirm that each data field for the plate and each sample is populated correctly, then click **Save**. (Figure 16)

- Refer to section 6.3.2 to save the newly generated CSV and LIVS files.

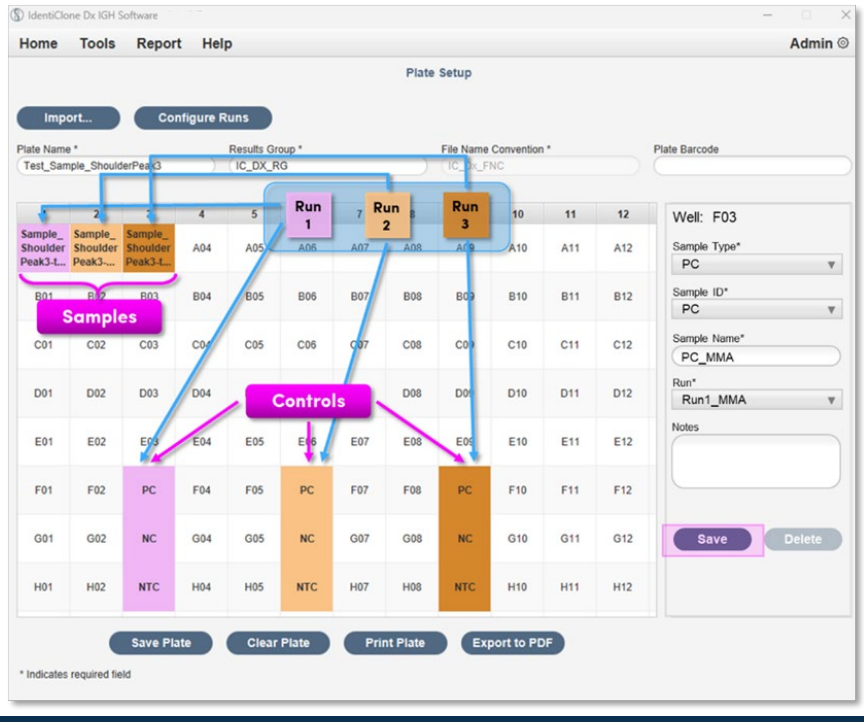
6.3.4.2.1. (Optional) Print a hardcopy of the plate map

6.3.4.2.1.1. Click the **Print Plate** button; if a printer is configured, the system directs the user to the print screen.

6.3.4.2.2. (Optional) Export the plate map as a PDF

6.3.4.2.2.1. Click the **Export to PDF** button, then select a destination folder to save the PDF.

Figure 16: IdentiClone Dx *IGH* Software Plate Setup ⇨ verify plate setup



6.3.5. Proceed to Fragment Analysis by Capillary Electrophoresis (refer to the Assay IFU section: *Fragment Analysis by Capillary Electrophoresis*).

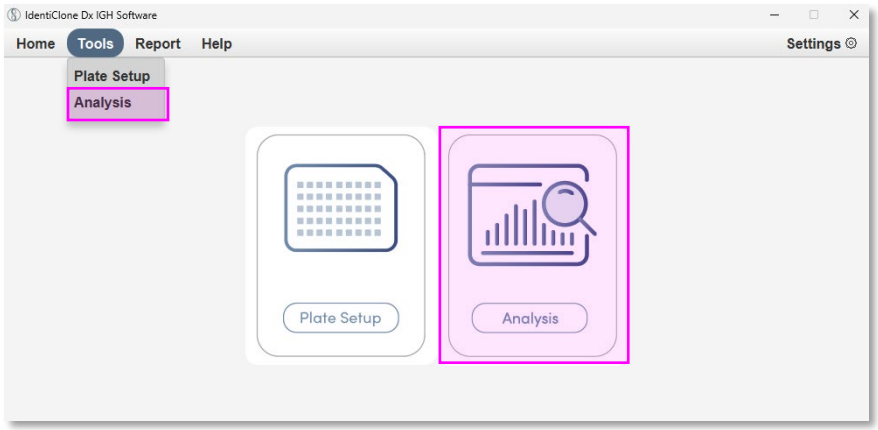
6.4. Select Data for Analysis

6.4.1. Select the *Analysis* tool from the home user Interface.

- Alternatively, *Analysis* can be accessed by navigating to **Tools → Analysis**. (Figure 17)

6.4.1.1. Verify that both FSA and LIVS files for the associated run(s) and plate(s) are located in the same directory file path.

Figure 17: IdentiClone Dx *IGH* Software home user interface ⇨ Tools ⇨ Analysis



6.4.2. Click **Select Directory for FSA and LIVS files.** (Figure 18)

6.4.2.1. Navigate to the directory file path containing the FSA and LIVS files, select the folder, and confirm the selection.

6.4.3. Click **Select Directory for Run Reports.** (Figure 18)

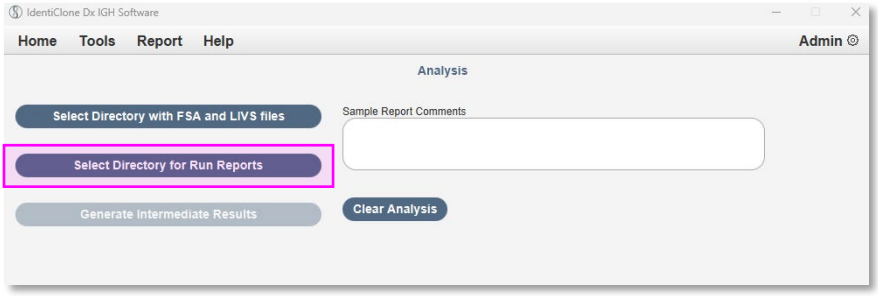
6.4.3.1. Select the directory file path for the desired location to save the Software reports.

6.4.3.2. Click **Select Folder** to confirm.

6.4.4. Click **Generate Intermediate Results.** (Figure 18)

- The software validates the FSA and LIVS files before generating run reports; software file validation requires the samples in the LIVS files to match the FSA files.
- Run reports will be generated in the directory file path selected in step 6.4.3.

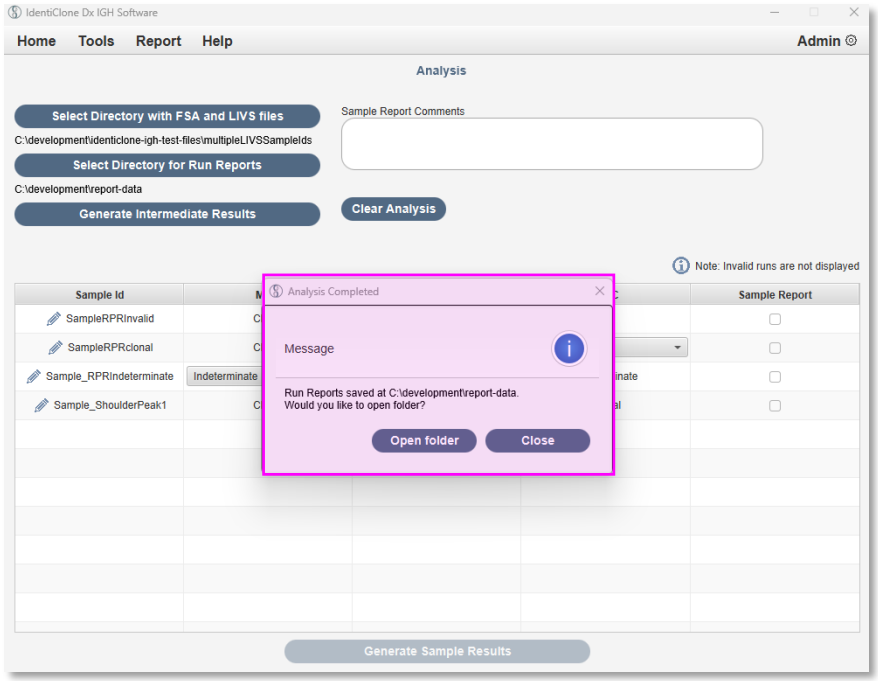
Figure 18: IdentiClone Dx *IGH* Software directory for Run Reports



6.4.4.1. After the run reports are generated, a prompt will appear providing the option to open the folder containing the run reports. (Figure 19)

- A password is set by the Admin user (see Appendix A, section 13.8) and is required to view the PDF reports.

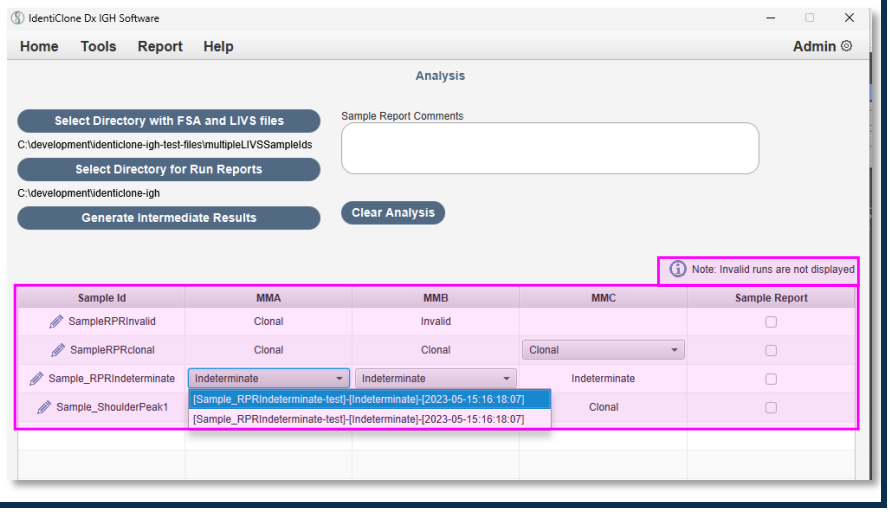
Figure 19: IdentiClone Dx *IGH* Software ⇨ Generate Intermediate Results



6.4.4.2. A table containing Intermediate Results for each Sample ID will be displayed in the Software window.

- Results are grouped by *Sample ID*, displaying Intermediate Results (*for each Sample Name*) in each column. (Figure 20)

Figure 20: IdentiClone Dx *IGH* Software ⇨ Intermediate Sample Results

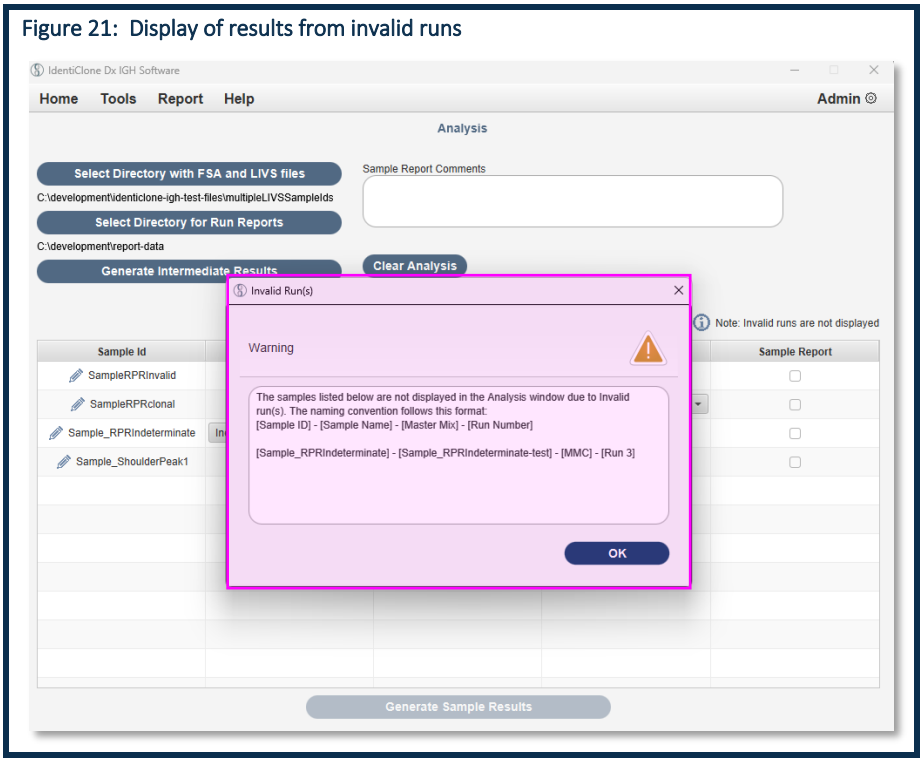


6.5. Determine final clonality status (*Sample ID*) and generate sample reports

IMPORTANT! **The clonality status associated with a *Sample ID* requires at least one *Sample Name* result (e.g. Clonal, Non-Clonal, Indeterminate, Invalid) from a valid run for each master mix is required. Otherwise, the *Sample Report* checkbox will not be enabled.**

6.5.1. The table only displays results from valid runs. All *Sample Names* from associated invalid runs can be viewed by clicking the icon next to the *Note: Invalid runs are not displayed.* (Figure 20 and Figure 21)

Figure 21: Display of results from invalid runs



6.5.2. For each *Sample ID*, select the *Intermediate Result* (indicated by *Sample Name*) for MMA, MMB and MMC.

6.5.2.1. By default, one *Intermediate Result* will be selected for each master mix.

6.5.2.1.1. If a *Sample ID* was tested with same master mix multiple times (i.e., retest), a dropdown menu will be available to select the proper result, based on following order of priority: Clonal, Non-Clonal, Indeterminate, Invalid.

6.5.2.1.2. When the dropdown is selected, a list including the *Sample Name*, Intermediate Result and Run Start Date are displayed, allowing the appropriate *Intermediate Result* to be selected for the final (*Sample ID*) clonality status.

6.5.3. For each *Sample ID*, select the **Sample Report** checkbox. (Figure 22)

6.5.3.1. The checkboxes under *Sample Report* column are enabled only if all Intermediate Results (for three master mixes) are present. The checkbox is disabled if any Intermediate Result is absent.

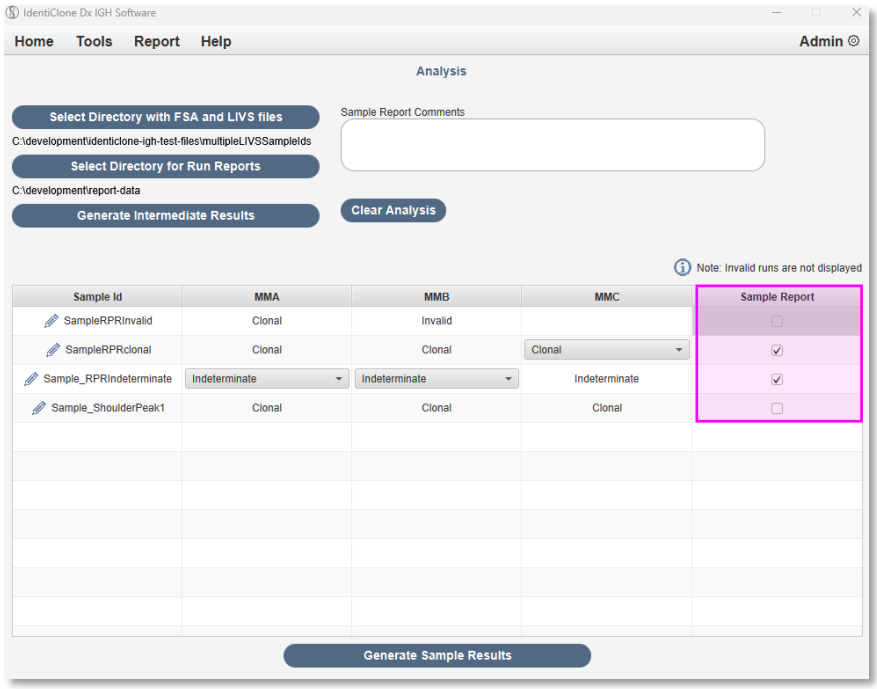
6.5.3.2. The information entered into the *Comments* is included in the sample report for the highlighted *Sample ID* at the time the information is entered.

6.5.3.3. The content in the *Comments* field can be cleared for each *Sample ID* to add associated comments based on the selected checkbox.

6.5.3.4. This field may contain up to 300 characters.

- If a typo is introduced to a *Sample Name* during plate setup, the *Sample ID* may need to be edited.

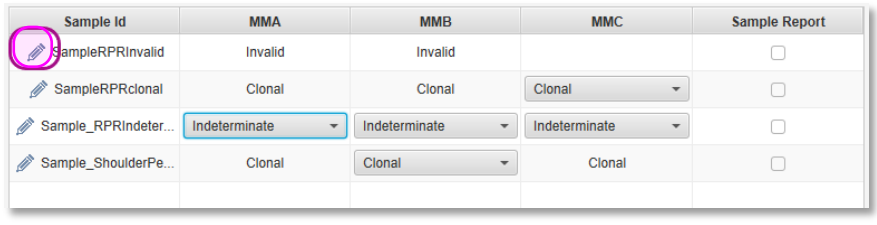
Figure 22: IdentiClone Dx *IGH* Software ⇨ Select Sample Results



IMPORTANT! **An edited *Sample ID* will be added to the intermediate results table after successful submission. Changes made will be logged in Audit logs (See Appendix A, section 13.6)**

6.5.3.5. (Admin user only) Edit a *Sample ID* using the *pencil* icon ( ) next to the respective *Sample*. (Figure 23)

Figure 23: IdentiClone Dx *IGH* Software ⇨ Edit *Sample ID*

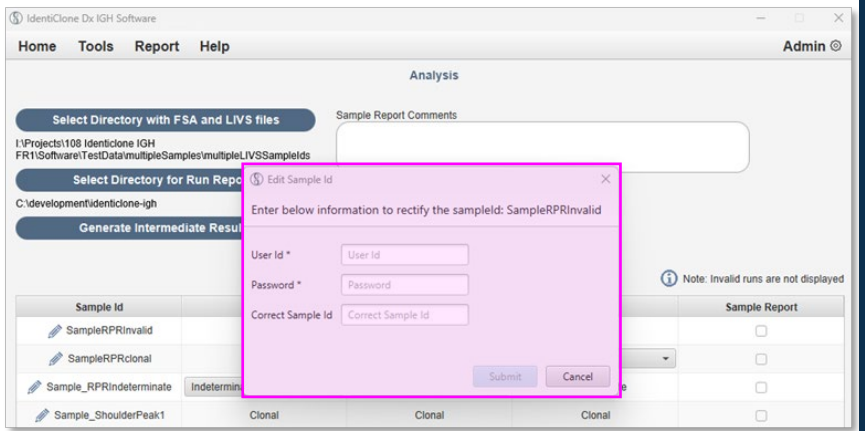


6.5.3.6. (Admin user only) Enter login credentials and the *Correct Sample ID*, then click **Submit.** (Figure 24)

- Verify the *Correct Sample ID* is included in the results table.

Note: This feature is provided as a convenience to the user and should not be used often.

Figure 24: IdentiClone Dx *IGH* Software ⇨ *Correct Sample ID*



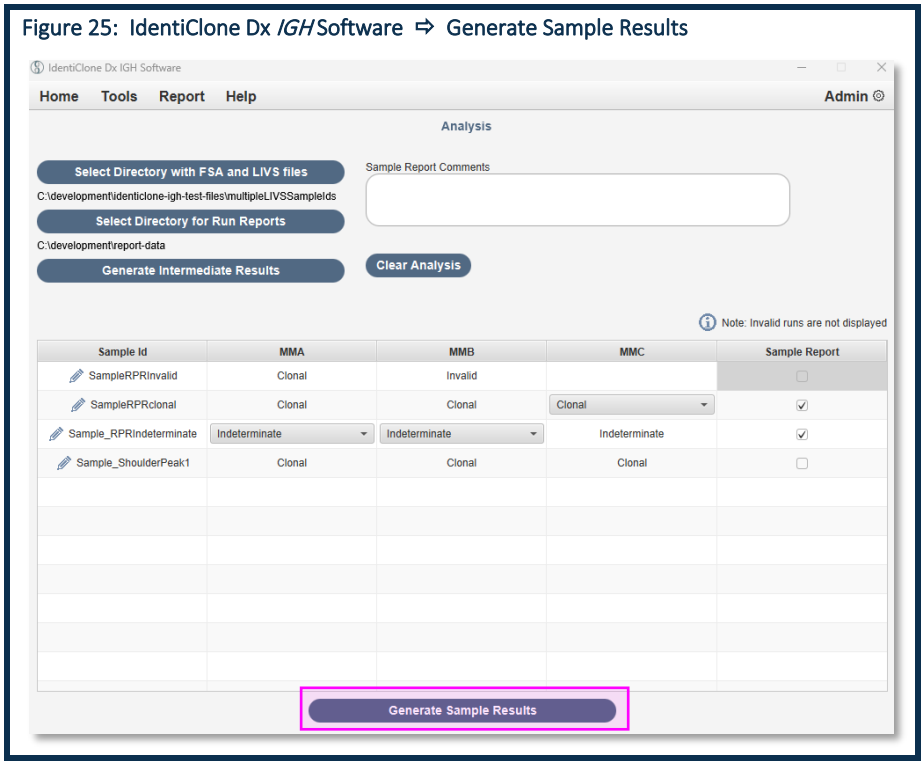
6.5.4. Click **Generate Sample Results**. (Figure 25)

6.5.4.1. Sample Reports will be generated in the directory file path selected in step 6.4.3.

- A prompt to open this folder will open after the Sample Reports are generated.

6.5.4.1.1. In order to view the Sample Reports, a password is required. The PDF report password must be set by Admin user. (Appendix A, section 13.8).

Figure 25: IdentiClone Dx *IGH* Software ⇨ Generate Sample Results



6.6. Example Software Reports

6.6.1. Run Report

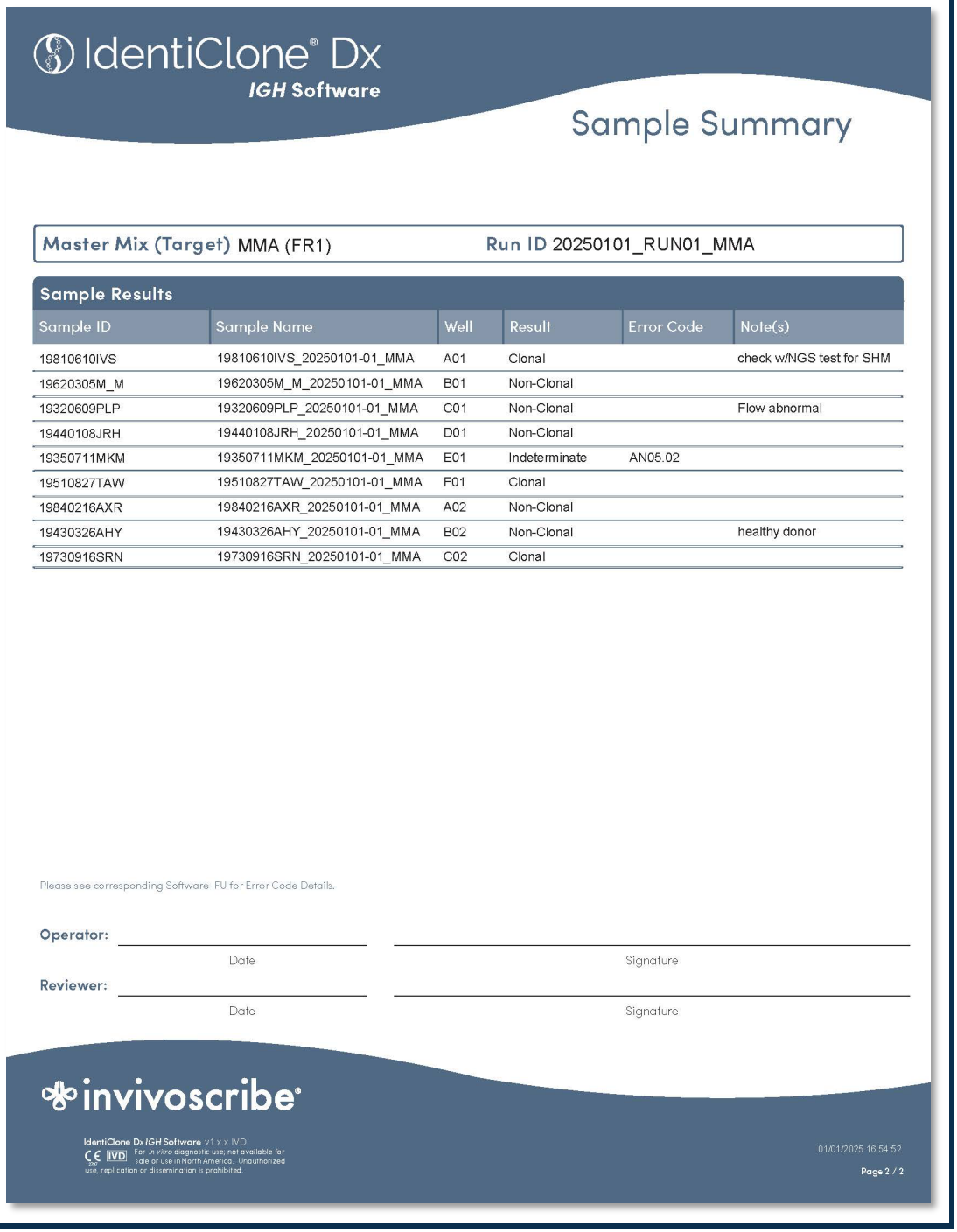
6.6.1.1. The first page of the Run Report is the *Run Summary*, which provides the reagent and ABI instrument traceability information, control results, and run validity status. (Figure 26)

Figure 26: An example IdentiClone Dx *IGH* Software Run Report, *Run Summary*

6.6.1.2. The second page of the Run Report includes the *Sample Summary* (Figure 27), detailing the results for all samples included in the master mix-specific run.

- The Sample Summary provides one (of three) master mix-specific Intermediate Result for each sample included in the run.
- The Sample Clonality Status is determined by evaluating Intermediate Results from all 3 master mixes and is provided in the Sample Report. (Figure 28)

Figure 27: An example IdentiClone Dx *IGH* Software Run Report, *Sample Summary*, which provides the sample results for the indicated master mix



IdentiClone® Dx
IGH Software

Sample Summary

Master Mix (Target) MMA (FR1) **Run ID** 20250101_RUN01_MMA

Sample Results

Sample ID	Sample Name	Well	Result	Error Code	Note(s)
19810610IVS	19810610IVS_20250101-01_MMA	A01	Clonal		check w/NGS test for SHM
19620305M_M	19620305M_M_20250101-01_MMA	B01	Non-Clonal		
19320609PLP	19320609PLP_20250101-01_MMA	C01	Non-Clonal		Flow abnormal
19440108JRH	19440108JRH_20250101-01_MMA	D01	Non-Clonal		
19350711MKM	19350711MKM_20250101-01_MMA	E01	Indeterminate	AN05.02	
19510827TAW	19510827TAW_20250101-01_MMA	F01	Clonal		
19840216AXR	19840216AXR_20250101-01_MMA	A02	Non-Clonal		
19430326AHY	19430326AHY_20250101-01_MMA	B02	Non-Clonal		healthy donor
19730916SRN	19730916SRN_20250101-01_MMA	C02	Clonal		

Please see corresponding Software IFU for Error Code Details.

Operator: _____ _____
Date Signature

Reviewer: _____ _____
Date Signature

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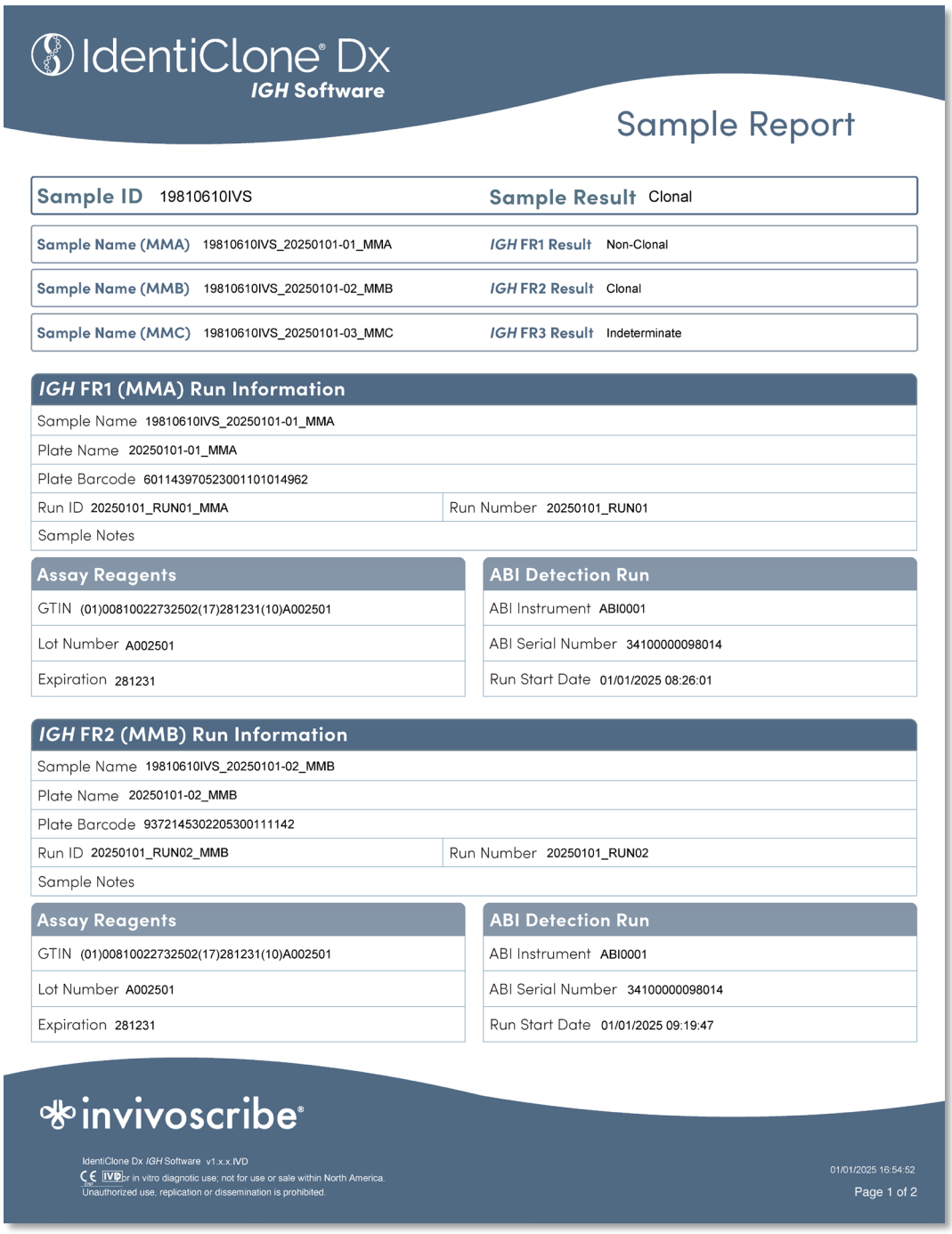
6.6.2. Sample Report

6.6.2.1. The IdentiClone Dx *IGH* Software Sample Report provides the results generated for each master mix, as well as the Sample Clonality Status.

- Additional traceability information is also indicated, including reagent and ABI instrument information. (Figure 28)

Figure 28: An example IdentiClone Dx *IGH* Software Sample Report



IdentiClone® Dx
IGH Software

Sample Report

Sample ID	19810610IVS	**Sample Result**	Clonal
Sample Name (MMA)	19810610IVS_20250101-01_MMA	***IGH* FR1 Result**	Non-Clonal
Sample Name (MMB)	19810610IVS_20250101-02_MMB	***IGH* FR2 Result**	Clonal
Sample Name (MMC)	19810610IVS_20250101-03_MMC	***IGH* FR3 Result**	Indeterminate

***IGH* FR1 (MMA) Run Information**

Sample Name 19810610IVS_20250101-01_MMA	
Plate Name 20250101-01_MMA	
Plate Barcode 60114397052300110101 4962	
Run ID 20250101_RUN01_MMA	Run Number 20250101_RUN01
Sample Notes	

Assay Reagents	**ABI Detection Run**
GTIN (01)00810022732502(17)281231(10)A002501	ABI Instrument ABI0001
Lot Number A002501	ABI Serial Number 34100000098014
Expiration 281231	Run Start Date 01/01/2025 08:26:01

***IGH* FR2 (MMB) Run Information**

Sample Name 19810610IVS_20250101-02_MMB	
Plate Name 20250101-02_MMB	
Plate Barcode 937214530220530011 1142	
Run ID 20250101_RUN02_MMB	Run Number 20250101_RUN02
Sample Notes	

Assay Reagents	**ABI Detection Run**
GTIN (01)00810022732502(17)281231(10)A002501	ABI Instrument ABI0001
Lot Number A002501	ABI Serial Number 34100000098014
Expiration 281231	Run Start Date 01/01/2025 09:19:47

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7. Error Messages and Corrective Action(s)

7.1. Plate Map (PM) Errors

Table 3 includes potential error codes associated with step 6.3. Follow the indicated corrective action in the event that any of these error codes appear during plate mapping.

Table 3: Plate Map Error Codes and Associated Corrective Actions

Error Code	Error Message	Corrective Action
PM04	Plate name cannot be blank	Verify the *Plate Name* field is populated.
PM05	Plate name contains illegal characters	Verify *Plate Name* contains only letters (A-Z, a-z) numbers (0-9), underscores (_) and hyphens (-). No spaces are permitted.
PM07	Result group cannot be blank	Ensure the *Results Group* field is not blank.
PM11	Plate contains no samples	Ensure each plate has at least one run containing one set of controls and at least one sample.
PM12	Sample name contains illegal characters	Verify *Sample Name* contains no more than 50 characters, and only includes letters (A-Z, a-z), numbers (0-9), underscores (_), and hyphens (-). No spaces are permitted.
PM14	Sample name cannot exceed 50 characters	Shorten *Sample Name* to be less than or equal to 50 characters.
PM15	Invalid sample type detected	Ensure the rules below are followed before importing a CSV file representing a plate map (this is created using a CSV file from a previous run): • A *Plate Name* must be entered. • The *Sample Type* column includes only values = *SAMPLE, PC, NC or NTC.* • The *Sample Name* and *User Defined Fields 1* and *2* in the CSV file must be empty or all the fields must be entered following the plate map rules. • *User Defined Field 1 => Sample Type* with values = *SAMPLE, PC, NTC, NC.* • *User Defined Field 2 => Run number* from *Run 1* up to *Run 24.* • *User Defined Field 3 => Master Mix* with values *A, B* or *C.* ○ Only one *Master Mix* can be assigned to a run at a time. • *User Defined Field 4 => Sample ID;* this field contains no more than 50 characters, only including letters, numbers, underscores, and hyphens (A-Z / a-z / 0-9 / _ / -). No spaces are permitted.
PM16	• Sample name cannot be blank; OR • Run number cannot be blank; OR • Sample must have a sample type assigned	
PM22	Run is missing a positive/negative/no template control or Run has too many positive/negative/no template controls	When adding a *Run*, verify it contains exactly one set of controls, i.e., one NC, one PC and one NTC.
PM24	Import file contains no samples	Verify the import file is properly formatted with the appropriate *Sample* information.
PM28	Plate name cannot exceed 50 characters	Decrease *Plate Name* to be less than or equal to 50 characters.
PM29	Sample notes contains illegal characters	Verify *Sample Notes* do not contain commas.
PM30	Barcode contains illegal characters	Verify the *ABI instrument Barcode* is correct.

Table 3: Plate Map Error Codes and Associated Corrective Actions

Error Code	Error Message	Corrective Action
PM34	Well is assigned a run, but is missing a sample information	Save the *Wells* assigned to a run with the associated sample or control information.
PM35	Sample notes cannot exceed 50 characters	Verify *Sample Notes* only include up to 50 characters.
PM36	Invalid run number detected	Ensure the rules below are followed before importing a CSV file representing a plate map (this is created using a CSV file from a previous run): • A *Plate Name* must be entered. • The *Sample Type* column includes only values = *SAMPLE, PC, NC or NTC.* • The *Sample Name* and *User Defined Fields 1* and *2* in the CSV file must be empty or all the fields must be entered following the plate map rules. • *User Defined Field 1 => Sample Type* with values = *SAMPLE, PC, NTC, NC.* • *User Defined Field 2 => Run number* from *Run 1* up to *Run 24.* • *User Defined Field 3 => Master Mix* with values *A, B* or *C.* ○ Only one *Master Mix* can be assigned to a run at a time. • *User Defined Field 4 => Sample ID;* this field contains no more than 50 characters, only including letters, numbers, underscores, and hyphens (A-Z / a-z / 0-9 / _ / -). No spaces are permitted.
PM37	Sample ID cannot be blank	
PM38	Sample ID cannot exceed 50 characters	
PM39	Sample ID contains illegal characters	
PM40	Master mix cannot be blank	
PM41	Invalid master mix detected	
PM42	Multiple master mixes assigned to a single run	

7.2. File Validation (FV) Errors

The error codes listed in Table 4 can occur while performing step 6.4; if any of these error codes appear while selecting data for analysis follow the indicated corrective action.

Table 4: File Validation Error Codes and Associated Corrective Actions

Error Code	Error Message	Corrective Action
FV03.5	Invalid FSA file	Repeat the Assay beginning from Fragment Analysis by Capillary Electrophoresis. • Do not edit the LIVS files after saving the plate • Do not edit FSA file output from ABI 3500
FV04.1	The format of the LIVS file is invalid	
FV06.1	All samples in LIVS file do not have matching FSA files. Ensure the ABI plate map is not manually edited.	
FV06.2	LIVS file cannot be located	Upload the corresponding LIVS file generated by the Software (containing the annotated plate information) in conjunction with the FSA files for analysis.
FV06.3	Path provided is not a directory	Ensure the correct directory is selected containing FSA and LIVS files.
FV06.4	Multiple LIVS files representing the same plate found	Only use LIVS files generated by the Software; do NOT duplicate any LIVS files – they include annotated plate information that allows traceability of samples to a plate.
FV06.5	Maximum LIVS files limit reached Note: A maximum of 15 LIVS files per analysis is allowed	Verify no more than 15 LIVS files are selected for analysis.

Table 4: File Validation Error Codes and Associated Corrective Actions

Error Code	Error Message	Corrective Action
FV06.6	Invalid ABI settings detected. Please confirm the ABI settings used match those specified in the IFU. Refer to IFU for further instructions.	Reset the ABI settings as recommended, then repeat the Assay beginning from Fragment Analysis by Capillary Electrophoresis. Only the FSA files generated by the ABI instrument using the recommended ABI settings can be uploaded to perform the analysis.
FV07.1	• The format of the import file is invalid; OR • There was a problem importing the plate.	Verify the correct CSV file was selected for importing into the plate map setup.

7.3. Analysis (AN) Errors

Table 5 includes error codes that can occur during data analysis. Follow the indicated corrective action below if any of the error codes below appear during data analysis.

Table 5: Analysis Error Codes and Associated Corrective Actions

Error Code	Error Description	Corrective Action
AN01.01	NTC invalid	Re-test entire run starting from Fragment Analysis by Capillary Electrophoresis.
AN01.02	NTC invalid	Re-test entire run starting from PCR Amplification.
AN01.03	NTC invalid	Re-test entire run starting from Fragment Analysis by Capillary Electrophoresis.
AN02.01	PC invalid	Re-test entire run starting from Fragment Analysis by Capillary Electrophoresis.
AN02.02		
AN02.03		
AN02.04	PC invalid	Re-test entire run starting from PCR Amplification.
AN02.05		
AN02.06	PC invalid	Re-test entire run starting from PCR Amplification. If the problem persists, contact IVS Customer Support.
AN02.07		
AN03.01	NC invalid	Re-test entire run starting from Fragment Analysis by Capillary Electrophoresis.
AN03.02		
AN03.03		
AN03.04	NC invalid	Re-test entire run starting from PCR Amplification.
AN03.05		
AN03.06	NC invalid	Re-test entire run starting from PCR Amplification. If the problem persists, contact IVS Customer Support.
AN04.01	Sample invalid	Re-test entire run starting from Fragment Analysis by Capillary Electrophoresis.
AN04.02		
AN04.03		
AN04.05	Sample invalid	Re-test entire run starting from PCR Amplification.
AN04.06		
AN04.07		
AN04.08	Sample invalid	Re-test entire run starting from PCR Amplification. Refer to *Run Report* for run failure error code.

Table 5: Analysis Error Codes and Associated Corrective Actions

Error Code	Error Description	Corrective Action
AN05.01	Sample indeterminate	If sample is non-clonal in the other two master mixes, re-test sample starting from PCR Amplification.
AN05.02		
AN05.03		

7.4. Other (OT) Errors

Error codes listed in Table 6 are categorized as "other" and can occur at any time while using software. Follow the corrective action indicated for the specified error code.

Table 6: Other Error Codes and Associated Corrective Actions

Error Code	Error Message	Corrective Action
OT01	Not enough disk space available in chosen result output location	Verify the output file location selected for file export has enough space (at least 10 MB).
OT02	Output location (file path) for results file is not writable	Verify the directory file path selected has write permissions.
OT03	Input location is not readable	Verify the directory file path selected has read permissions.

8. References

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11. Zhang J-J, Xie Y-X, Luo L-L, et al. "A comparison of capillary electrophoresis and next-generation sequencing in the detection of immunoglobulin heavy chain H and light chain κ gene rearrangements in the diagnosis of classic hodgkin's lymphoma." *Bioengineered*, 2022; 13:3, 5868-5879.

- IdentiClone Dx *IGH* Assay Instructions for Use (English) (Invivoscribe 📖: 280495)
- ABI 3500xL Dx Genetic Analyzer User Manual (Thermo Fisher: 100079380 Revision D)
- ABI 3500xL Genetic Analyzer User Manual (Thermo Fisher: 100079380 Revision E)

9. Technical and Customer Service

We appreciate your business. We are happy to assist you with understanding this software and will provide ongoing technical assistance Monday through Friday to ensure our reagents are performing efficiently in your laboratory.

Contact Information

Invivoscribe, Inc
10222 Barnes Canyon Road | Building 1 | San Diego | California 92121-2711 | USA
Phone: +1 858 224-6600 | Fax: +1 858 224-6601 | Business Hours: 7:00AM - 5:00 PM PST/PDT
Technical Service: support@invivoscribe.com | Customer Service: sales@invivoscribe.com | Website: www.invivoscribe.com

10. Symbols

The following symbols are used in labeling for this product.

REF	Catalog Number	TAQ	Taq DNA Polymerase
VOL	Reagent Volume	CONTROL + *IGH*	*IGH* Positive Control
LOT	Lot Number	CONTROL - *IGH*	*IGH* Negative Control
	Storage Conditions	CONTROL NTC	No Template Control (NTC)
UDI	Unique Device Identifier	MMA *IGH* FR1	*IGH* (FR1) Tube A Master Mix
	Expiration Date	MMB *IGH* FR2	*IGH* (FR2) Tube B Master Mix
	Protect from light	MMC *IGH* FR3	*IGH* (FR3) Tube C Master Mix
	Manufacturer		Consult Instructions for Use
CE	European Conformity	CH REP	Swiss Authorized Representative
IVD	For *In Vitro* Diagnostic Use	EC REP	Authorized Representative in the European Community
		UKRP	UK Responsible Person

11. Legal Notice

For Legal Notices related to this product, visit: https://invivoscribe.com/legal-notices/

12. Revision History

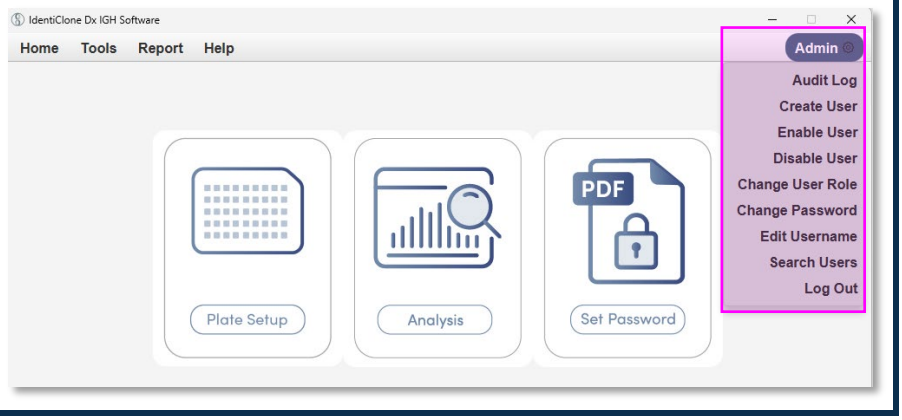
Table 7: IdentiClone Dx *IGH* Software IFU Revision History and Notified Body Validation

IFU Revision	Date Issued	Change Description	Revision Validated by the Notified Body
B	August 2025	Initial Release for Submission to Notified Body	☑ Yes Validation language: **English** ☐ No
C	February 2026	• Implemented non-functional updates including branding alignment and clarification of warnings and precautions. • Updated system requirements and software distribution information to align with the Invivoscribe Software Portal. • Alignment with the software update to version 1.2.0. • Updated symbols and revision history	☐ Yes Validation language: **English** ☑ No

13. Appendix A : Admin User Access

The Admin user has additional privileges as compared to a basic user, including additional menu options to allow multiple user management features to be accessed. (Figure 29)

Figure 29: Additional Admin menu options



13.1. Audit log

13.1.1. Only users with Admin privileges have access to view the Audit logs, which allows all activities performed with the Software to be viewed by category based on the event type and corresponding action(s). (Figure 30)

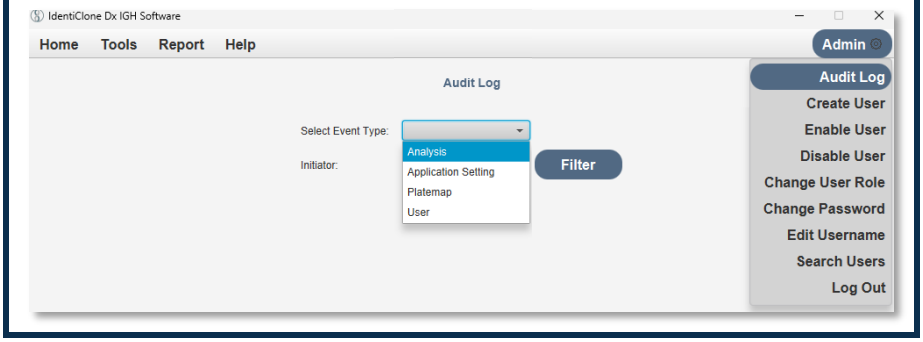
13.1.1.1. **Analysis Event Type:** All analysis activity is logged from start of analysis to the report generation activities for sample reports.

13.1.1.2. **Application Setting**: The setting activity that applied throughout the application. For example, setting PDF password and backup location activities are logged.

13.1.1.3. **Plate Map**: All plate setup activities, e.g., saving the plate map or importing a CSV file for plate setup.

13.1.1.4. **User**: All user activities, such as editing *username*, *change role*, *login*, *logout*, etc., are logged.

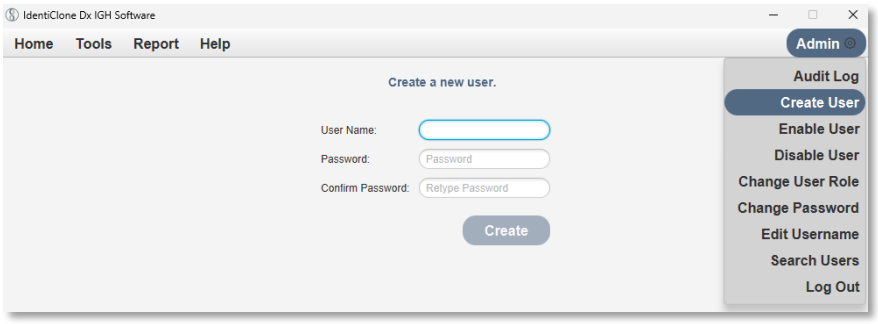
Figure 30: Audit Log categories and event types



13.2. Create User

13.2.1. Only users with Admin privileges have the ability to create other users with basic role privileges; this requires a username and password. (Figure 31)

Figure 31: Create a new user



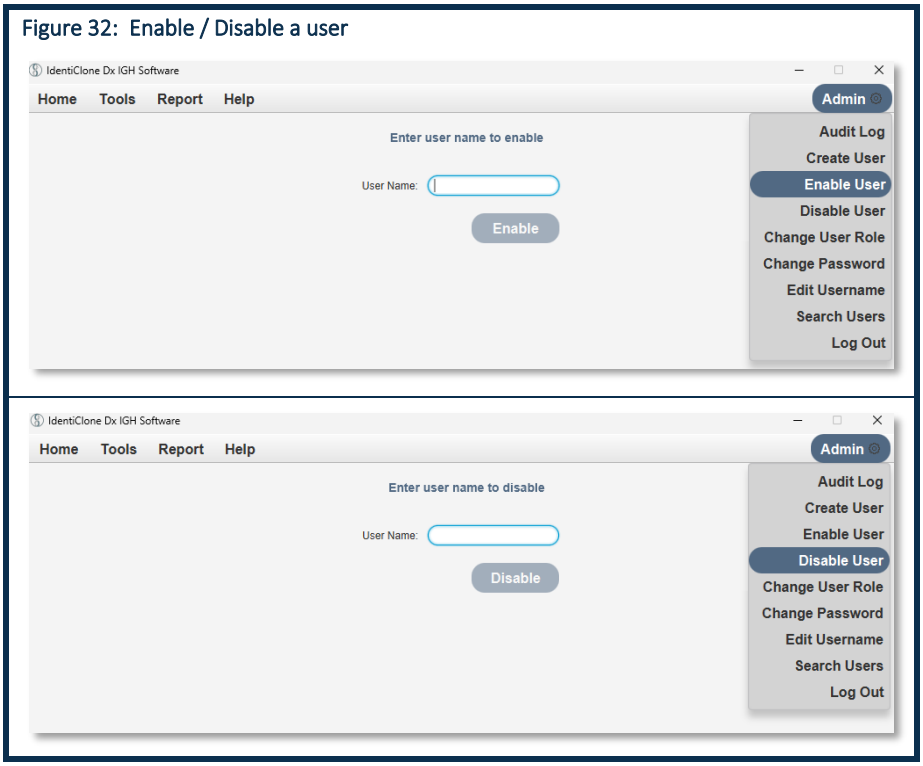
13.3. Enable and disable a User

13.3.1. Only users with Admin privileges have the ability to enable and disable users assigned a basic role. (Figure 32)

13.3.1.1. Admin level users cannot be disabled.

13.3.1.2. If a user is disabled or deactivated, they cannot login to the Software until the user is enabled and activated.

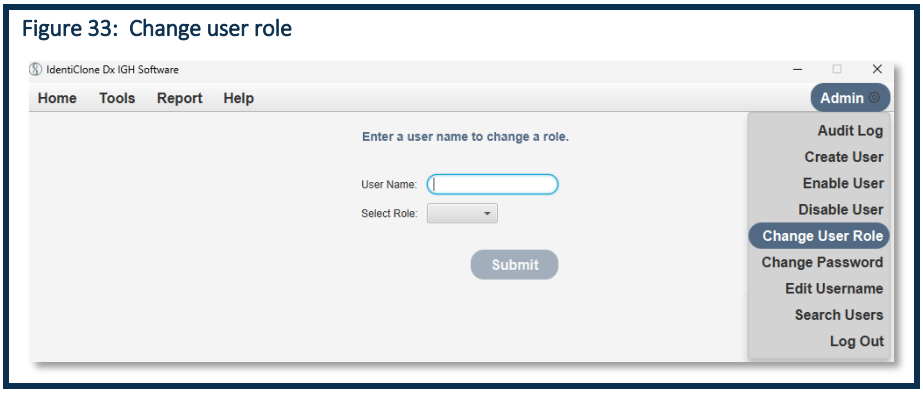
Figure 32: Enable / Disable a user



13.4. Change User Role

13.4.1. Only users with Admin privileges have the ability to change a user role from *Basic* to *Admin* or vice versa. (Figure 33)

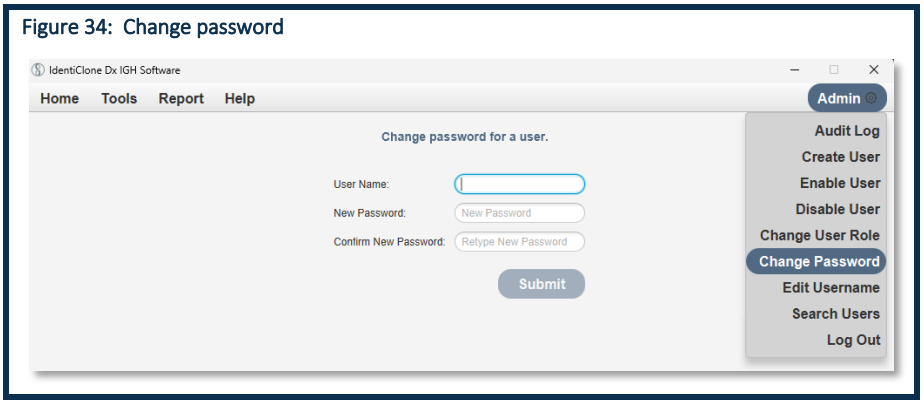
Figure 33: Change user role



13.5. Change User Password

13.5.1. Only users with Admin privileges have the ability to change their own and other user passwords by providing a username and a new password. (Figure 34)

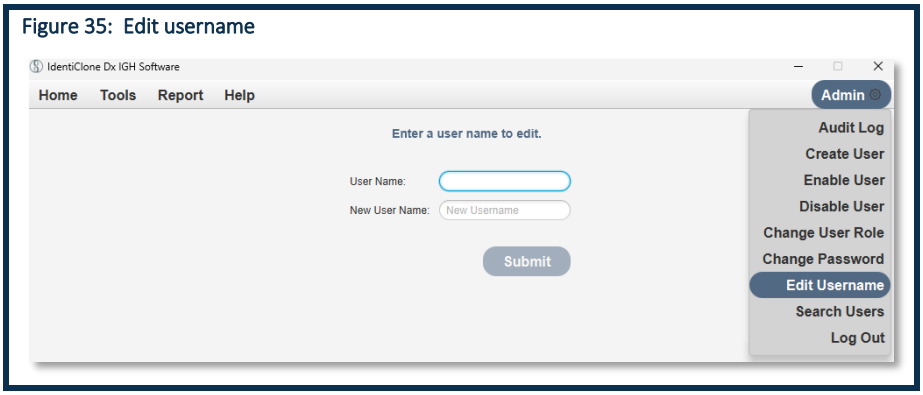
Figure 34: Change password



13.6. Edit Username

13.6.1. Only users with Admin privileges have the ability to edit their own and other usernames by providing the old (former) username and new username. (Figure 35)

Figure 35: Edit username



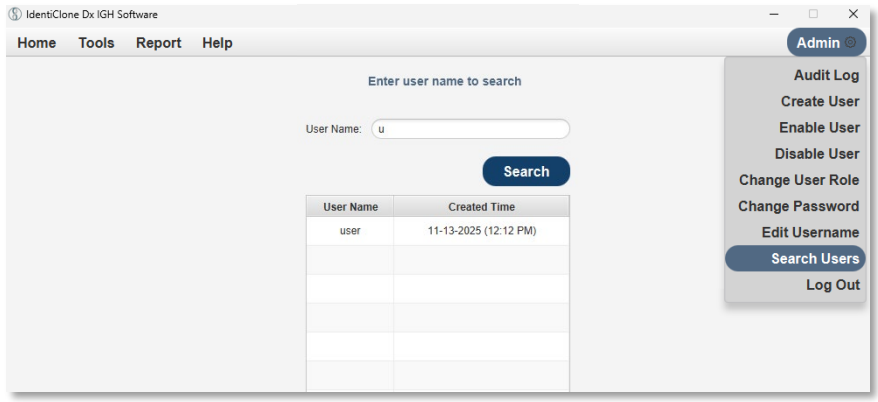
13.7. Search Users

13.7.1. Only users with Admin privileges have the ability to search for the users with access to the Software. (Figure 36)

13.7.1.1. Click **Admin** and select **Search** from the dropdown menu, then search by entering part of a username.

13.7.1.1.1. The software returns the list of users matching the username search criteria.

Figure 36: Search for user



13.8. Set PDF Report password

13.8.1. Only users with Admin privileges have the ability to set the PDF password. (Figure 37)

- After the initial Admin user is configured, set the PDF password prior to the first analysis with the Software.
- If the analysis function is used before setting the PDF password, a prompt will appear, displaying a warning message to *Set PDF report password.*

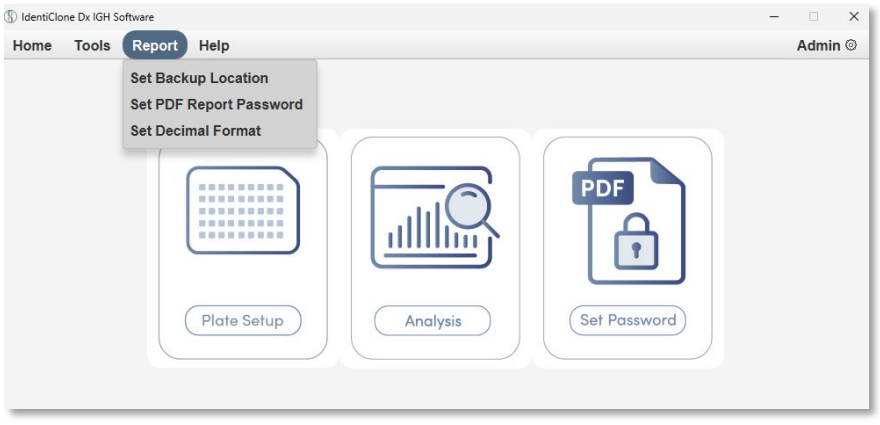
IMPORTANT! **All PDF reports generated by the Software require a password to view.**

13.8.1.1. Navigate to the *Home page* of the Software or click on the **Report** menu.

13.8.1.2. Enter a password and enter it again to confirm, then select **Submit.**

- After setting the password, any user can perform analysis by navigating to *Analysis* ⇨ *Dx Analysis*.

Figure 37: Administrator Report Menu



13.9. Set Back up location

13.9.1. By default, the software will use a folder named ***backup*** located one level above the installation directory. (Figure 38)

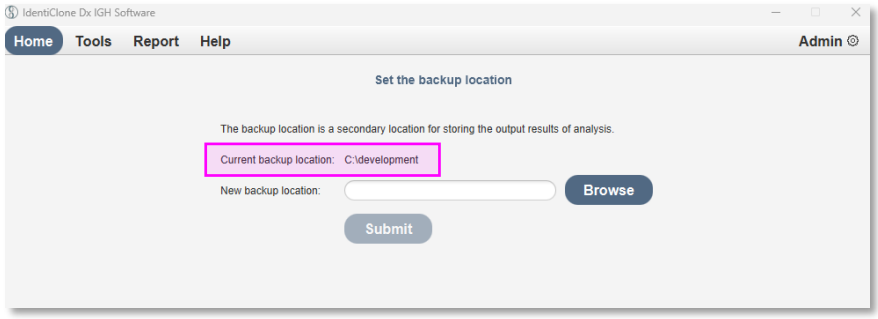
- Only users with Admin privileges have the ability to configure the backup directory path for the PDF reports.

13.9.1.1. Click the **Report** from the dropdown menu, then click **Set Backup Location**.

13.9.1.2. Click the **Browse** button and navigate to the directory file path to store the PDF report backup files, then click **Submit.**

- The file path for a previously configured backup location will display in the *Current Backup Location* field.

Figure 38: Set Backup location function



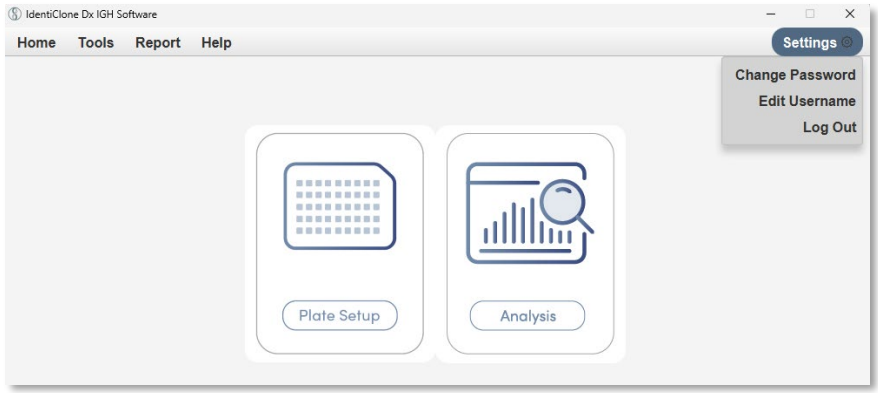
13.10. Basic user access:

13.10.1. The role of basic user includes limited permissions, allowing access to perform *Plate Setup*, *Analysis, Edit Username* and *Change Password*. (Figure 39)

13.10.1.1. User management features are accessed under the *Settings* menu.

13.10.1.2. Change a basic user password or username by clicking on the respective options in the dropdown menu.

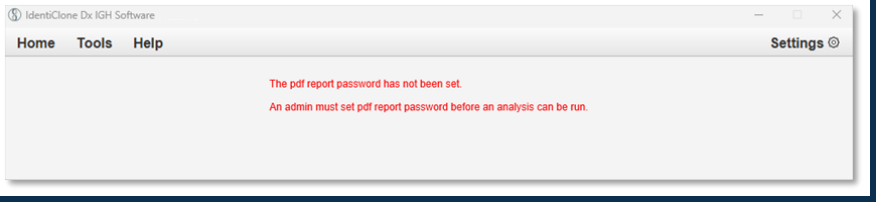
Figure 39: Basic User settings



13.10.2. If the *PDF report password* was not configured by an Admin user, a basic user will receive a warning as shown below upon login. (Figure 40)

13.10.2.1. An Admin user must first set the *PDF report password* prior to implementing the Software.

Figure 40: PDF report password warning



13.11. User Inactivity

13.11.1. The Software application is programmed to provide a warning after 5 minutes of inactivity, which includes a prompt to *Continue* or *Cancel* the session. (Figure 41)

13.11.1.1. If this prompt is ignored, the Software will log out the user and return to the Login screen.

13.11.1.2. When the user logs in again, the Software will continue to the same screen / function before the user was logged out.

Figure 41: Inactivity warning and prompt