HLA Typing Software

release 2.0

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1.1   What is the HLA Typing Software?

The HLA Typing Software by Biotest is used to present, evaluate and store typing results in a clearly arranged format. It does not matter whether you process HLA assays manually or use a reader or automated system. The HLA Typing Software enables you to quickly establish, print or export reports after the evaluation of the data.

The HLA Typing Software also has a Multi-User option. This means, the same data can be accessed from several workplaces. This option, first implemented for big laboratories, makes also sense for smaller ones, because it is a perfect backup solution for your workplace.

The present manual contains a short set of instructions for the installation and use of the Typing Software.

1.2   System requirements

Computer:

*   Operating system Windows 2000 or Windows XP Professional Service Pack 2
    (The software can be used with other Windows operating systems but has not been tested.)
*   Min. available local disk storage: 100 MB
*   Min. working storage: 256 MB
*   screen resolution: 1024 x 768

> ### Attention:
> The option "large fonts" must not be selected!

*   For operation via server: network connection to the server

> ### Attention
> If the server is firewalled (as for example with Windows XP Service pack 2), communication port 3050 must be enabled.

*   For multi-user operation: if a Firebird server is already in operation, a user 'ADMIN' must have been created on it.
    This new user is created by the database server command "gsec.exe -user sysdba -pass masterkey -add admin -pw nimda" (Folder "\Program files\Firebird\Firebird_2_0\bin").
*   Internet update of assay lot data requires Internet connection and an Internet browser.

> ### Attention:
> If these requirements are not met by your computer, this could lead to errors, slow performance and eventually even to program crashes!

Recommendations for the connection of a reader:

*   Shielded serial cable, length $\leq$ 2m
*   Transmission rate $\leq$ 9600 Baud
*   The line should not be in the vicinity of electromagnetic fields.
*   Parameter adjustment in reader setup

1.3   Installation on Server

This installation will be carried out:

- for single-user operation - on the respective computer
- for multi-user operation - on the server that makes the data and program available to all workstations

Start the installation by double clicking "BiotestHLAtypingSetup.exe". The Installation Assistant will then guide you through the entire installation procedure.

The installation starts with the Firebird "welcome" screen:

Click <Next>

→   The license agreement is displayed. Select " I accept... ". Only then will you be able to click <Next>.

→   Information on the installed data is displayed, this information can be found in the file readme.txt in the installation folder of the database server. Click <Next>

→   Proposal of the installation folder for the database server. Please follow the proposal and simply click on <Next>

→   An options menu is displayed. As before, you should not change the options but continue with <Next>.

There are two additional screens to confirm with <Next> without changing any options. Finally, an overview of the settings is displayed. This time, click <Install>.

→   Another information is displayed. Continue with <Next>.

Finally, installation takes place. Finish this first part of installation with <Finish>.

> ### Note:
> For HLA typing 2.0, the usage of Firebird 2.0 Database Server is recommended. If you are working with Interbase 6.0 in combination with HLA Typing Software only, please install Firebird Server first and then uninstall Interbase 6.0 via the Windows Control Panel.

After the database has been installed, the actual software is then installed. The following screen display will pop up when you start to install the HLA Typing Software:
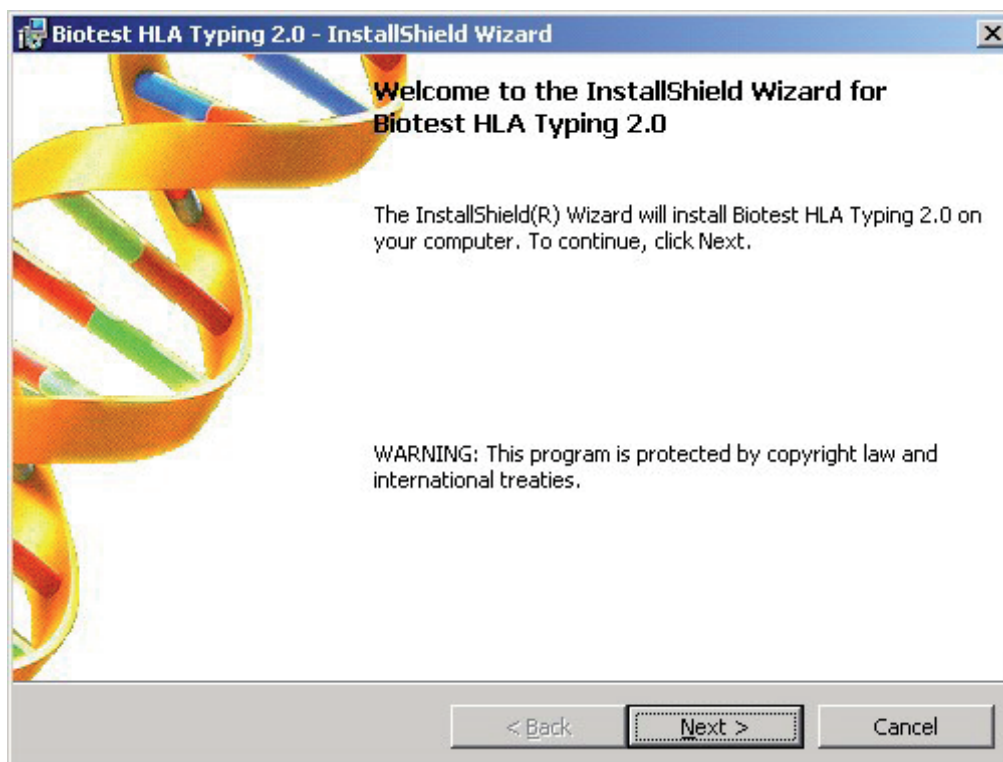
It is strongly recommended to leave the default settings unchanged and to confirm all prompts in the Installation Assistant by clicking the <Next> or <Finish> key.

There is of course one exception: You must actively accept the license agreement by clicking the button <I accept...> or else the <Next> key will not be available.

After accepting the license agreement, important information for configuration is displayed. This can also be viewed in the readme.txt file:
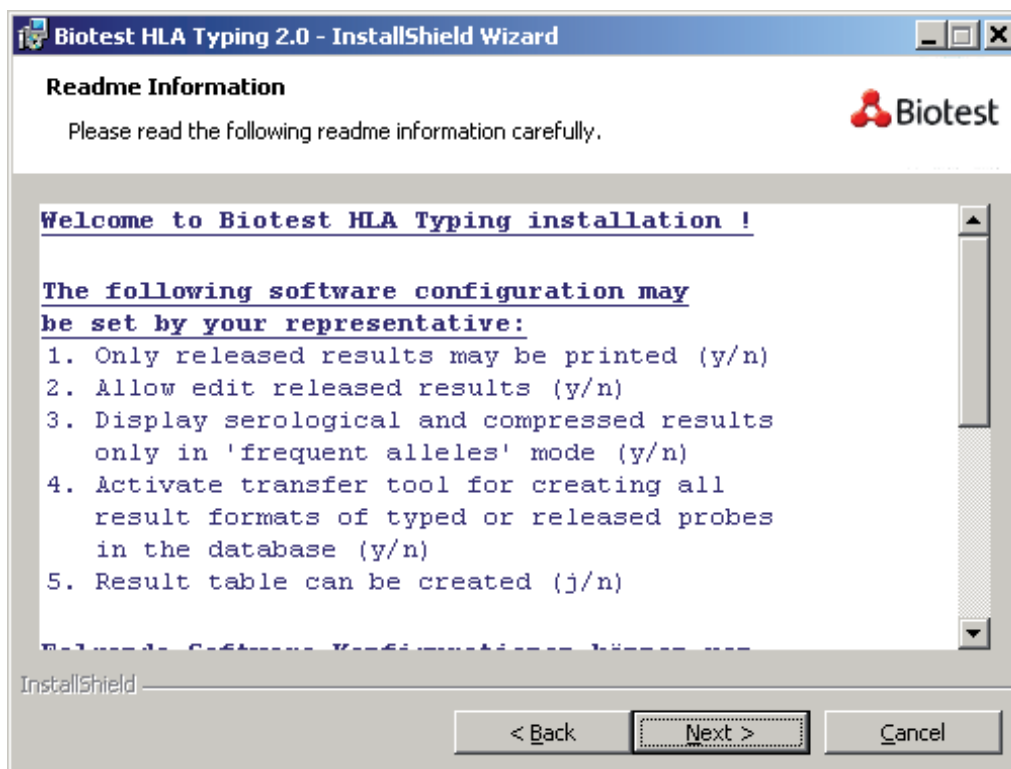
Please enter your name on the next screen display. You also need to enter if the software will be available for any user who uses this computer, or just for the user who is logged in:
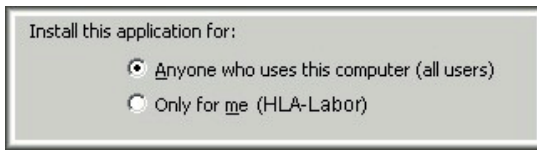
Click <Next> to select the installation place. You should not change the proposed settings.

Please wait a moment until the screen display below appears:
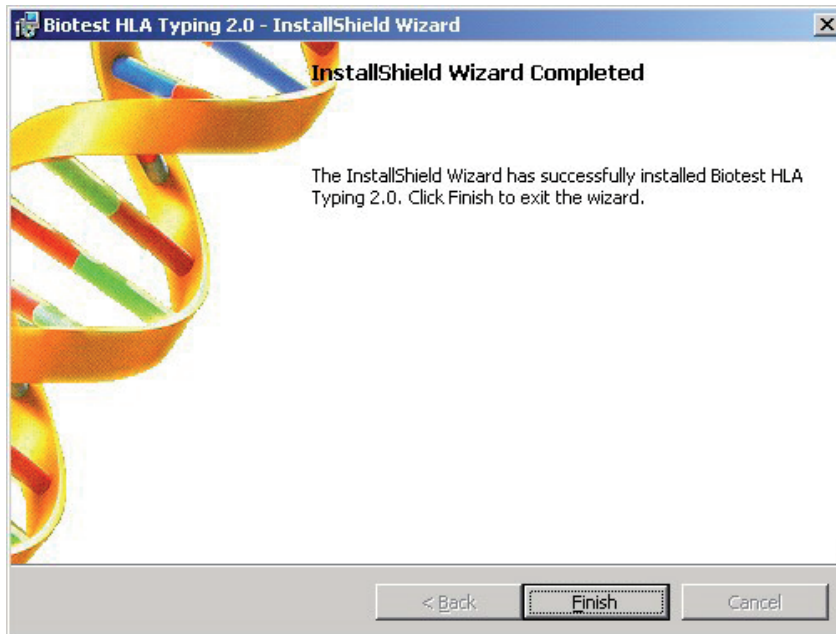
After clicking the <Finish> button, the software is installed but important settings are still missing.

During an update, the option to uninstall the old software is offered in the next window:
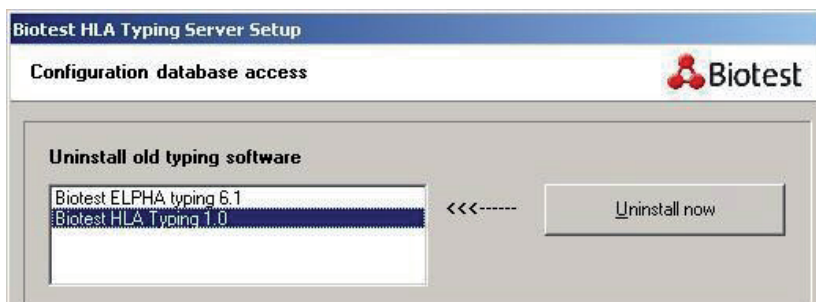
Attention:

It is strongly recommended to uninstall the software. All changed files such as the old data bases will not be uninstalled. They can be transferred to the new version during the next step.

Up to this moment, the installation for a single-user system and for the server of a multi-user system is identical. It is only now that procedures change.

In the case of a **single-user system**, the first option in the lower section of the window
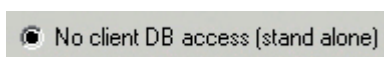
is selected.

In the case of a multi-user system you select how to identify the server: via its IP-address or via its name:
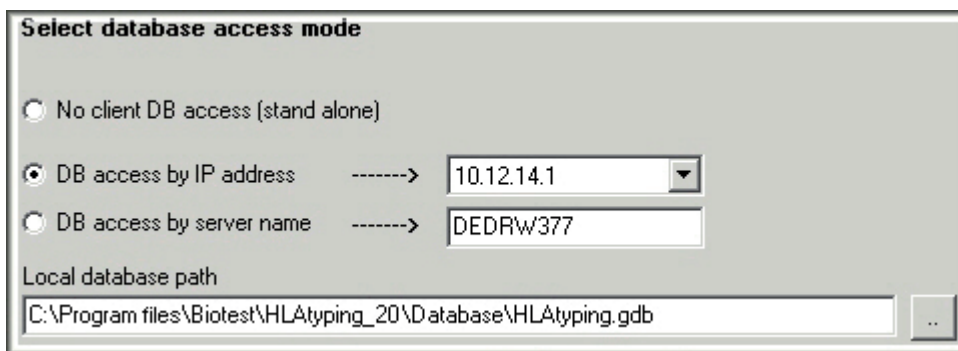
After clicking <OK> you will be asked whether the database is to be transferred from a current installation:
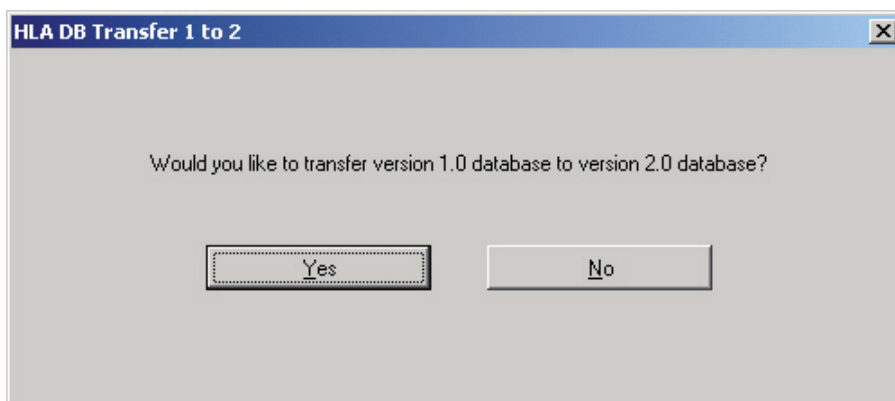
If this is a new installation, you continue with <No>.

If you update the software you select <Yes>. As the structure of the database differs between version 1.0 and 2.0, the old database needs to be converted to ensure that it can still be used. Here, you enter the path to the database.

The default path

C:\Programs\Biotest\HLAtyping_1005\Database\HLAtyping.gdb has already been entered:
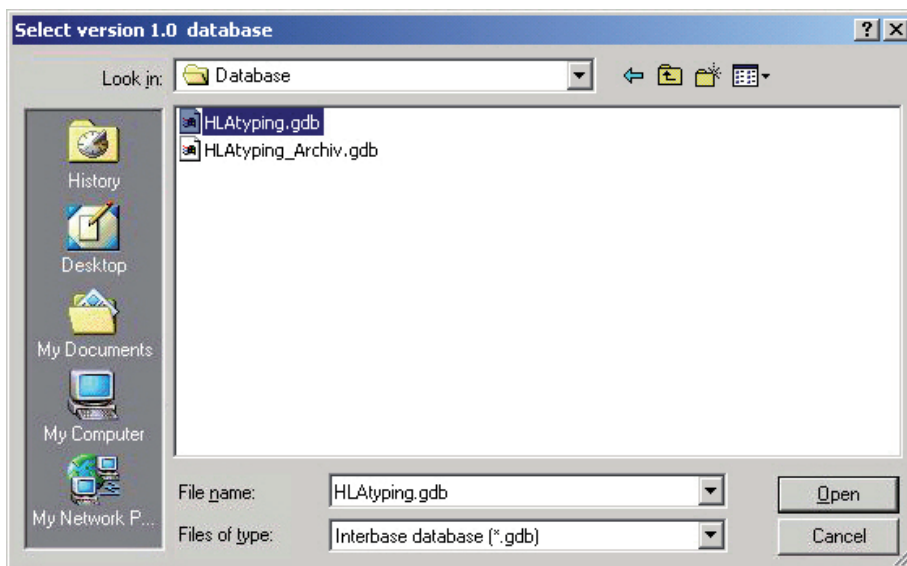
Click <Open> to start the conversion.

Depending on the size of the database, the conversion can take some time. During this time, a window indicating "Transferring database..." is displayed.

→   After the conversion, the following message will be displayed:
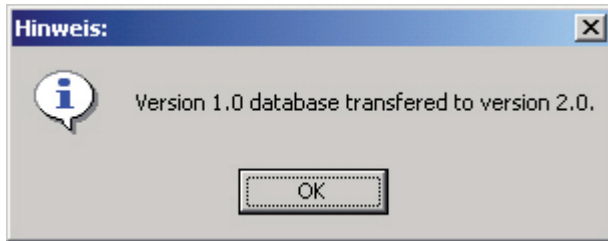
Attention:

If the conversion fails, a warning message will appear.
The old database is not deleted after the conversion!

The Biotest HLA Typing Software has now been installed!

On a multi-user system, proceed with the Installation of the clients.

But - also on a single workplace you cannot start working just yet. Typing can only begin if you have worked your way through the "First Steps"!

1.4   Checking the installation

After the installation of the HLA Typing Software 2.0, the color-coded folders and files will be found in the installation directory:
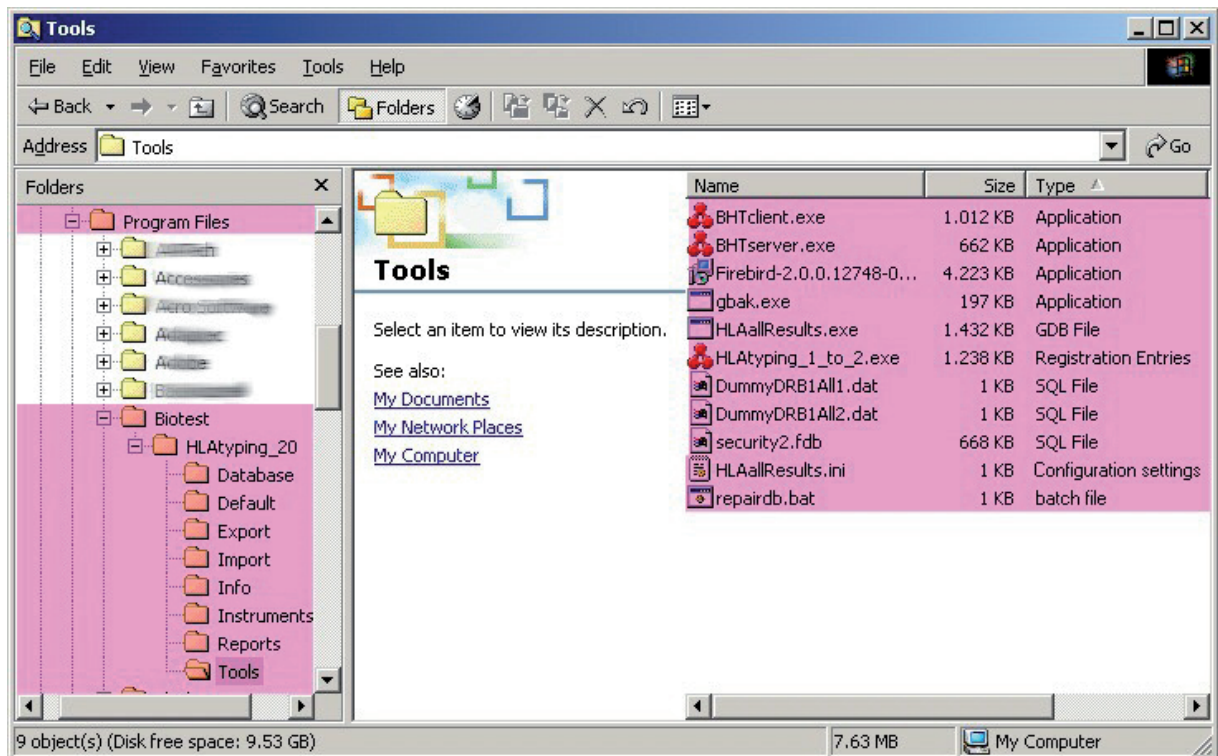
1.5   Installation on clients

In multi-user systems, this installation is carried out on each workstation.

> ### Attention:
>
> Before you install the clients, the installation of the server must have been completed.
>
> ---
>
> The network administrator needs to ensure access to the server. On the server, the installation directory of the software needs to be released for the Client and the Client computer must have a network drive for this release.
>
> ---
>
> It must be known how the server can be identified by the Clients (IP address or server name).

The **BHTClient.exe** program is located on the server in folder **\Biotest\HLAtyping_20\Tools**. This is now executed on each workstation via the connected network drive.

Important!

From HLA Typing Version 2.0 onwards, Clients of version 1.0.0.5 can no longer be used! They must be uninstalled during an update in order to avoid incorrect operator inputs.

→   For this purpose, the old software is selected and uninstalled by clicking <Uninstall now>.
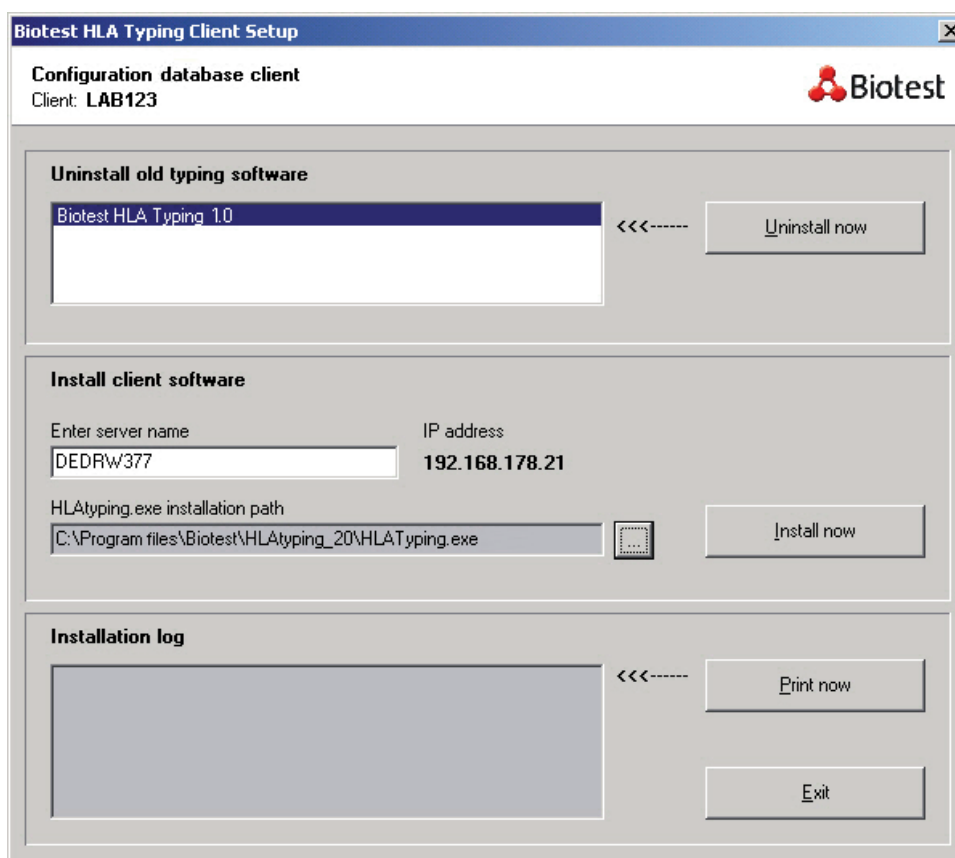
Next, you select the path to the server and to **HLAtyping.exe** in the **Install Client Software** area. After clicking <Open> this is entered in the "installation path" field.

By clicking <Install now> the workstation is configured for use of the HLA Typing software.

You can check in the **installation log** what precisely has been installed. This can also be printed by selecting <Print now>:

```
Installation log                                    12

11.08.2006 12:11:58 System services file: Interbase port already exists.  <<<------   Print now
11.08.2006 12:11:58 C:\WINNT\system32\gds32.dll already exists.
11.08.2006 12:11:58 Start menu link 'Biotest HLA Typing 2.0' created.
11.08.2006 12:11:58 Desktop link 'Biotest HLA Typing 2.0' created.
                                                                          Exit
```

Click <Exit> to close the setup window.

On the desktop of the computer this icon will appear:

Biotest HLA Typing 2.0

The Biotest HLA Typing Software has now been installed!

But - you cannot start working just yet. Typing can only begin if you have worked your way through the "First Steps"!

1.6 Database transfer

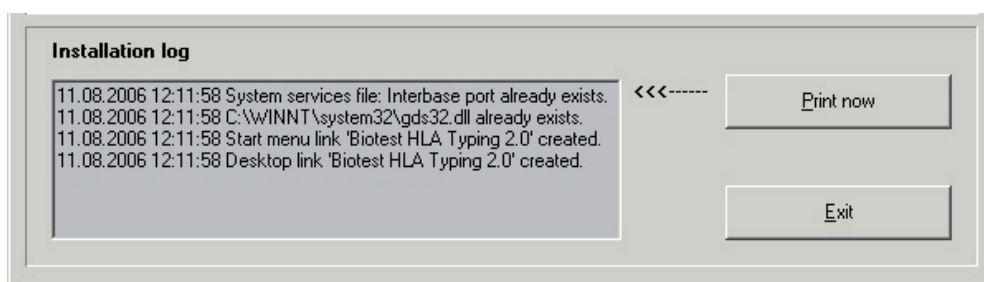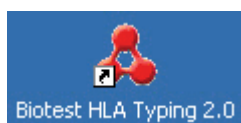When updating the HLA Typing Software from version 1.0.0.5 to version 2.0, the structure of the database changes. Therefore it is essential to transfer old databases that you still want to use to version 2.0.

> ### Attention:
>
> During installation you will be asked whether you want to transfer an existing database. If, up to now, you have only ever worked with one database and if you have already updated it, there is no need to do any more.
>
> If, however, during the update, you answered the question "Would you like to transfer...?" with <No>, you can transfer the database retrospectively.

On the server, you will find the directory**...\HLAtyping_20\Tools**. In it there is the program

HLAtyping_1_to_2.exe

At the start, the following display appears:


```
HLA DB Transfer 1 to 2                                        X

      Would you like to transfer version 1.0 database to version 2.0 database?

            Yes                              No
```
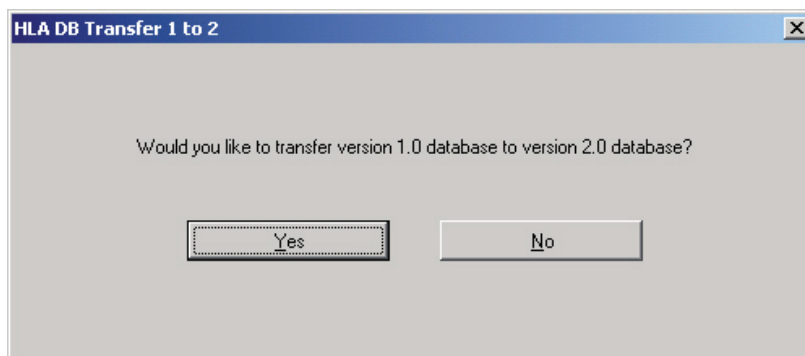
When you click <Yes>, the Windows **open** menu appears with the standard path having already been selected. If your database has been saved at another place, you can select it here:
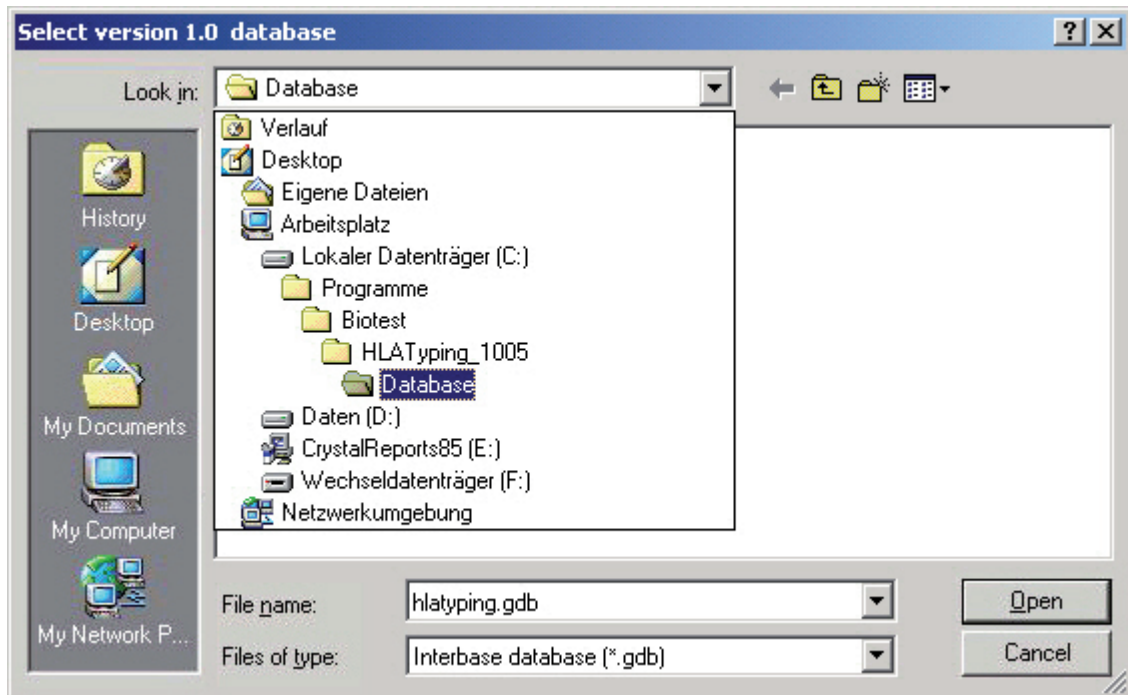
After clicking <open>, the display on the screen indicates that the transfer is being carried out:
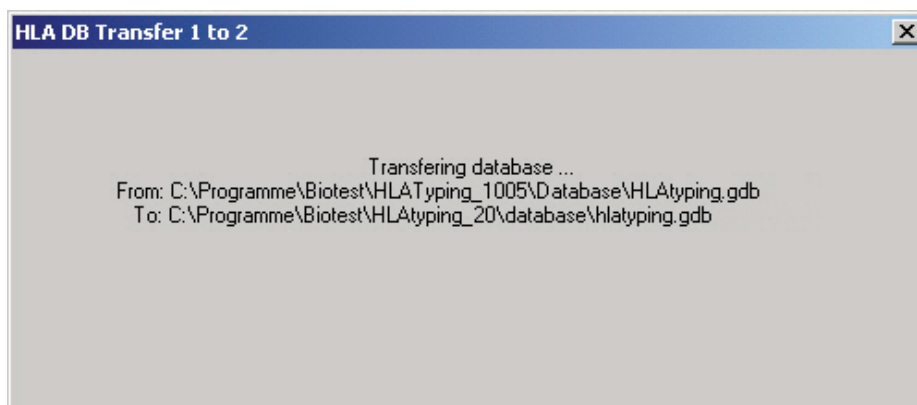
Depending on the size of database this can take some time.

→   The display will show whether the transfer has been successful:
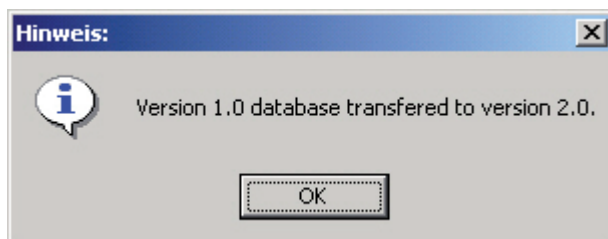
Attention:

If several databases are to be transferred to the new format, please note that, after the transfer, the database will be called **HLAtyping.gdb** and saved in the directory...\Database. If a database that is to continue to be used has already been filed there, this database must be saved at a different place in order to avoid loss of data through overwriting!

1.7   Features of HLA Typing Software

HLA Typing software features the following functions:

	Module
	Module
1	import of assay lots, informations about every imported lot in the assay list
2	display and administer active lots
3	define carriers
4	Search - database: administration of all data, extensive filter functions
5	variable path settings for import and database
6	variable setting for automatically generated plate name
7	Use of NMDP codes, as an addition to DNA and serological nomenclature
8	create tests manually
9	assign patients, change patient data
10	enter reactions
11	typing in batch mode or single typing with the typing dialog, individual release of each sample
12	online help and <F1> help
13	Import of automated platform data
14	interpretation of reader data
15	print results
16	export results
17	Import of patient data
18	administer allele frequencies
19	administer more than one lab
20	Multiuser features
21	Delete samples
22	Calculate result table for all results

2   First Steps

2.1   UserManager

It must be clearly traceable at any time which operator created a specific typing report. This is why the HLA Typing Software features the user management function which has proven valuable in the Biotest ELPHA and SSP Typing Software.

The software distinguishes between the Administrator, (who administers the users) and the Users, who are authorized to create the reports.

The administrator assigns the user names and determines which requirements a password must fulfill. He defines the rights for each user. An example: The confidence principle can be ensured by defining the rights for the evaluation and release. However, the administrator himself is not authorized to perform typing assays or release reports.

The user can change his password, but has no further access to the User Management feature. He can, however, carry out all laboratory tasks within the scope of his authorization (examples: administer, type or release lots or print reports).

When leaving his work station, the user can log out with a mouse click without closing the program.

While using the user management the following prompts may be displayed:

Do you really want to delete the user?
This appears if a user is accidentally about to be deleted from the list.

Password does not meet the criteria.
The password entered does not match the password criteria established by the system administrator.

Password not confirmed!
The repeated password is incorrect.

User name already present!
Attempt to enter a new user whose name already exists.

Password expired! Please enter a new password.
This appears if the password has expired according to the criteria established by the system administrator.

More than 3 failed attempts! Please inform the system administrator.
The system administrator has allowed a maximum of 3 failed attempts to enter a password. This limit has been exceeded.

User language not selected.
Each user needs to enter his dialog language.

2.1.1 The Administrator

The administrator assigns the user names and determines which requirements a password must fulfill. He defines the rights for each user. An example: The confidence principle can be ensured by defining the rights for the evaluation and release. However, the administrator himself is not authorized to perform typing assays or release reports.

After logging in, the administrator has access to the user management:

The password for the first log-in is ADMIN - admin. The administrator should change the password thereafter.

→   The user management dialog is displayed:
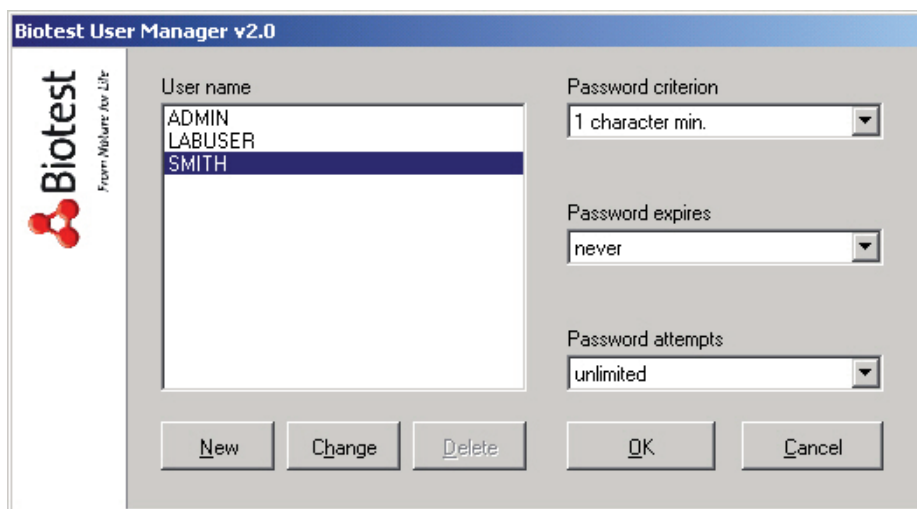
New: A new user is created → see User Management

Change: This is where the administrator can change his password.

Delete: The administrator cannot be deleted!

General settings for all users are made in the right column.

Password criterion: This is where you define how many characters a password must have and whether it must include digits.

Password expires: After a defined amount of time a new password must be entered upon logging in.

Password attempts: If the defined number of attempts is exceeded, the user can no longer log in and must see the administrator. (Are you the administrator? And you forgot your password? Please contact Biotest's Technical Support!)

Attention:

As shown below, the administrator has only limited authorizations within the HLA Typing Software. This feature is to ensure that not too many people use the software in their role as "Admin" and warrants proper documentation and traceability of the reports.
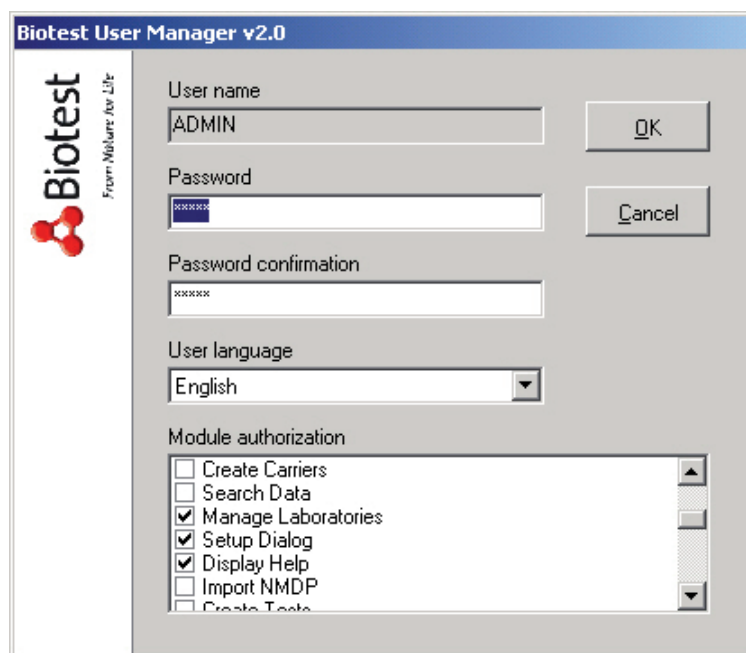
2.1.2 User management

The user can change his password, but has no further access to the User Management feature. He can, however, carry out all laboratory tasks within the scope of his authorization (examples: administer, type or release lots or print reports).

User management is the administrator's task, he is the only one who has access to this feature.
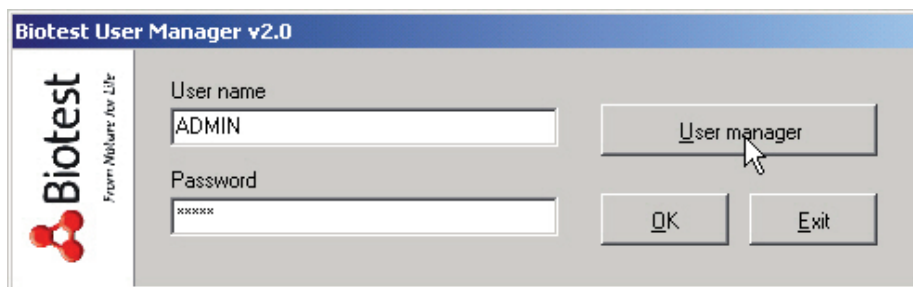
- Clicking on <User manager> displays the user management dialog:
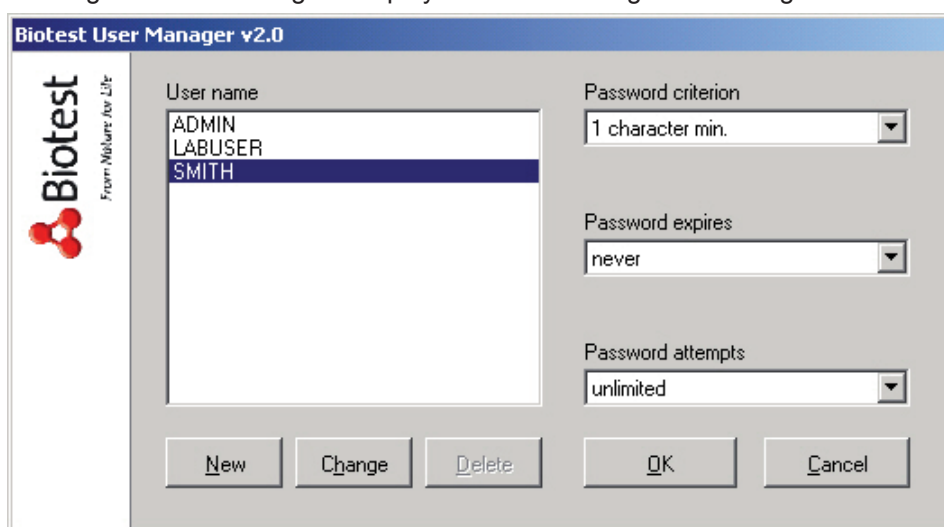
- General settings are made in the window to the right of the user list. They are described in the chapter The Administrator.

- Click on <New> to create a new user:
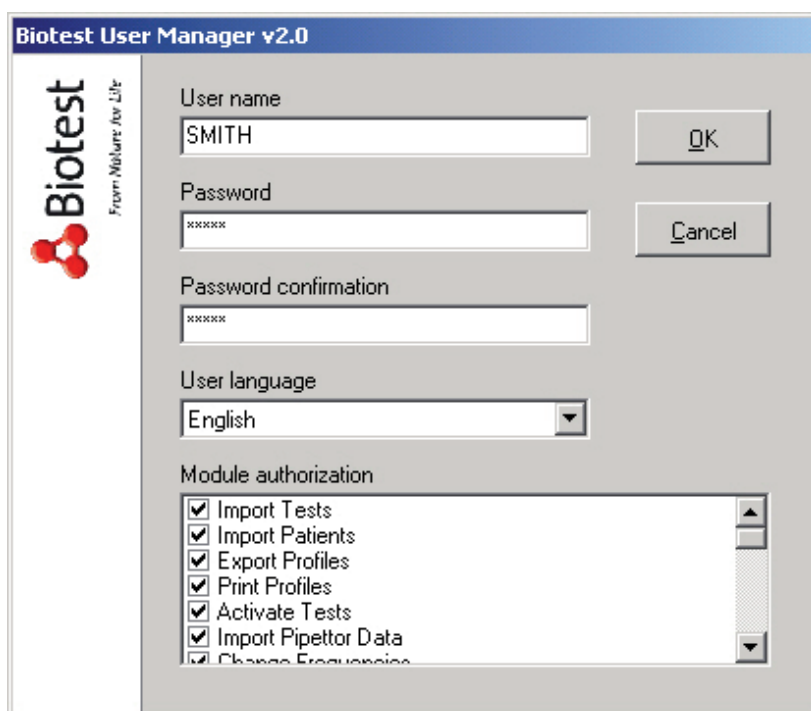
User name:

The user must enter this name during login. It should therefore be easy to memorize and not be too long.

Password:

When creating a new user, the user name in lower-case letters should be used as the password. The user is then to change his password upon his first log-in.

User language:

Please define for each user the language in which he works (currently German or English).

Module authorization:

User rights may also be granted only for certain modules of the software. In order to ensure the confidence principle, the rights for typing and the rights for results release may be granted to different users.

- By clicking the right mouse button you can activate a context menu to select or deselect all modules at the same time:
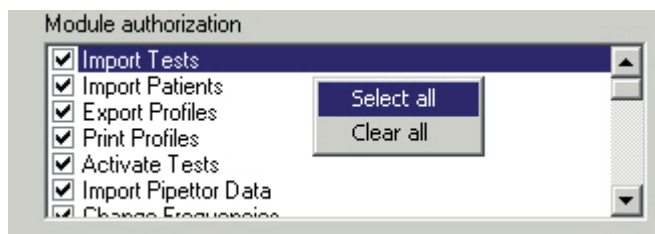
- Click on <OK> to save the user data.

2.1.3 ☺ ☹ User log-in/log-out

When leaving his work station, the user can log out with a mouse click without closing the program: just click on the sad face ☹!

- The new user clicks on the smiley face ☺: The log-in screen is displayed.
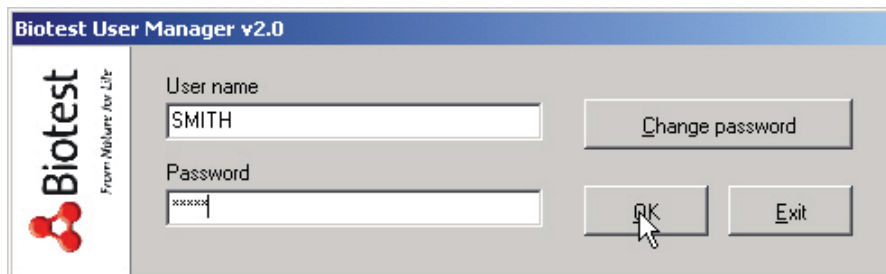
> → Enter your password, click on <OK> and start working!

- After entering the user name and the password, you can change your password (for example because it has expired). Do not click on <OK>, but on <Change password>. The following window will be displayed and allows you to enter your new password:
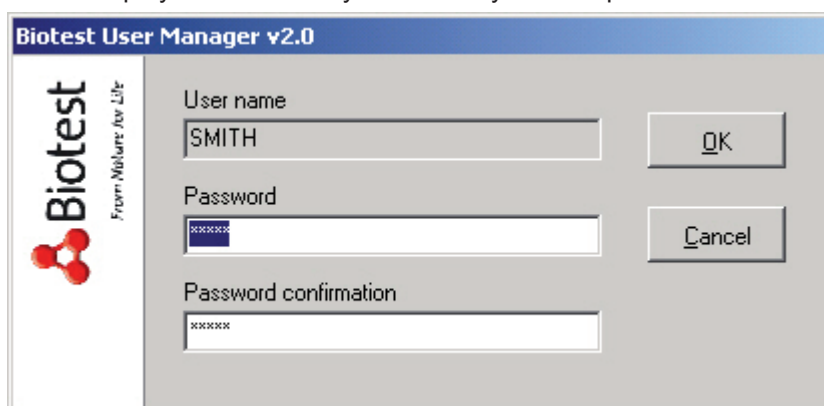
- Click on <OK> to get to the HLA Typing Software.

Attention:

You forgot your password? See your administrator for help!

2.2 Laboratory management

Select **Lab – Laboratory management**

This is where the basic settings for your laboratory are entered.
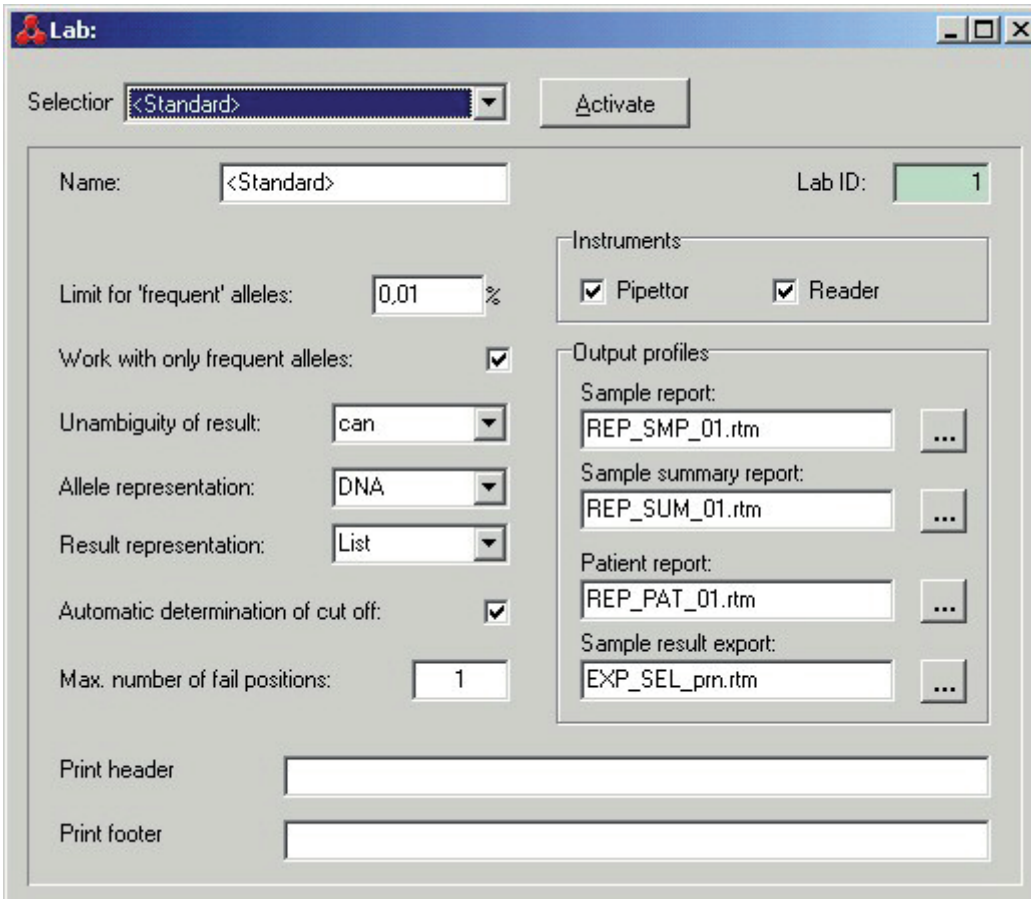
The Laboratory management allows for several laboratory profiles. Thus, you may enter different requirements for results representation, different print-outs etc. for the individual working areas.

Create a new laboratory profile

Select **Lab – Laboratory management** and click on ▯ "New" (at the top). You can now enter a name for the new laboratory profile.

Set options

On the left side, enter the conditions under which the newly created laboratory will routinely do its typing. If necessary, you can change these settings for a single typing. Thus you may, for example, set the maximum number of false reactions to 0 for your laboratory in order to obtain the clearest possible report. In case a sample does not produce any result, you can increase the number of false positions by increments until reasonable typing is ensured.

The individual options:

Limit for 'frequent' alleles

The limit defines from which frequency onwards an allele is considered to be frequent. An allele combination is classified as frequent if the frequency of all alleles of the combination is equal or highter than the limit. The higher the limit, the fewer results will be obtained when you have only frequent allele combinations displayed.

Only frequent alleles

Check this box when you want only frequent allele combinations displayed.

Unambiguity of result

> **can** – Result can be released without the user having to mark a specific allele combination as the most probable one.

> **should** – Upon release, a message is displayed saying that one allele combination should be selected as the most probable one. The result can, however, be released without this selection.

> **must** – One result must be marked as the most probable one or else the results cannot be released.

Allele representation

Nomenclature of results: DNA, serological or compressed

Results representation

List, string or NMDP codes

It is recommended to calculate NMDP Codes with the „Calculate result tables" routine (calculator icon in **Search** dialogue or "create result table" option, see chapter 4.1.7 and 4.1.8).

> ### *Note:*
> ---
> If „NMDP codes" is selected as result display for your lab, this could lead to extended waiting time while opening the typing window!
> ---

Automatic determination of cutoff

Turn automatic adaptation of the cutoff to current reaction strengths on/off

Max number of fail positions

Basic settings: 0, 1 or 2. Can be increased to 5 for individual typing.

Print Header

Freely definable header for all printouts

Print Footer

Freely definable footer for all printouts

Lab ID

This ID is assigned by the software.

Instruments

Check this box when using a reader and/or pipettor.

Output profiles

Output profiles are set on standard defaults. In case you have to change them, please proceed as follows:

- Click on "..." to display the selection window below in which you choose the appropriate profile for the results print-out. This selection must be made for the sample result, summary result and patient result.
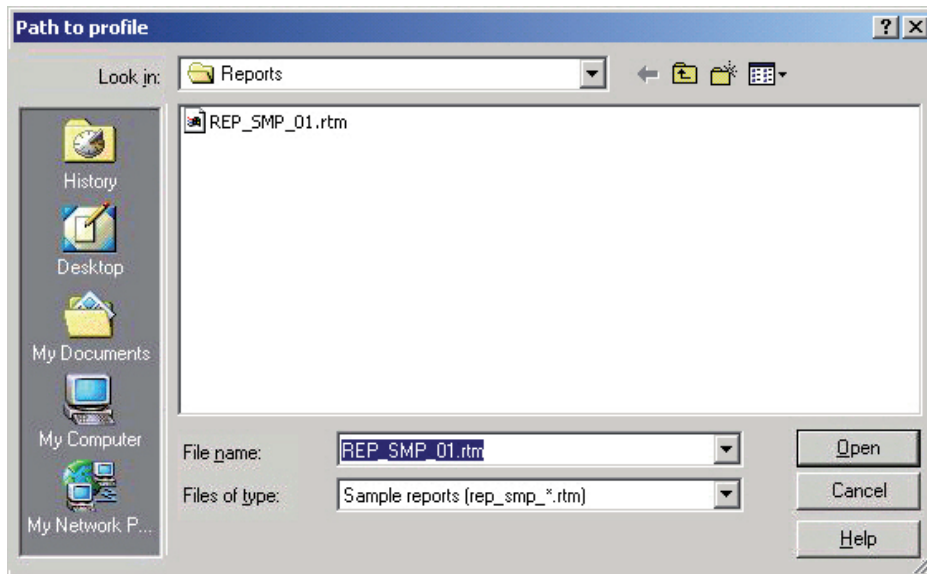
- Click on <Open> to enter the print profile.

→   This is an example of the completed laboratory management configuration:
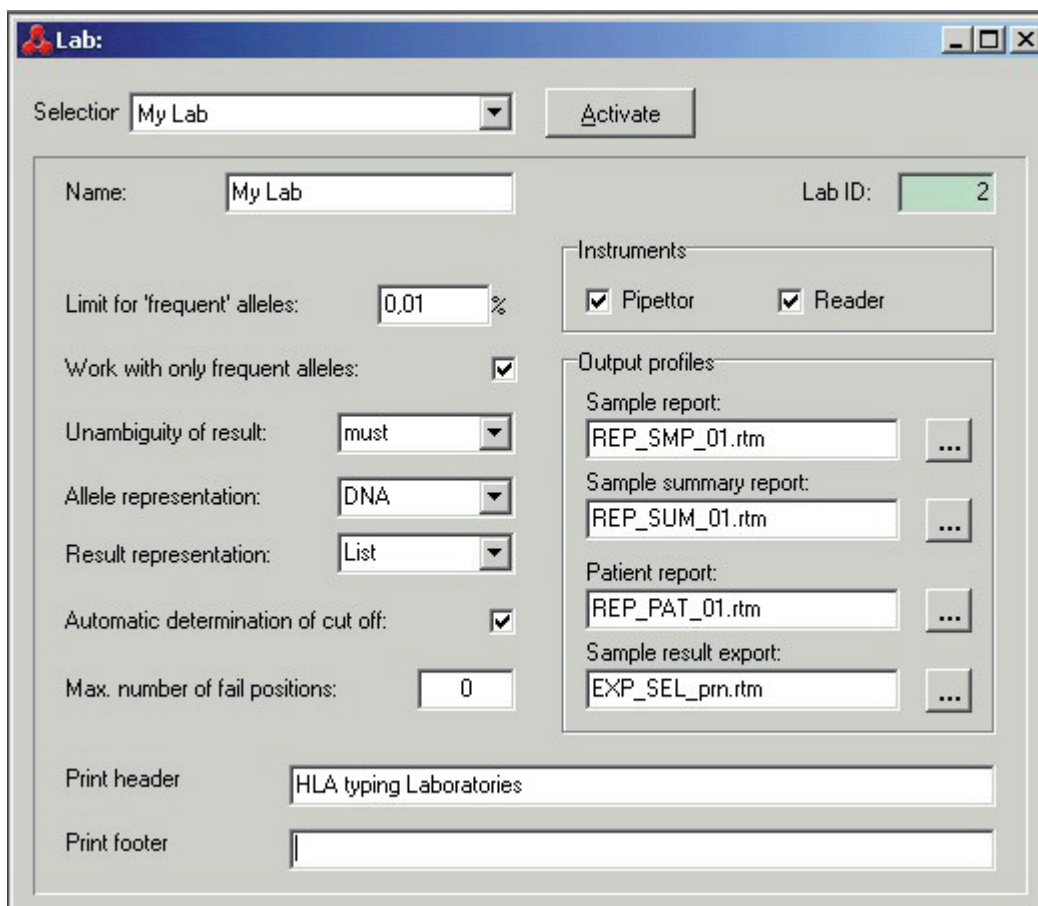
Activate lab profile

The individual labs or working areas can be selected in the "Selection" list. Activate your choice by pressing <Activate>.
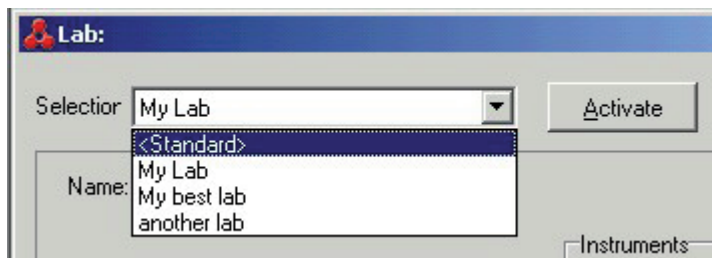
→   The selected lab is now active. The current lab is displayed in the status line of the program at the bottom left, next to the logged-in user:

2.3   Settings

Select **Extras – Setup**

These basic settings are required for the proper functioning of the software.
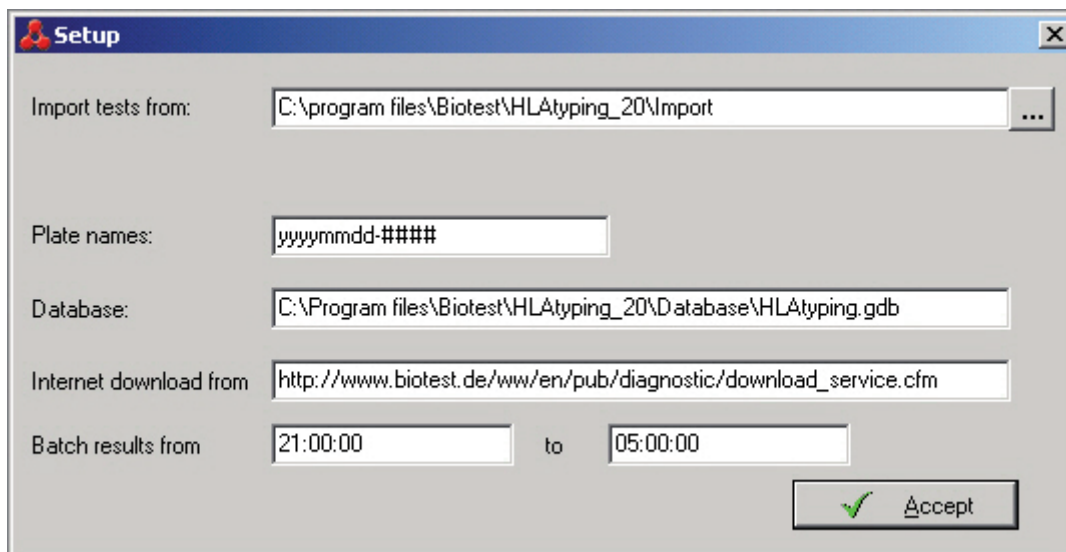
The fields should already be filled out as these paths were already created upon installation. This is where they can be changed if required.

Import tests from

Where do the assay lots come from?

→   Enter path here.

Plate names

Each plate needs an unique unambiguous name which can be generated automatically upon manual creation of a plate. This is where you define the system to be used to create a plate name. In the present example, the plate name consists of 4 digits for the year (=YYYY), two digits for the month (=mm), two digits for the day (=dd) and a four-digit serial number. If no entry is made here, the following error message will be displayed upon manual creation of a plate:

Hint: ✕

ⓘ Too few dummy positions (#) for automatic plate name

[OK]

Database

This is where all data are filed: lot data, typing results, patients…

In case you are part of a multi-user system, the database is provided centrally on the server for all work stations. The path entered here is therefore the path to the server.

Important information for your data-processing department:

If this file is lost, all patient and sample data are irretrievably lost. Regular backups are required!

Internet-Download from

In addition to the data on the batch disk, Biotest also makes the batch data available on the Internet. From here it can be imported as from a batch disk if you have Internet access. The entered path is the path to the Biotest Internet download area.

Batch results from... to...

If, during installation, the 'Result Tables' function has been activated, it is possible to use this function to set the times when these result tables are to be generated (see chapter 4.1.7).

Note:

It is recommended to set a time when nobody works with the software (e.g. at night) because this function takes up a great deal of the main memory.

2.4 ⊞ *Update of assay lots*

2.4.1 Download from the Internet

Before typing, the current lots must be imported to the software. Current lots are located in the "Import" folder after installation. For every new assay lot, you need to download the lot data from the internet and import them into the software as described in this chapter.

Biotest makes assay lot data available on the Internet where it is presented as ZIP data. It can be downloaded using the HLA Typing software.

First you must secure Internet access. You need to be online if you want to download batches from the Internet. The HLA Typing software cannot establish an Internet connection on its own.

Call up the menu **file- import – Lot download from Internet**…..

→ The Biotest download page will be activated in your browser:
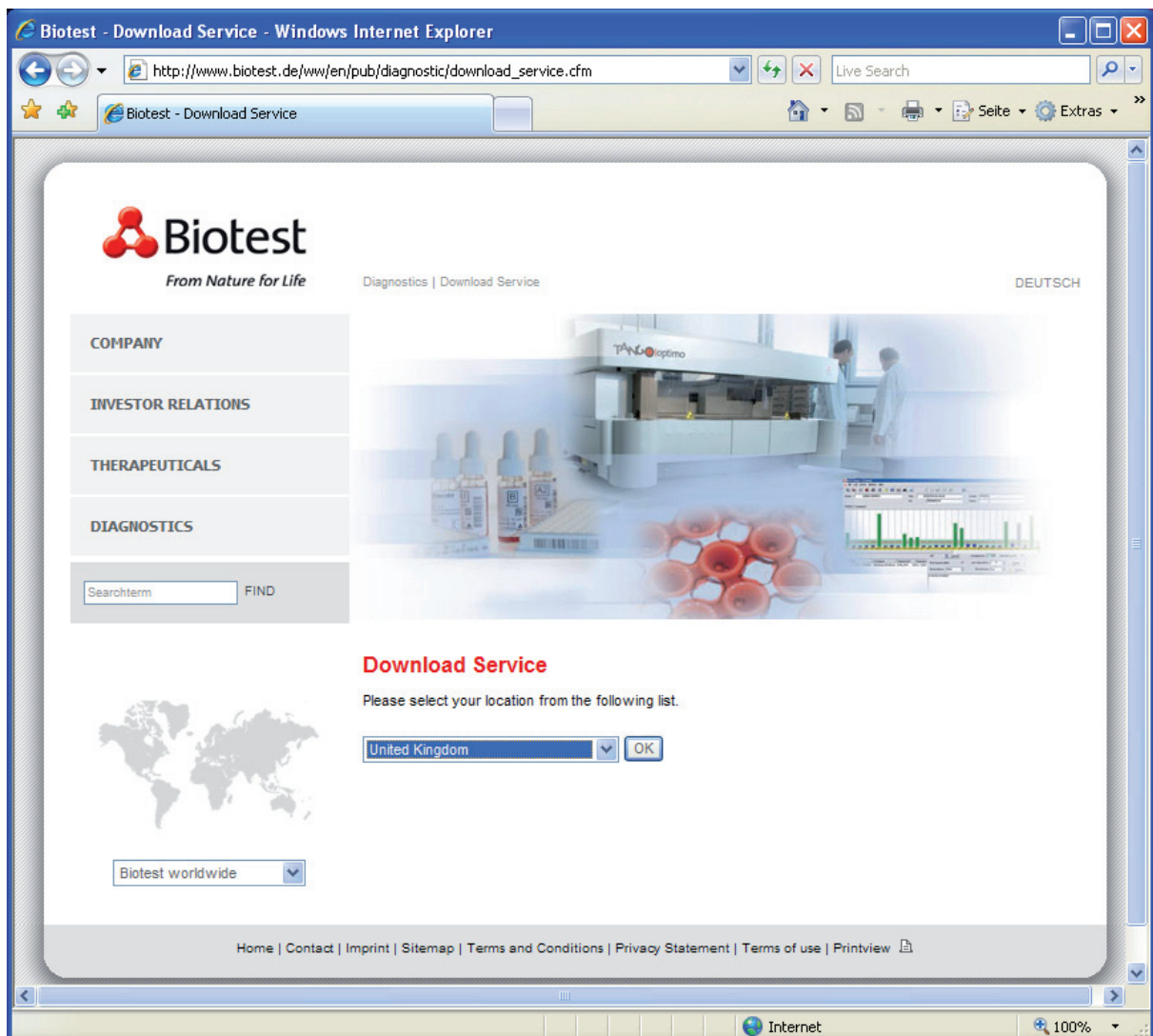
Select your country and click on the <OK> button beside the country list.

A list of the Biotest Diagnostics Divisions is displayed. Select **Transplantation ELPHA**:

A list of the ELPHA products is displayed. Select the assay you need lot data for:

All available lots and informations for this assay are displayed. You get the lot data by clicking on <SW>:

Further information is available for this batch:

PC (Pattern Chart): contains the current reaction patterns in PDF format, which is ideal for printing.

TI (Test Information): contains a file in *.zip format with the reaction pattern in Excel, details on the positioning of probes on the sequence in amino acid presentation, information on changes within this batch compared with preceding batches.

Software: the file name gives an indication as to which allel database and which variant of the reaction pattern the batch is based on. "DB2007-10V1" stands for: database from October 2007, reaction pattern version 1.

Depending on the settings of your computer, a security message is displayed. Proceed by clicking <OK>. On the next screen, store the data on your computer by clicking on <Save>:
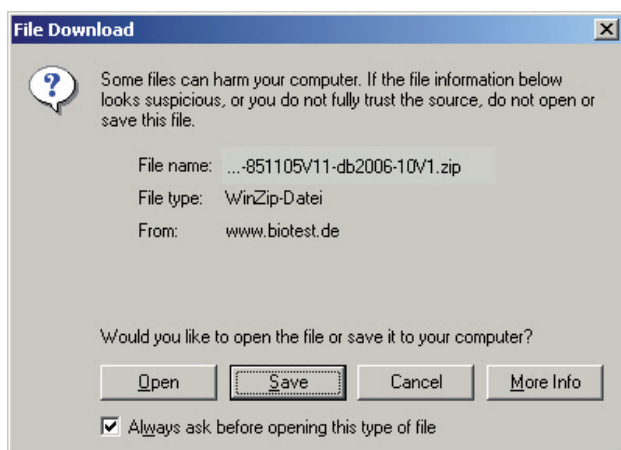
Next, you can select where you want to store the file: on the disk or on the USB stick (= removable medium) or directly in the import directory of the HLA Typing software:
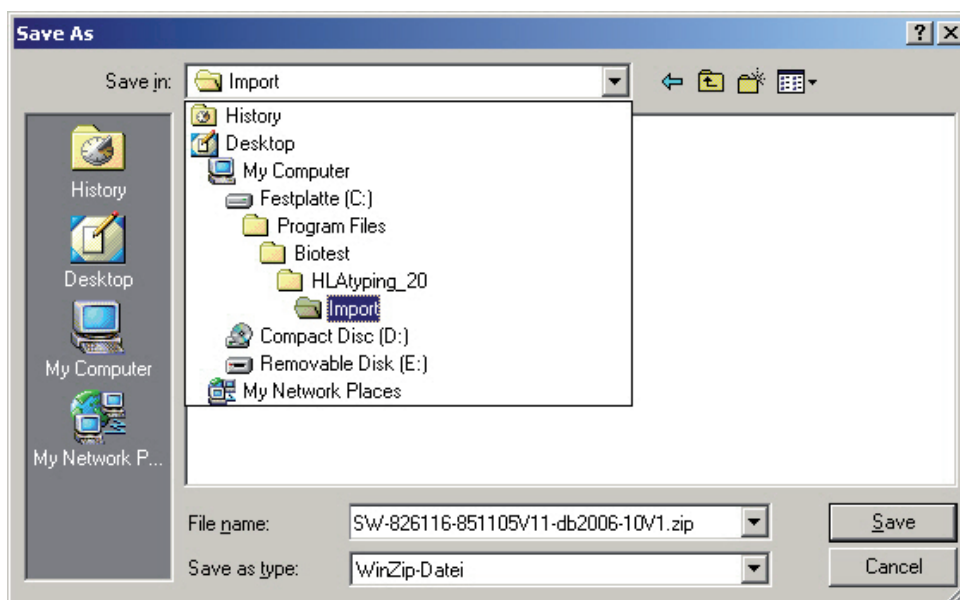
At this point, the file is not yet ready for import. The ZIP file needs to be unpacked first. This happens outside the HLA Typing software using a program such as WinZip. Only the *.tst file, which is contained in it, can be imported.

> ### Attention:
> Depending on the assay, you need to import one or more *.tst files. The other files contained in the ZIP file are not used in the HLA Typing Software.

2.4.2 Import of assay lots

Select **File - Import - Lot import from file** or

Press the <F3> key or click or the ![icon] icon.

→   The following screen is displayed:
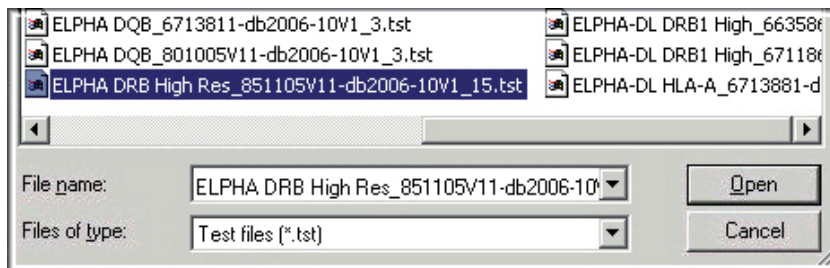
This is where you can select, if necessary, the location where lot data are stored. Select the assay to be added or updated. Click on <Open> to obtain the following display:
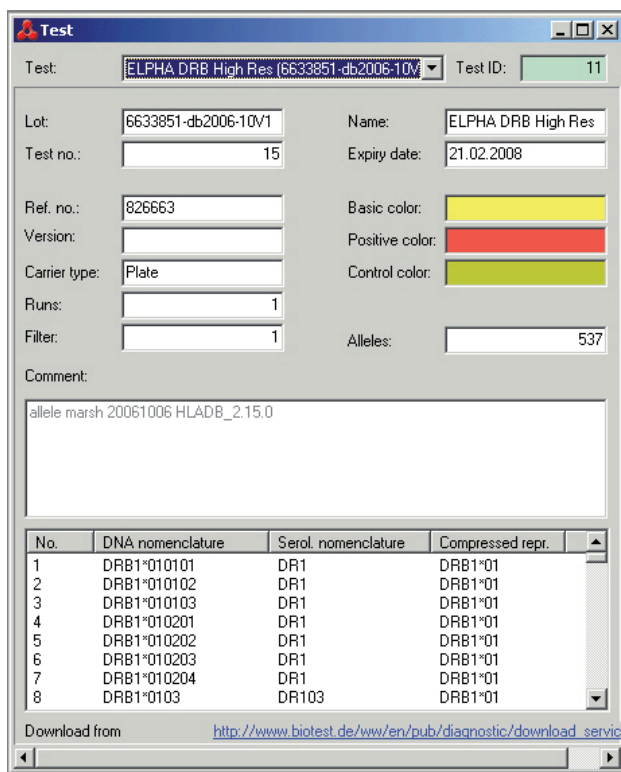
Subsequent to the data input, the new lot is stored by clicking on the ![save icon] key.

> *Attention:*
>
> Depending on the assay, the storage of lot data can take a few minutes.

In case you forget to save the data, the system will prompt you as follows:
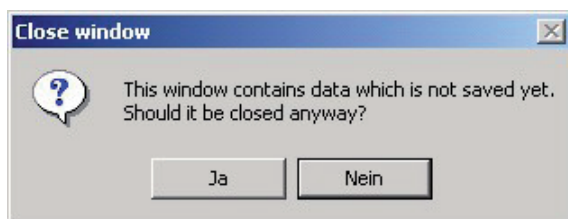
Click on <No> and save the data by clicking on the ![save icon] key.

You can import further assay lots by clicking on ![icon] key again.

A list of the imported, active assay lots will be displayed under **File – test list:**
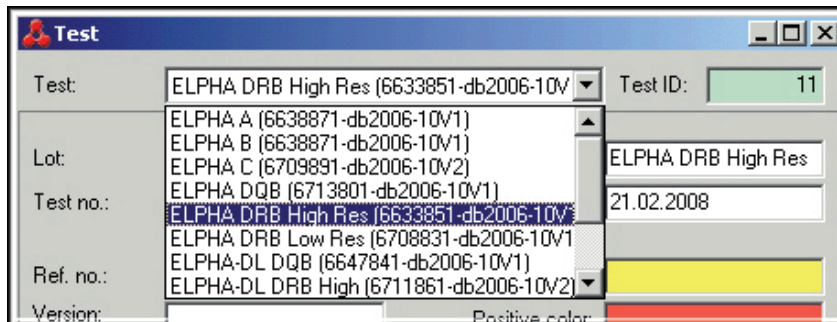
On selecting an entry, the allele list of this lot is displayed.

2.5 ![icon] *Activation of assay lots*

Before you can work with the newly imported lots you must activate them. You also have to tell the HLA Typing Software upon starting it which lots you are going to work with. To make things easy for you, the lots used the last time are displayed as active when starting the software.

The following display appears after logging in:
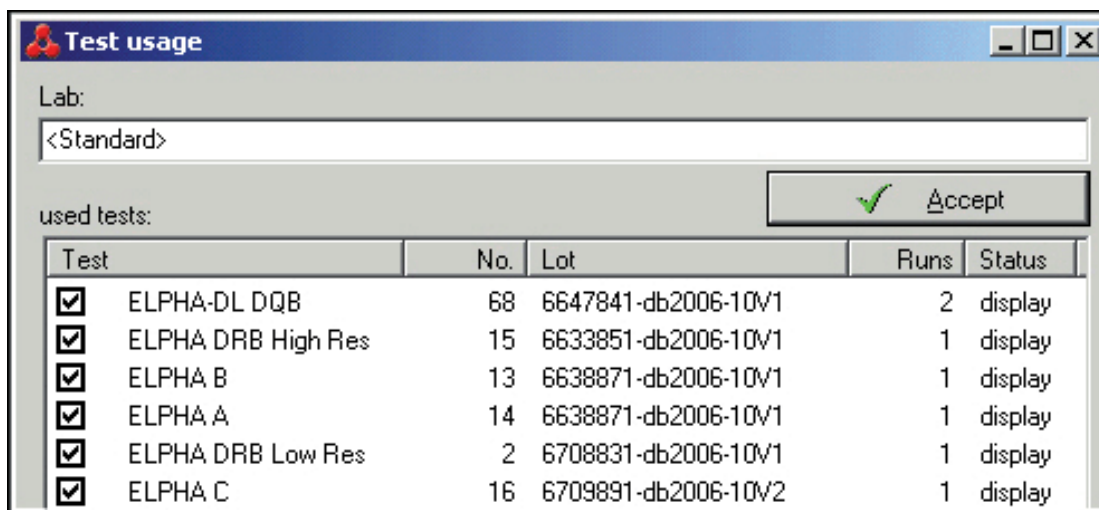
You can now switch to a new lot if appropriate.

> ### *Attention:*
> Only one lot per test can be active.

A new lot can be activated while the software is running. This means that if you are using two lots on one day you can switch to another lot before assigning or importing a test. Pressing the ![icon] key or using the menu option **Lab - Activate test lots** you will access the lot management screen.

To ensure optimum clarity even when handling long batch lists, you have the opportunity to hide batches that are no longer used from view:
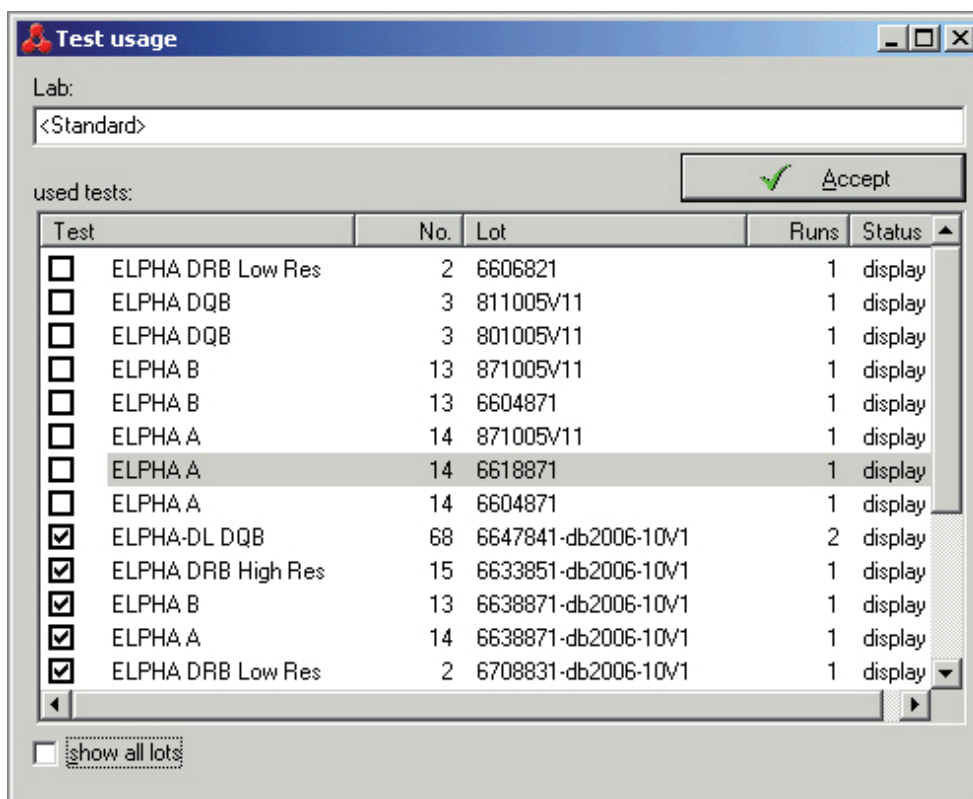
- First you tick "show all lots"
    - → A new <change status> button appears

- You use the mouse to mark the batch that you no longer need and click <change status>
    - → The status changes from "display" to "hidden":
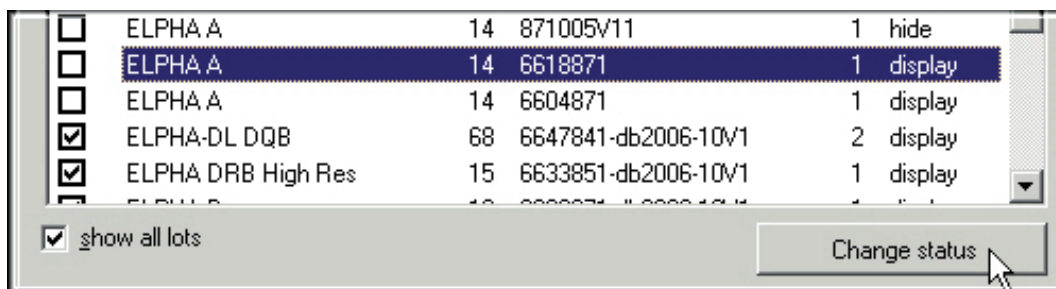
- This is repeated for each batch that is no longer required.

    Attention:

    This does not mean that the batches are deleted.

- After the status has been set for all batches, you untick "display all batches"
    - → Now the screen is much tidier

You can re-use a hidden batch by doing the following:

- Activate "display all batches"
- Set the status of the batch to "display" by using <change status>
- Activate batch
- To shorten the list, deactivate "show all lots"

2.6 ⬛ *Define carriers*

Before evaluating the first plates, you must tell the software which tests are located in which positions of your microtiter plate. This pattern is stored under a specific carrier name. Such a plate configuration is stored once and can subsequently be assigned to the microtiter plate to be read upon manual creation of a test.

If you load up data obtained by an automated instrument, the carrier is automatically assigned. The carriers for the import of data from automated instruments must be manually created once prior to the first import of a specific plate configuration. In this case it is essential that the plate configurations in the Pipettor settings (see Annex) and the configuration of the carrier defined in this place be identical. The carrier denomination must also be identical in both dialogs.

> ### Attention:
> After the standard installation, you will find all usual carriers that are required to work with Quickstep in the laboratory **Standard**, and you will find the carriers necessary to work with Tecan RMP in the laboratory **My Lab.**

If your individual test setup is missing, define the carriers as follows:

Either select **Lab – Define carriers** or click directly on ⬛ to display the following entry mask:
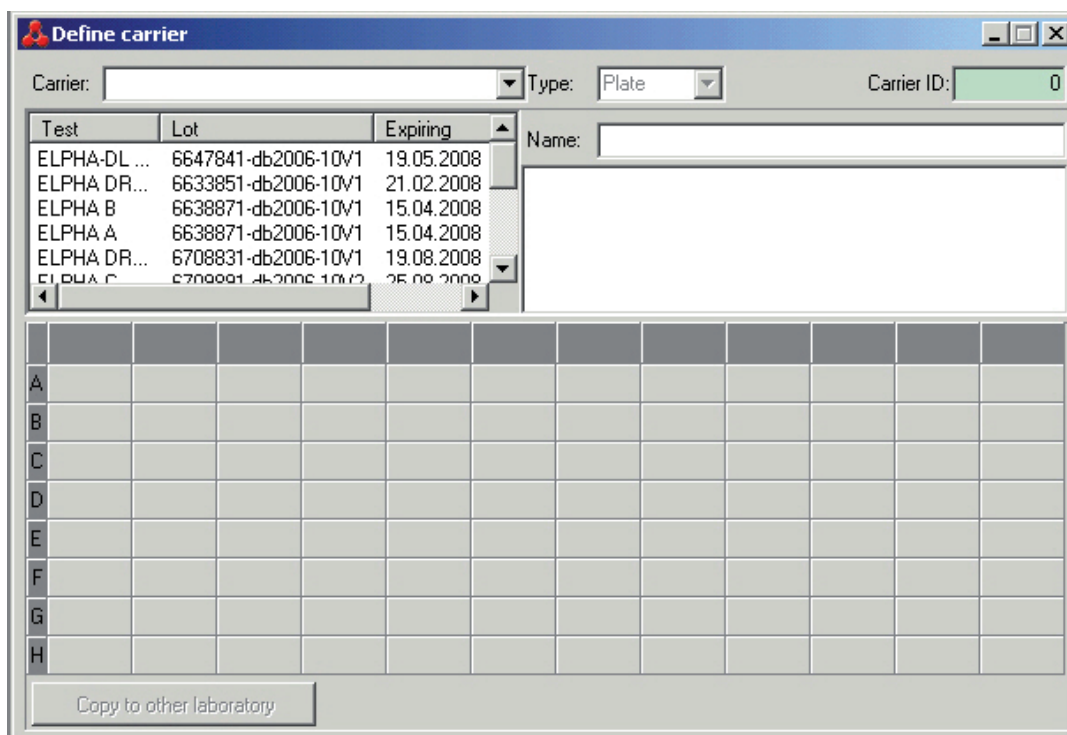
- First assign a name to the new carrier by entering it into the empty field "name".

  Without pipettor: Use a meaningful name such as "HLA-AB DL 2x"

  Tecan: Carrier name and plate configuration must be identical with the name and configuration used in the pipettor settings.

  For Tecan, this is always >TEC_*Test no.1_Test no.2_Test no.3*... For "HLA-AB DL 2x" it would therefore be**>TEC_63_64_63_64** , as HLA-A is test no. 63 and HLA-B is test no. 64.

  Quickstep: Carrier name and plate configuration must be identical with the name and configuration used in the pipettor settings.

  For Quickstep, this is always >QS_*Test no.1_Test no.2_Test no.3*... For "HLA-AB DL 2x" it would therefore be **>QS_63_64_63_64**, as HLA-A is test no. 63 and HLA-B is test no. 64.

- Then load the assays onto the plate. In the list at the left top of the mask you will see the available test lots. Only imported and activated test lots are displayed. Mark the lots on the plate by double-clicking on them. At the same time the selected tests are entered in the list at the top right-hand corner.

Don't forget to save your entries! Press ![save icon] at the top of the main screen.

This is what it looks like when it's finished:
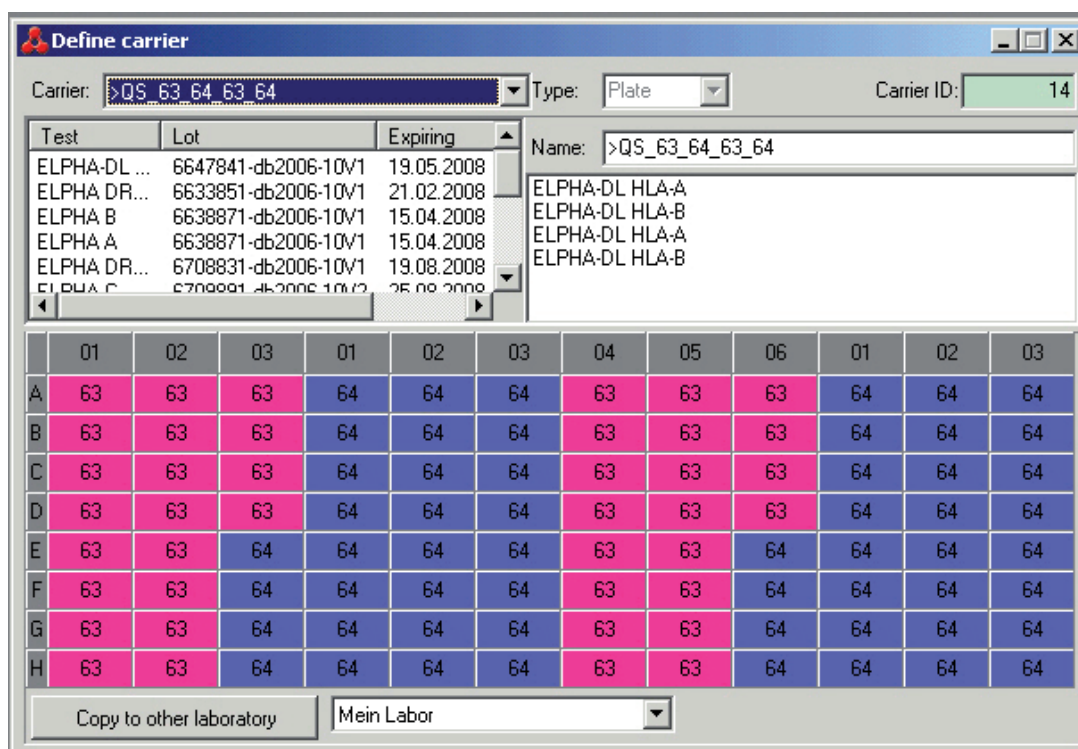
In case you want to create another carrier immediately after saving the previous carrier, press ![new icon] (new) at the top of the main screen.

If you require the same carrier in another laboratory, it needs to be set up only once. Afterwards, the laboratory that requires the same carrier can be selected underneath the microtiter plate. Then, you click on <Copy to other laboratory>. This will be followed by a confirmation that the carrier has been copied successfully.

2.7 Delete carriers

Made a mistake while defining a carrier? No problem! Click on

![icon] to display the entry mask. Select the carrier to be deleted:
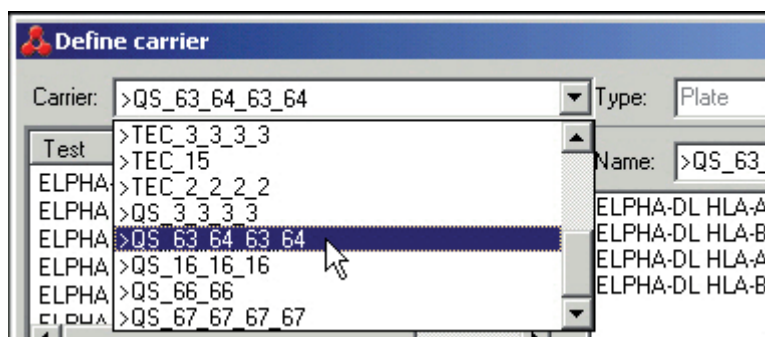
Then click on the waste bin at the top of the main screen: ![waste bin icon] Deleted!

> *Attention:*
> If a carrier was already used for typing, it can not be deleted.

3 Working with the Software

3.1 Patients

The following patient data can be stored and assigned to a sample:
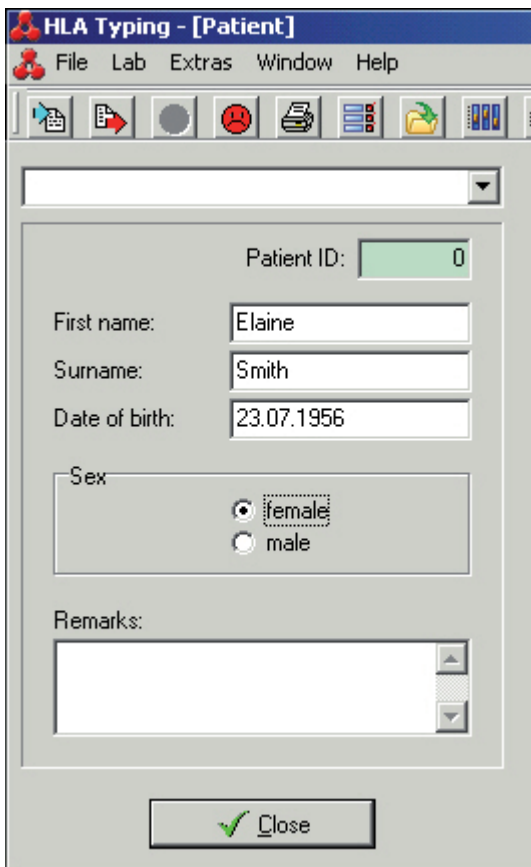
- Last name
- First name
- Date of birth
- Sex
- Comments

This allows you to print out patient-related result reports.

3.1.1 Create patients

Please proceed as follows to create a new patient:

- **File – Patient list** → The patient list appears
- **New** → A new patient can be added.
- Entry of patient data

> **Attention:**
> From version 2.0 ownwards the comments entered here will be printed too.

- Click on **save** und **new**, to create the next patient
- Click on <Close> to save the data and close the function.

3.1.2 Import patients

Patient data can also be imported from a LIMS.

These need to bear the file name "patient.pat".

Procedure:

- Select File – Import – Import patient data
    - →   The following window appears:
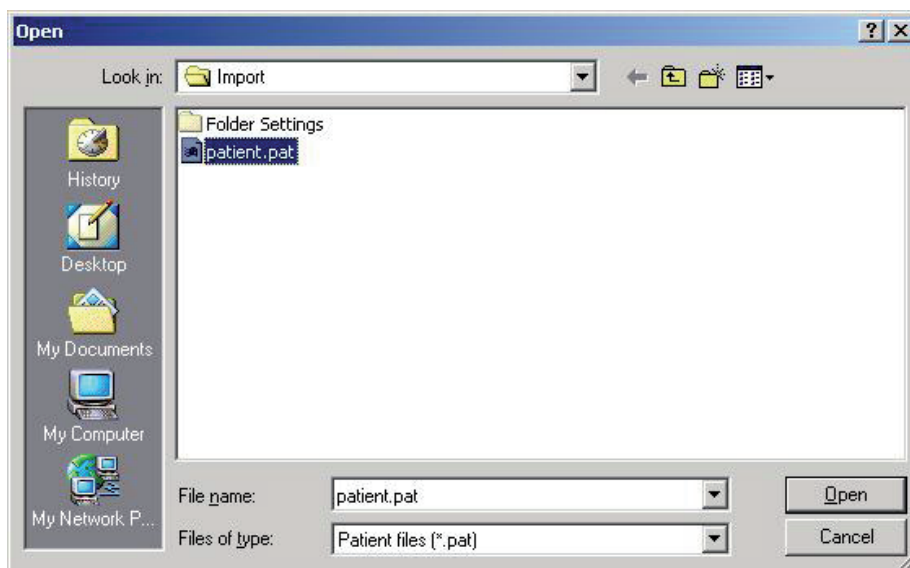
- Click on file and <Open>
    - →   The patient data in the file are imported.
- After the patient data have been imported, the transfer protocol is displayed:
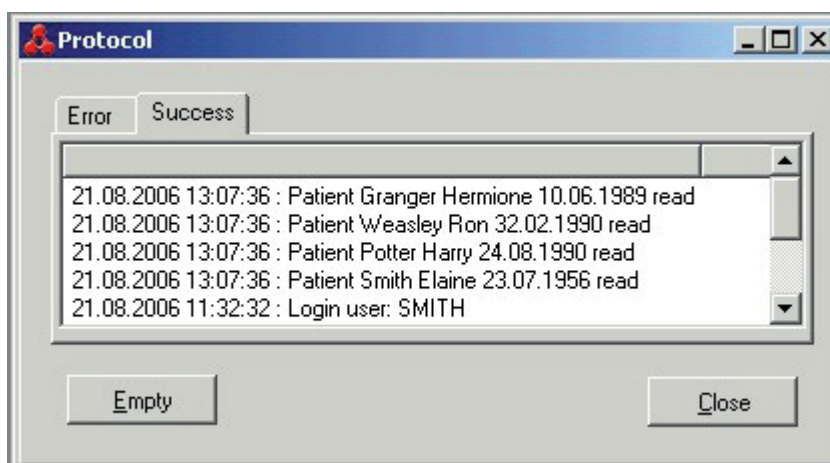
- Use <Close> to return to the Main Menu.

3.2   📂 Import of pipettor data

The HLA Typing Software can evaluate OD data generated by a pipettor such as Tecan RMP or Quickstep. Thus the automated processing is immediately followed by automatic evaluation.

The configuration of the pipettor interface is described in the annex. However, this task should be completed by your Biotest product specialist!

- Select **Lab - Automation platform** or press 📂 directly.

  → The system displays a list of plates that can be processed.

  ### Attention:

  If this function is not available, please verify that the pipettor is activated in the settings of the active laboratory (see Lab management). If this is not the case, check the "Pipettor" box and restart the software.

  In case this list is empty even though plates have been pipetted, please verify the following:

  - Is the path of the folder for the output files of the pipettor in the pipettor settings correct?
  - Has the proper pipetting instrument been selected?
  - Did the product specialist design the corresponding pipettor tests for your test (see chapter 5.2 'Pipettor configuration')?

Biotest Pipettor Interface 2.0.6.1

Biotest Quickstep   quickstep.dev

Instrument files folder

`C:\Program files\Biotest\HLAtyping_20\Import`   [...] [Start import]

| Status	Date	Time	Test name	Plate ID	File name
❗ not processed	06.10.2006	09:35:08	HLA_ABdl	AB_DL-011	AB_DL-011.TXT
❗ not processed	03.04.2006	14:17:16	HLA_ABdl	AB_DL-07	AB_DL-07.TXT
❗ not processed	04.04.2006	20:29:08	HLA_ABdl	AB_DL-11	AB_DL-11.TXT
❗ not processed	05.04.2006	13:59:44	HLA_ABdl	AB_DL-12	AB_DL-12.TXT
❗ not processed	03.04.2006	14:11:20	HLA_ABdl	AB_DL-13	AB_DL-13.TXT
❗ not processed	03.04.2006	14:14:02	HLA_ABdl	AB_DL-14	AB_DL-14.TXT
❗ not processed	02.06.2005	17:22:04	HLA_C	C-01	C-01.TXT
❗ not processed	30.03.2006	10:27:16	HLA_C	C-02	C-02.TXT
❗ not processed	13.03.2006	16:40:32	HLA_C	C-03	C-03.TXT
❗ not processed	10.07.2005	15:12:00	HLA_DQB	DQB-01	DQB-01.TXT
❗ not processed	04.05.2006	14:50:12	HLA_DQB	DQB-2	DQB-2.TXT
❗ not processed	04.05.2006	14:33:12	HLA_DQB	DQB-3	DQB-3.TXT
❗ not processed	04.05.2006	14:18:16	HLA_DQB	DQB-4	DQB-4.TXT
❗ not processed	03.04.2006	12:30:54	HLA_DRB1_dl	DRB1ALL-04	DRB1ALL-04.TX
❗ not processed	03.04.2006	12:32:50	HLA_DRB1_dl	DRB1ALL-05	DRB1ALL-05.TX
❗ not processed	29.04.2005	15:31:20	HLA_DRB1high_dl	DRB1HIGH-02	DRB1HIGH-02.T
❗ not processed	29.04.2005	15:38:30	HLA_DRB1high_dl	DRB1HIGH-03	DRB1HIGH-03.T

[Refresh] [Setup] [Exit]

☐ Archive imported files   `D:\HLAtyping_20\Archive`   [...]

- Highlight plate using the mouse or
- Keep the shift key pressed down and use the mouse (or use the Control key and the mouse) to highlight several plates at once.
- Click on <Start import>

  → When import is complete, imported plates are marked with a green tick and the file name is changed. This ensures that the plate will not be processed again during the next import.

After the import, the import protocol is displayed:
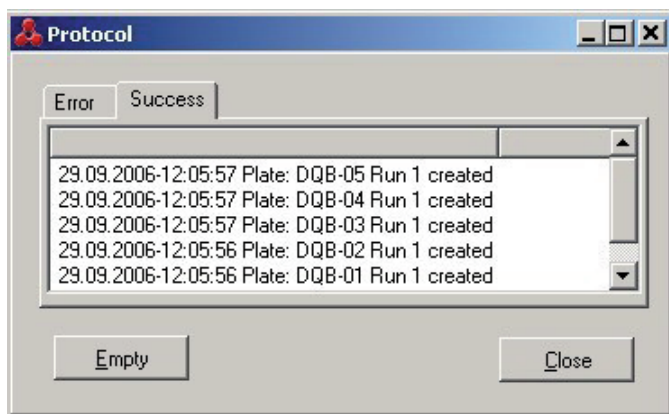
In case a plate could not be imported, the reason for this is displayed in the sheet <Error>. The protocol can be displayed any time by the menu **Help - Pipettor protocol**.

Imported plates can now be evaluated by batch typing.

Archive imported files

Check to activate the option. Then enter or select the path to the archive folder.

All imported files are transferred to the archive. So they are no longer displayed in the file list. This helps to keep the list clear.

3.3   Undo import

Import failed, for example because no carrier had been created?
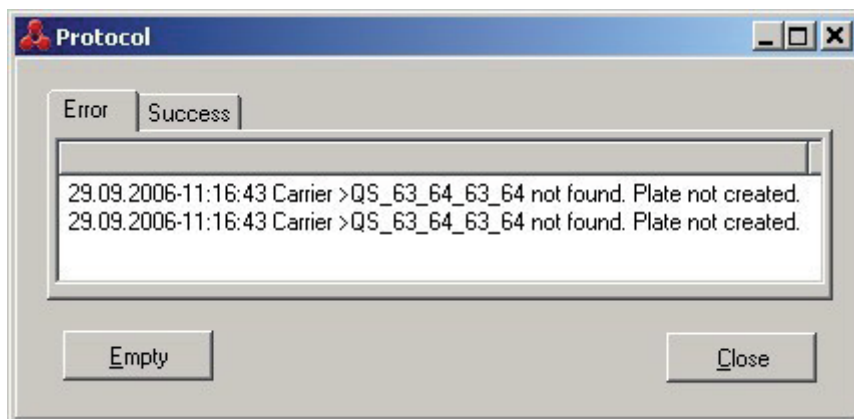
No problem – the import can be repeated at any time.

- First solve the problem causing the import failure (e.g. define carriers).

- Select ![folder icon]

- If the 'Archive imported files' option has not been activated: on the list of imported data, mark the plate that needs to be re-imported .

- If the 'Archive imported files' option has been activated: copy the desired plate file from the archive folder back into the 'Device files folder'.

- Right mouse key - Reset Status

  → The plate is classified as "not processed" (note the blue **!** and the re-established file name).

- If you would like to re-import all imported plates, just select "reset all status" of the context menu.
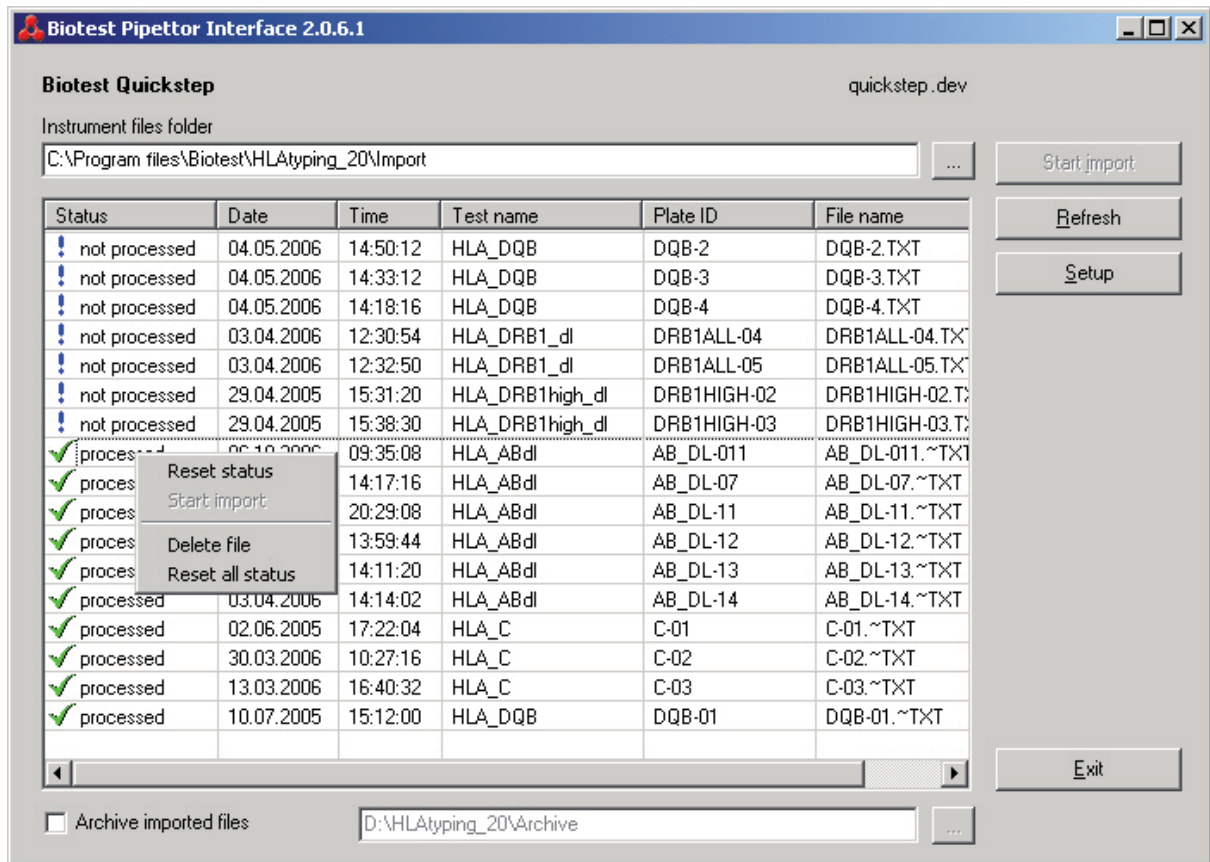
- The plate(s) can now be re-imported

4 📖 *Search*

4.1 Search - Main Window

This is your main working area. Samples are managed in the **Search** window. All tasks from creation to evaluation and report print-out are carried out in the **Search** window.
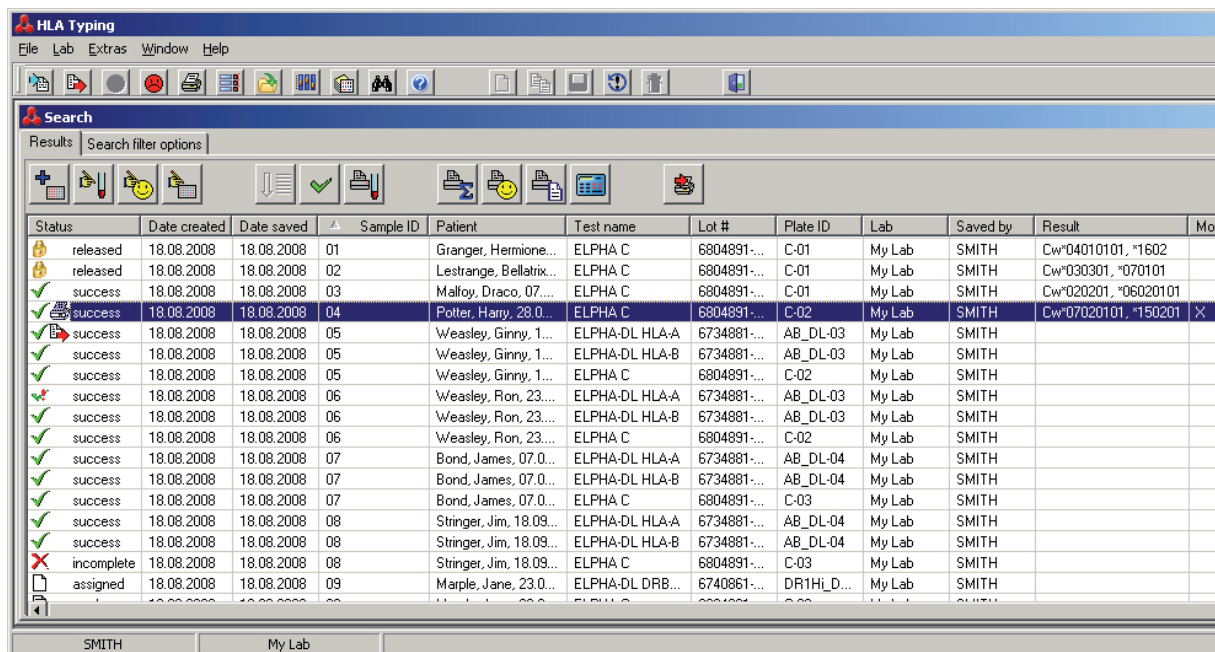
Explanation of the individual menu options

Buttons on the left side of the Main Menu: These are not used in the "Search" window.

Buttons on the right side of the Main Menu: These can be selected when appropriate.

Sample list:

Sample database. This is where the samples are displayed according to the filter settings. Samples can be selected and processed. Double clicking on one entry opens the next function that is required to process the sample (if the status of a sample has been "assigned", the "enter reactions" window appears).

Column headers:

Click on the column headers to sort the list by the corresponding column in the Search dialog.

Filter settings:

The filter settings determine which results will be displayed (see chapter 4.1.1).

Buttons

Create test:
Enter a new test: distribution of samples on the plate, sample IDs etc.

Change Sample ID:
As long as the sample is not released, the sample ID may be amended.

Assign patient:
This is where you can assign a patient to a sample that has not yet been released.

Enter reactions: Status ☐ assigned
Reactions are entered manually or using the reader.

Batch typing: Status 📄 read
Allows for the typing of several samples in one go.
The course of the typing will be displayed afterwards:

✔ successful typing

✔ successful typing. With the setting "only frequent alleles" in the laboratory management, the setting was changed to "all alleles" in order to find a result.

✘ typing incomplete: typing parameters and reactions need to be checked

Typing: Status 📄 read
Typing of a single sample

Print sample result:
Print results for the selected sample

Print summary result:
Print all test results for this sample ID.

Print patient result:
Print all test results for this patient.

Print Search list:
The list shown in the search window is being printed. The print-out lists the filter settings with which the print-out has been produced.

Calculate all results / Update NMDP codes:
All results are calculated for the chosen assays.

After the registration of new codes at the NMDP, the NMDP results can be updated.

This can take time. During this time, it is not possible to continue working with the software.

Export result:
Export the sample to programs such as Excel.

If required, in addition to the standardized laboratory profile, a XML file can be issued, which can be imported using the Helmberg Score. When doing so, consider the standardized setting for the issue profiles in the laboratory administration and the options for the XML file in the **File – Export** menu.

Delete sample: This Button is only accessible if you are authorized to delete samples. A security check will be carried out. If you answer this with <Yes>, the samlpe will be deleted:
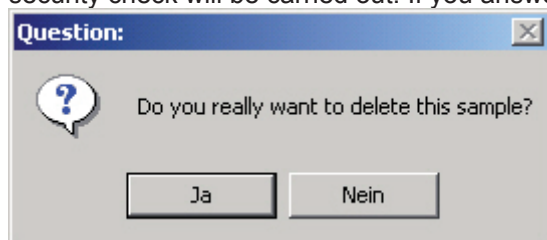
The plate entries/raw data referring to the sample will also be deleted.

| SMITH | <Standard> |

Bar below the sample list:

This is where the current user and the current lab profile are displayed.

4.1.1 Filter settings

Search – click on "Filter settings" tab.

Without filters, your **Search** window would soon become too crowded. This is where you select which samples should be displayed. Examples:

- only today's samples
- only results of untyped samples
- only the results for patient John Public
- only the DQB tests of the last 5 days that were processed by you
- searching for a specific sample or plate etc.
- searching for a specific allele, while "%" as a wildcard must be set in front of the exact allele name, e.g. %A*2301

> *Attention:*
>
> If the database is extensive, the search for alleles can be time consuming!

4.1.2 Manual creation of tests

If the tests are evaluated visually or using the reader, the plate is created manually. This takes only a few steps:

Search - **Create test**

→ A window appears into which you enter all required data from top to bottom:

Carrier
Select the matching plate layout from the list.

Plate
Select a unique plate number by pressing <Create> or enter data manually

Sample ID
Can be entered here.

Patient
Can be assigned here. Press <...> to view the patient list. Select patient and click on <Accept>. The smiley 😊 shows you that a patient was assigned to this sample.

> ***Attention:***
> Make sure that the entered data (selection of carrier, sample sequence, ...) really match your assay configuration!
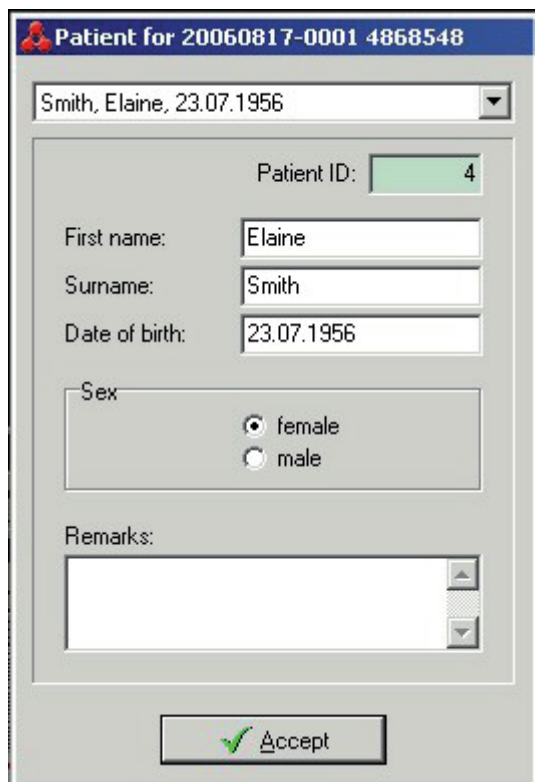
💾 Don't forget to save the data!

Newly created samples are marked as 🗋 "assigned" in the **Search** window.

4.1.3 Patient assignment

Patients can be assigned in two places:

1. Upon manual creation of the test

2. Select Sample in the Search window in order to access the function <Assign patient>. Click on <Assign patient> to display the patient list.
   In the header, the plate number and the sample number is displayed:

You can now highlight one patient in the list. Press <Accept> to return to the **Search** Menu.

> ### *Attention:*
> Patients can be assigned only as long as the sample has not been released!
>
> Exception: if, when installing the software, you chose the option that released results can be edited, the assignment of a patient is possible ever after the release.

4.1.4 Enter reactions

4.1.4.1 Enter reactions manually

Search - highlight the selected entry (Status ☐ assigned)

Enter reactions

→ An entry mask is displayed showing the plate with the corresponding sample IDs.

Positive reactions are highlighted by a single mouse click.
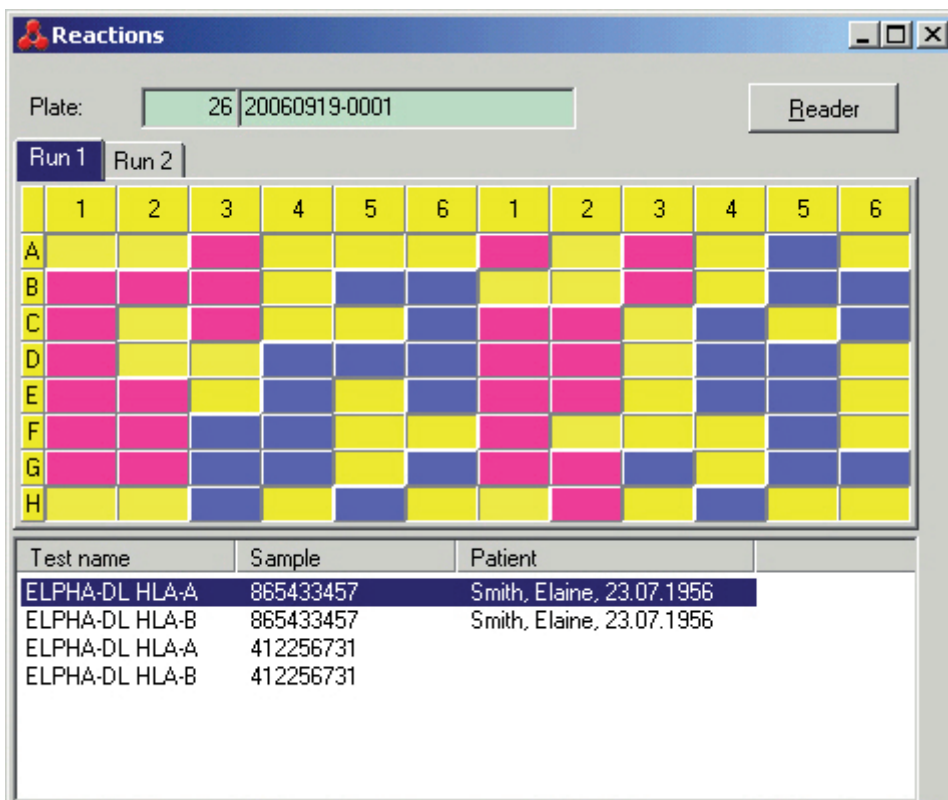
Don't forget to save your data 💾!

→ The sample will be highlighted in the "Search" window as 📄 "read".

4.1.4.2 Enter reactions using the reader

Search - highlight the selected entry (Status ☐ assigned

Enter reactions

→ An entry mask is displayed showing the plate with the corresponding sample IDs.

Press <Reader> to display the Reader window.

> ***Attention:***
>
> Should the screen not show the <Reader> button, please check the Reader box for your active laboratory (see Lab Management).
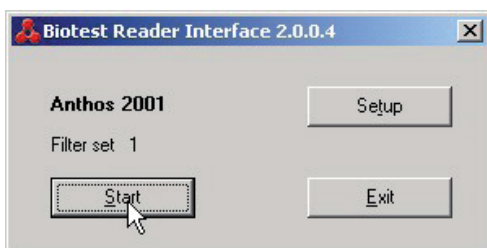
Press <Start> to read the plate. The reactions are displayed.
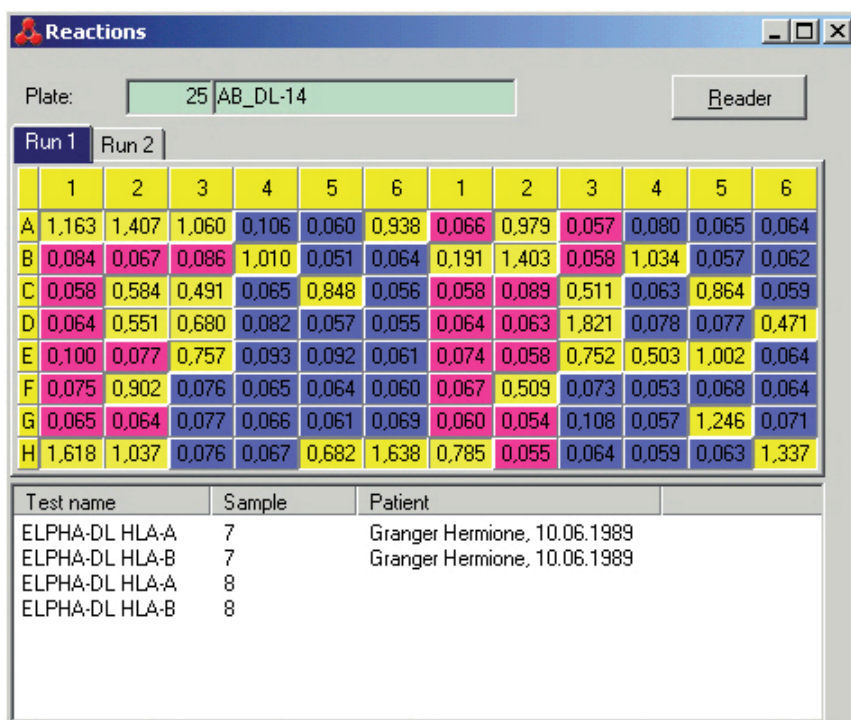
Attention:

In case the message

is displayed, please verify that
- the reader is switched on
- the reader is connected to the PC
- the appropiate reader driver is selected
If these measures don't help, there could be a problem with the reader settings.
Please contact your Biotest product specialist.

Don't forget to save your data !

The sample will be highlighted in the "Search" window as "read".

Attention:

If, by mistake, you read a plate incorrectly, it is possible to re-read the plate after a warning query.

Prior to using the reader for the very first time to read plates, please have your Biotest product specialist set the correct parameters for your reader (see Annex – Reader configuration).

4.1.5 Batch processing

Search - highlight several samples with read status 📄 "read" using the Control key + left mouse key or using the shift key + left mouse key

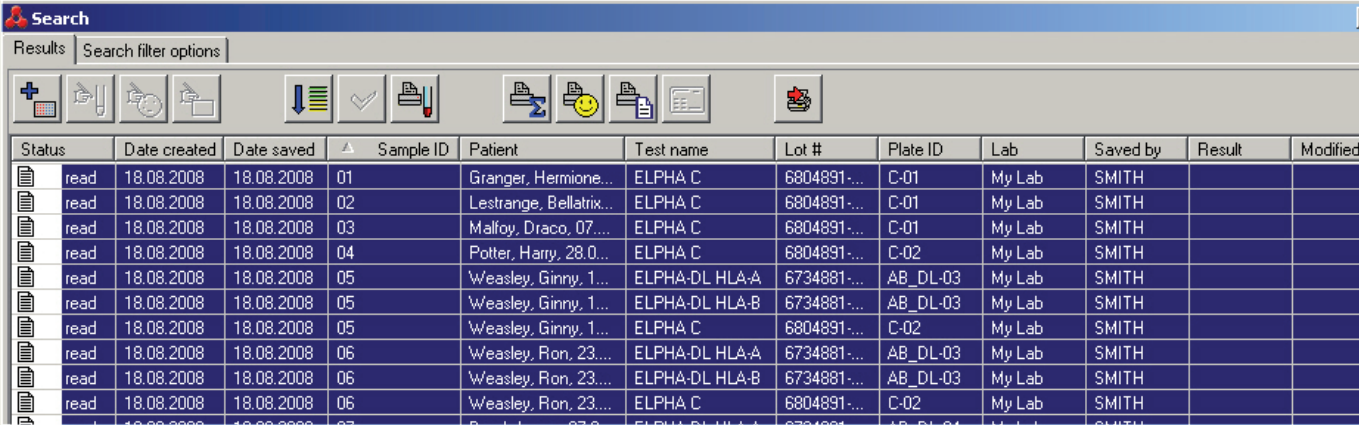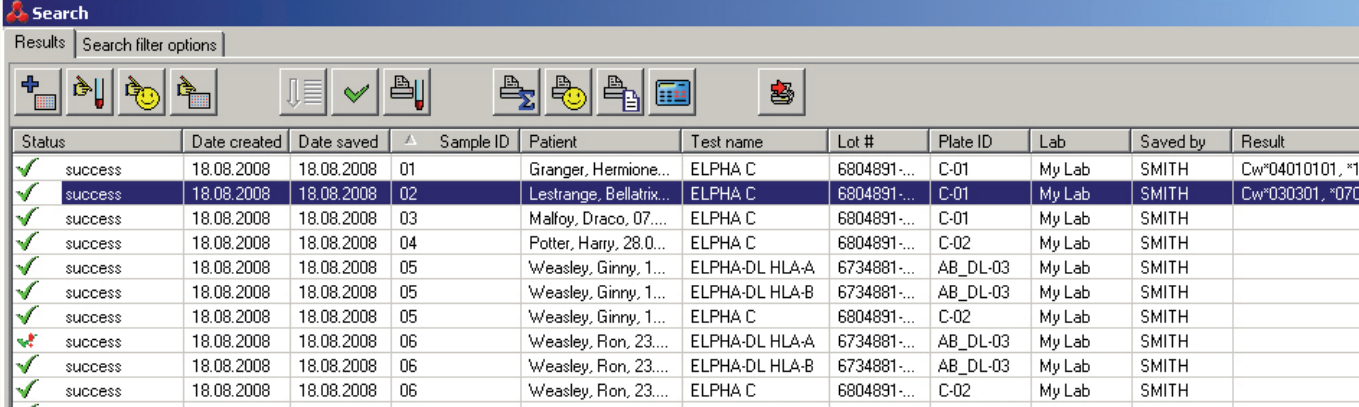| Status		Date created	Date saved	▲	Sample ID	Patient	Test name	Lot #	Plate ID	Lab	Saved by	Result	Modified
📄	read	18.08.2008	18.08.2008		01	Granger, Hermione...	ELPHA C	6804891-...	C-01	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		02	Lestrange, Bellatrix...	ELPHA C	6804891-...	C-01	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		03	Malfoy, Draco, 07....	ELPHA C	6804891-...	C-01	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		04	Potter, Harry, 28.0...	ELPHA C	6804891-...	C-02	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		05	Weasley, Ginny, 1...	ELPHA-DL HLA-A	6734881-...	AB_DL-03	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		05	Weasley, Ginny, 1...	ELPHA-DL HLA-B	6734881-...	AB_DL-03	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		05	Weasley, Ginny, 1...	ELPHA C	6804891-...	C-02	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		06	Weasley, Ron, 23....	ELPHA-DL HLA-A	6734881-...	AB_DL-03	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		06	Weasley, Ron, 23....	ELPHA-DL HLA-B	6734881-...	AB_DL-03	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		06	Weasley, Ron, 23....	ELPHA C	6804891-...	C-02	My Lab	SMITH		
📄	read	18.08.2008	18.08.2008		07	Bond, James, 07.0...	ELPHA-DL HLA-A	6734881-...	AB_DL-04	My Lab	SMITH		

The selected samples are typed.

-   The sample status is set on ✔ "successful" if a result has been identified for the sample.

-   ✔ successful typing. With the setting "only frequent alleles" in the laboratory management, the setting was changed to "all alleles" in order to find a result.

-   ✗ typing incomplete: typing parameters and reactions need to be checked

Status		Date created	Date saved	▲	Sample ID	Patient	Test name	Lot #	Plate ID	Lab	Saved by	Result
✔	success	18.08.2008	18.08.2008		01	Granger, Hermione...	ELPHA C	6804891-...	C-01	My Lab	SMITH	Cw*04010101, *1
✔	success	18.08.2008	18.08.2008		02	Lestrange, Bellatrix...	ELPHA C	6804891-...	C-01	My Lab	SMITH	Cw*030301, *070
✔	success	18.08.2008	18.08.2008		03	Malfoy, Draco, 07....	ELPHA C	6804891-...	C-01	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		04	Potter, Harry, 28.0...	ELPHA C	6804891-...	C-02	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		05	Weasley, Ginny, 1...	ELPHA-DL HLA-A	6734881-...	AB_DL-03	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		05	Weasley, Ginny, 1...	ELPHA-DL HLA-B	6734881-...	AB_DL-03	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		05	Weasley, Ginny, 1...	ELPHA C	6804891-...	C-02	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		06	Weasley, Ron, 23....	ELPHA-DL HLA-A	6734881-...	AB_DL-03	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		06	Weasley, Ron, 23....	ELPHA-DL HLA-B	6734881-...	AB_DL-03	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		06	Weasley, Ron, 23....	ELPHA C	6804891-...	C-02	My Lab	SMITH	
✔	success	18.08.2008	18.08.2008		07	Bond, James, 07.0...	ELPHA-DL HLA-A	6734881-...	AB_DL-04	My Lab	SMITH	

> ### *Attention:*
>
> If, in the laboratory administration, the automatic cutoff has been chosen as standard setting, this will only be used during batch typing if the software was unable to establish a result without shifting the cutoff.
>
> In order to produce clear results, batch typing always works with the "0 error" setting.
>
> The samples are just typed, not released. Each sample must be verified and released individually in the typing dialog!
>
> In batch processing mode, the software uses the lab settings selected while importing reader or pipettor data.

4.1.6 Typing dialog

Search – Select unreleased sample - Typing.

Not only the obtained results are displayed in the typing window; this function offers additional options to edit a result.
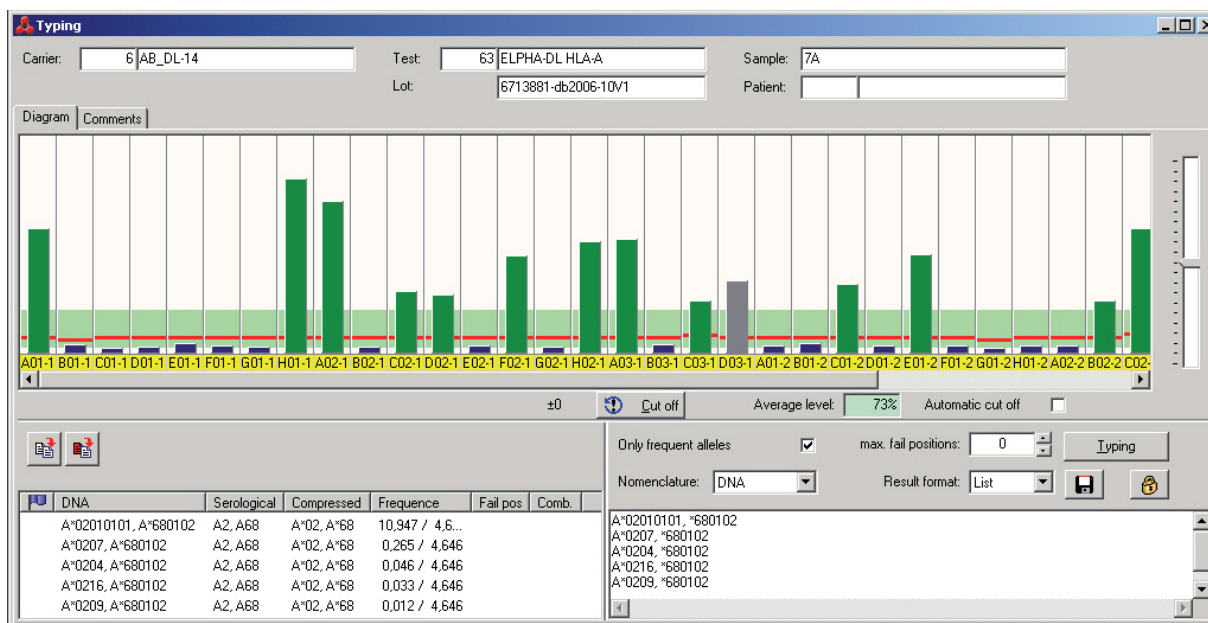
4.1.6.1 Typing

After the cutoffs and typing options have been entered, click on <Typing> to start the process.

In case no result is displayed or the display shows another result than the optimal one, the settings can be changed prior to re-typing. The result is released only when you press <Release>.

> **Attention:**
>
> Unknown reaction patterns are not inevitably due to faulty PCR reactions. They could also be the result of contamination, handling errors during the assay process or the existence of a new allele. As necessary, the assay has to be repeated.

The list of results contains the names of alleles, the serological equivalents, the allele groups and a number indicating the "frequencies" of the alleles in percent. The values refer to the proportions of the alleles in typing studies. An update of the data is published every 2-3 years in the "HLA Dictionary". Even though this analysis is not meant for an exact calculation of allele frequencies, the numbers are useful for an estimation of the probability of a combination.

> **Attention:**
>
> If you do not release the result, it must be stored before you leave Typing!

4.1.6.2 Sample data

The following data are shown:

- Carrier (Plate number)
- Test ID and Test name
- Sample ID
- Lot number
- Patient's last name and first name (if available)

4.1.6.3 Graph and cutoffs

Graph

Each OD value is displayed in the form of a bar; the height of the bar is proportional to the strength of the reaction. The bars can have different colors:

control: gray
positive bar: green
negative bar: dark blue
false pos./neg.: red
weakly reactive probes for all alleles (weak): yellow
probe with unknown or not assessed reaction (uncertain): violet

The permitted range for the cutoff is shown in light green, the cutoff itself as a red line.

Upon manual entry of results, positive reactions are shown with their maximum OD value, while negative reactions are displayed with an OD value near 0.

If you wish to change a reaction from positive to negative or vice versa, you can click on the corresponding bar using the **right mouse key** and select "Toggle wrong". The color of the bar changes to red. Upon typing, this reaction will only be assessed the way you marked it and not on the basis of its OD value. To undo a change, proceed the same way.

Changes will not only be marked in colors but appear in the system commentary, too.

If you click on one individual probe, information on this probe is displayed in the bar chart.
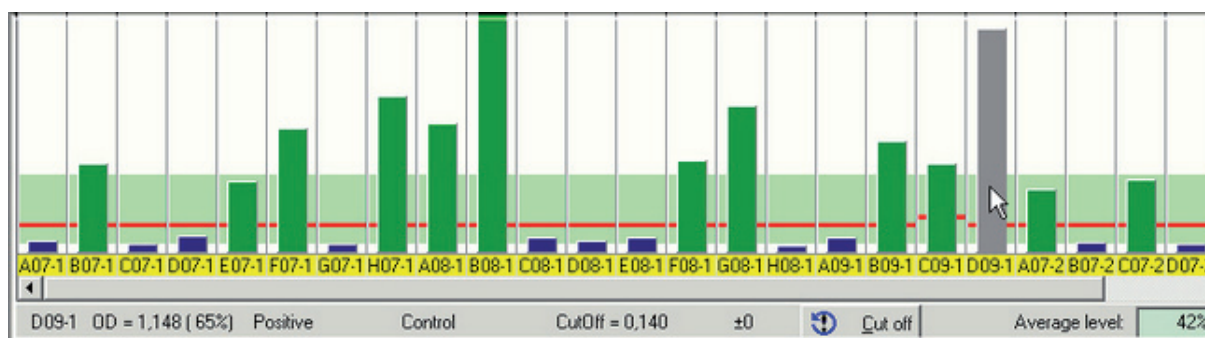
D09-1	Position of the probe on the microtiter plate and the reading (first or second run)
OD=1,148	OD value of the reaction
(65%)	Relative divergence from the reference OD of the probe
Positive	Evaluation of the reaction (positive / negative / false positive / false negative)
Control	Probe characteristics (control/ undecided / weak)
CutOff=0,140	This cut-off value is used to evaluate the probe
±**0**	The cut-off value has been shifted by these percentage points (automatic cut-off or manual using the slide control on the right hand side)

Cutoff

There are various ways to optimize the cutoff for a sample:

- Use the slide control on the right-hand side to increase or decrease the cutoff for all reactions.
- You can change the cutoff for each individual reaction by "dragging" with the mouse.
- Activate "Automatic Cutoff" here or in Lab Management in order to recalculate the cutoff based on the reaction strength of specific probes.

Use to undo cutoff changes.

> ### *Attention:*
> If, in the laboratory administration, the automatic cutoff has been chosen as standard setting, this will only be used during batch typing if the software was unable to establish a result without shifting the cutoff.

Average level

The average level shows you the discrepancy between the reactions of this plate and the average reaction strenght for this assay. A positive value indicates a stronger than average reaction. A negative value indicates a weaker than average reaction.

4.1.6.4 Typing options

The typing options routinely used by the software were defined in Laboratory Management.

These defaults can be adjusted for an individual typing run at any time in the typing dialog.

- Frequent allels only: ON or OFF.
- Automatic cutoff: ON or OFF. If this is not activated, the system will use the cutoff stored for this lot.
- Max. number of false reactions: 0 to 5 false positive/false negative reactions are accepted.
- Nomenclature: DNA, serological or compressed.
- Output format: list, string or NMDP

All parameter settings for typing are stored and documented correspondingly in the results printout.

4.1.6.5 Results display

 All Results

If all results (or a NMDP code) have already been calculated for this assay, this 'pocket calculator' symbol appears. Calculating all results has the advantage that all variants of nomenclature and output format are displayed without delay.

Please note that renewed typing results in the deletion of the data entered in the result table.

Window at the bottom left

The results are shown in full in the left window, i.e. with all 3 nomenclatures, indicating potential failed positions.

If a result that contains errors is marked (click once), this will be color-coded red in the bar chart:
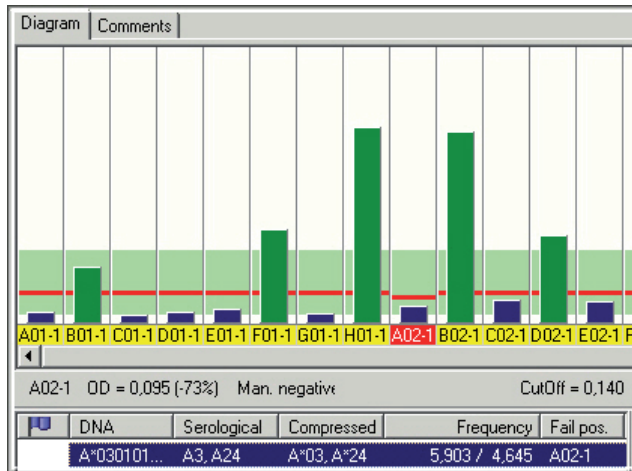
Depending on the entry in Lab Management (unambiguity of the result), the most probable result of several entries must, should or can be highlighted:

Highlight the selected result by double-clicking on it. The highlighted DNA result is displayed in the 'Result' column of the 'Search' window. If no DNA result was selected, but a valid NMDP result for both allele combinations was evaluated for these typing settings, the codes are displayed in the result column.

> *Attention:*
>
> While results with error positions can be selected, they cannot be marked.
>
> It may be useful to add further results from this list to the findings, for example results with error positions. From version 2.0 onwards, the entries can copied to the commentary in the bottom left window. The commentaries are printed on the findings report. To do this, proceed as follows:

- Merge the columns that are not wanted on the print-out.

- If you want to import all results or all results with fail positions:

  Click on ![icon](All Results) (All Results) or ![icon](All results with fail positions) (All results with fail positions)

  → The view changes to "Comments". The results are shown in the right-hand field.

- If you want to import individual results into the 'Comments' field:
  Mark the results by using the mouse and pressing the shift or control key.
- Call up the context menu by clicking the right mouse button and select "copy":

DNA	Frequency	Fail pos.
DQB1*030101, DQB1*0602	23,544 / 10,629	C02-1
DQB1*030302, DQB1*0602	5,173 / 10,629	C02-1,C03-1,D03-1
DQB1*030101, DQB1*060501	23,544 / 0,630	D01-1,H01-1,D02-1
DQB1*030101, DQB1*0609	23,544 / 0,250	D01-1,H01-1,D02-1
DQB1*0304, DQB1*0602	0,200 / 10,629	C02-1,F03-1,G03-1

- Click on the <Commentaries> tab to change to the commentary window
- Using the mouse, click on the right hand commentary window
- Using the right mouse button, call up the context menu, select "insert"
  - → The results from the window are entered as commentary:
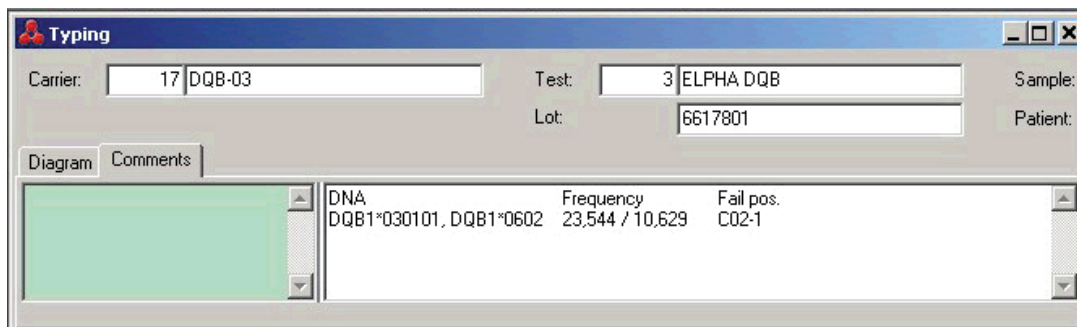
Don't forget to save!

DRB LowRes and DRB HighRes

Due to the options resulting from different combinations of DRB1* alleles with involved DRB3*/DRB4*/DRB5* alleles, the display of a complete list of results would take a long time. This is why an additional window "Associated alleles" appears when you highlight a result. This window lists the possible allele combinations for the selected result. The involved DRB3*/DRB4*/DRB5* alleles of the marked result are bundled into strings and issued on the findings print-out.
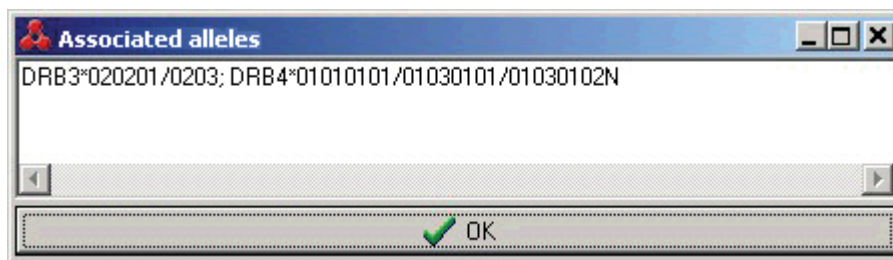
Attention:

Determination of frequent allele combinations using DRB assays detecting DRB3*, DRB4* and DRB5* additionally to DRB1*:
An allele combination is listed as "frequent" if the frequency of all alleles associated is higher or equal to the limit value set in the laboratory management. Besides the frequency of the DRB1* allele the frequency of its associated DRB3*, DRB4* or DRB5* allele is taken into consideration.
The following assays are concerned: ELPHA DRB SL LowRes, ELPHA DRB SL HiRes and ELPHA DRB DL HiRes.

Window at the bottom right
This is where the result is shown in the selected nomenclature – the way it will appear in the results printout.

4.1.6.6 Comments

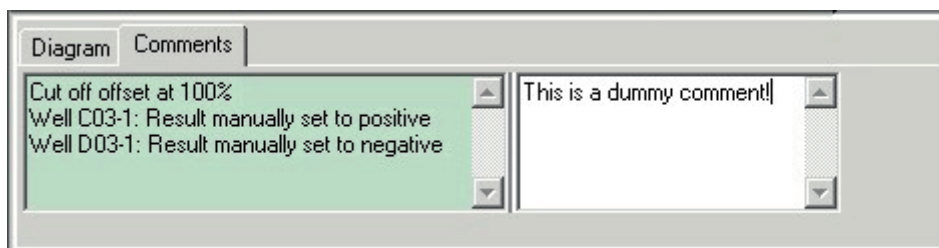Click on the tab <Comments> at the top left to obtain a split window. Comments generated by the system are displayed in the bright green window on the left. On the right hand side, you can enter your own comments (250 characters max.):

The previous chapter describes how to copy results from the window at bottom right of the typing dialog to the commentary window.

4.1.6.7 Release

If you agree with the typing as done by the software, you release the result by clicking on <Release>. The result can then no longer be changed!

→ The sample is marked as 🔒 released in the **Search** window.

> *Attention:*
>
> Upon the explicit request of the customer, the Biotest product specialist can release the option to process released samples.

4.1.7 Evaluation of result tables

HLA typing software features the „Create result tables" function, which stores all typing result formats in the database.

This function is called by the menu option **Extras – Create result table**. Working period for the routine is chosen in the „Setup" screen at "Batch results from… to …" (see chapter 2.3).

While the function is activated, all successfully typed samples with results of only one format are sequentially processed during the time set.

If the working period for the routine was long enough, all result tables for the samples of the previous day are available the next morning. It has the advantage that all nomenclature and output formats are displayed without delay.

Once called, the generation of the result table will run once during the selected period, even if you close the HLA Typing software after having called the routine.

If you would like to calculate a result table in this way again the next day, you need to start the routine again.

If necessary, a result table for a single marked sample can be created by clicking on the „calculator" icon in the „Search" window.

During this time, it is not possible to continue working with the software.

The same routine for evaluation of result tables is also used for the update of NMDP codes after the registration of new allele combinations with the NMDP (see also the next chapter "Evaluation of NMDP Codes").

4.1.8 Evaluation of NMDP codes

For HLA typing 2.0 or higher, NMDP codes are updated online by a HTML document from the NMDP web page.

This way it is guaranteed that you are always up-to-date concerning these codes.

After a allele database update within the lot data, the allele combinations found might not yet be registered with NMDP.

In this case, the software cannot find a code for some combinations.

It would e.g. look like this in the result field:

```
B*1402/1406
=>B*14BF
---
B*1501/1512/1519/1526N/1527/1532/1533/1534/1535/1538
/1560/1575
->No code exists for the above combination!
```

For combination B*1402/B*1406, code B*14BF was evaluated.

Combination B*1501/........./1575 is not yet registered at NMDP.

A comment is displayed, meaning that there was no code found for this combination.

If „Save typing" or the result table calculation routine was used, all combinations without valid NMDP code are written to a log file in the "export" folder. (by default C:\Program files\Biotest\HLAtyping_20\Export)

The "NMDP_no_results.log" file is used for the registration of the combinations at the NMDP.

For the above example, the file entry looks like this:

```
NMDP_no_results.log - Editor
Datei  Bearbeiten  Format  ?
2008-05-15 17:10:51    ALL    B*1501/1512/1519/1526N/1527/1532/1533/1534/1535/1538/1560/1575
```
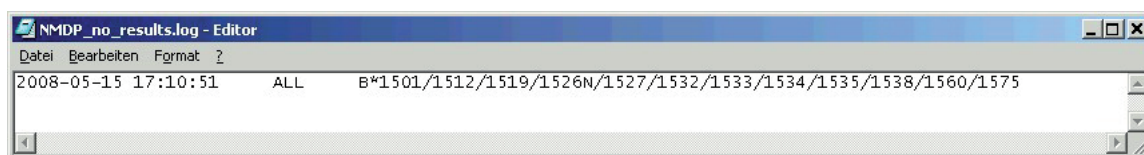
Please delete the log file after having sent the combination to the NMDP, to avoid double registration of allele combinations.

As soon as the new codes are provided by the NMDP, you can update the results in the database with the "calculate result table" routine.

The option to create a new result table by running the "calculate result table" routine (see chapter 4.1.7) stays active, until valid codes for your settings (only frequent/all) are found and written to the result table.

As soon as valid codes are calculated for a sample, they are displayed in the "Result" column of the **Search** window.

The "calculator" icon for this sample has changed to "inactive".

> *Notes:*
>
> Precondition for the evaluation of NMDP codes is a working connection to the internet.
>
> ---
>
> When creating the log file, it is ensured that there are no double entries.

4.1.9 Print/Export

The **Search** window offers you the following options for a released sample:

Print sample report:
The selected result (selected sample with the corresponding test result) is printed.

Print summary report:
All tests are printed for the selected sample (sample ID).

Print patient report:
All tests will be printed for the selected patient, including tests run under different sample IDs.

Export results:
Same as sample report. A file containing the test result is generated for each selected entry. The file of the standard laboratory profile is filed in the ...\Export folder. If required, the XML file to be imported in Score is filed in the directory that has been entered under **File - Export**.

Print Search list:
The list shown in the search window is being printed. The print-out lists the filter settings with which the print-out has been produced.

If you don't need to print some of the columns, reduce them to the minimum size on the **Search** dialogue. These columns are not printed.

Attention:

When printing non-released samples, this is pointed out on each page of the printout.

Each printout contains information on the batch number, the test kit as well as the used carrier.

From version 2.0 onwards, each sample will be provided with the sample number and the date as well as - in the case of patient findings - the patient number, which will be printed in the footer.

Via the ![printer icon] –button further printing options are available.

4.2   Print/Export: additional functions

Besides the Print buttons in the **Search** window, there are additional print options.

Definition of standard profiles in Lab Management

Several different output profiles can be stored for each lab. These will be used for printing in the **Search** window.

Additional print options

Select **File - Export** or **File - Print**

or click directly on 🖨

→   A mask appears, which will allow you to freely combine all printing/exporting parameters:

Basically, you can print out the same reports as via the Search menu. It is recommended to use this menu if you need to print or export individual profiles of single samples not covered by the standard laboratory settings.

The necessary information is requested depending on the print mode.

The figure shows the settings required for a sample export. For a patient result, for example, you will be asked for the patient's name.

From version 2.0 onwards, on top of the findings-specific information (sample name, test name etc.), further options will be available in the printer dialog:

Display print preview

If this option is chosen, it is possible to review the findings and their layout before they are printed.

Display printer dialog

If findings are printed on different printers, this option must be selected. This way, the respective printer can be chosen each time findings are printed.

XML-Export to the Helmberg Score

This is an interface to the Helmberg Score. The findings of the HLA Typing software can be exported as XML and be input in the Helmberg Score software from version 3.3.1.5F. To do this, tick *file export/list report* and *XML-export*. Via the ⋯-button you can select the standard directory in which XML files are to be filed.

Attention:

The XML file is always generated in addition to an export profile (e.g. in the PRN or TXT format). Therefore, when exporting an individual result to XML you need to enter an additional profile under *profile name*.

Export/Report with own SQL command

If you use an export/report profile that has been set up specifically for your requirements, this option may need to be selected. You will receive the necessary information from the Biotest customer service.

Profile name

A suitable print profile and/or export profile needs to be selected!

Attention:

The print profile **EXP_SEL_txt01.rtm** generates a daily export file where the sample numbers represent the search key. If, on the same day, a sample is typed several times and if the result is exported via this profile, the result that has been exported last will always be kept and the result that has been exported before will be overwritten.

4.3 Define allele frequencies

With the allele lists, the lot data are complemented by the frequencies of the allels. In case your population's allele frequencies differ from those stored in the lot files, they can be changed using .

→ An entry mask will be displayed.

1. Choose the laboratory where you want to adjust allele frequencies.

2. Choose a test. You can only choose tests that are currently worked on by the laboratory ("active tests").

3. Use the <search> button.
   → The list of alleles is displayed:

By default, the list is sorted by allele name. By clicking on a column, another arrangement can be

selected. This is indicated by an arrow in the selected column.

4. When searching for a specific allele of the selected test, enter the % allele name in the "allele name" field (e.g. %DRB1*040101) and press <search>.

5. The desired allele can now be selected from the list. The default frequency is shown on the right; you can enter the desired value below that.

6. When activating the green tick, the value is entered in the "laboratory value" column.

Warning!

This change affects all typing results! Please also note the cutoff value for "frequent allels" stored under Lab Management.

7. After you have entered the changes, the new values will be activated by clicking on <Save Changes>:

> **Warning:**
>
> ⚠ Changes will be transfered for all lots of the selected lab!
>
> OK
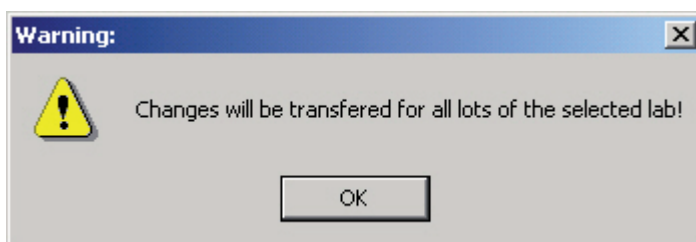
If you wish to reestablish the default values, delete the entry for "lab value".

4.4 Window

The HLA Typing Software allows you to have several windows open at the same time. For example, if you select an entry in the **Search** list and edit it, an additional window for this sample will open next to the window with the list. Use the menu option **Windows** to sort your windows as you wish.

This will also display a list of open windows so that you can easily locate "lost" windows.

4.5 ![icon] Online help

Press the <F1> key to get to the online help file. This will automatically display the help text matching the currently open window. If you need help for another topic, there are several methods to find it quickly:

1. Use the index on the left side; it is identical with the printed manual.

2. Select "Index" or "Keywords" to enter the topic for which you need help. This will display all the topics containing this key word.

Use the arrow keys to scroll back and forth. This is quite useful when you are trying to familiarize yourself with a complex topic such as, for example, typing.

4.6 Close program

- You can close the program by using the ☒ at the top right corner (as in any Windows application)

- by selecting **File - Close**

- or directly by using the ![icon] button.

5   Annex

5.1   Reader configuration

Configuration of reader settings requires the corresponding access rights.

> **Attention:**
>
> **This is usually the task of the Biotest product specialist!** In case you change this configuration without speaking to Biotest, we cannot be held liable for problems regarding the functioning of the reader interface!
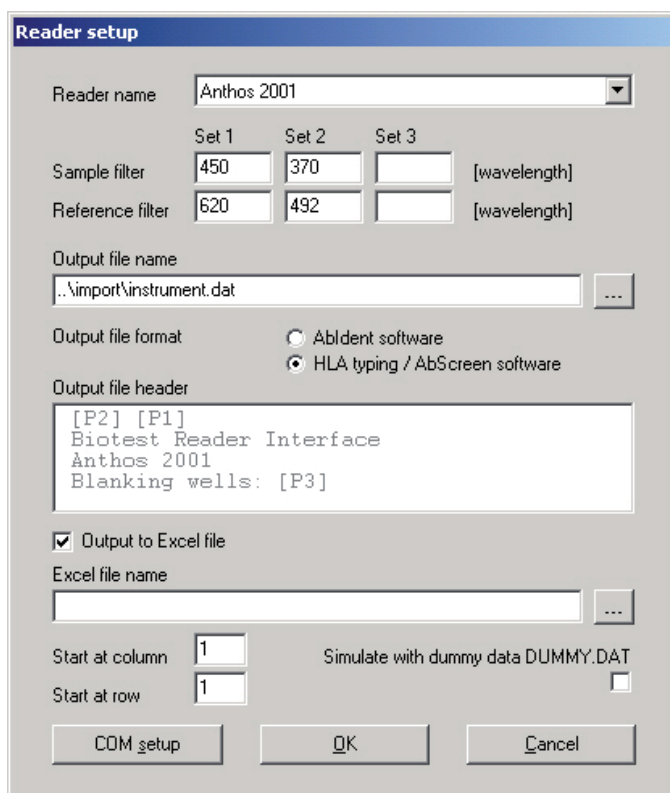
- Select Search – select an assigned sample – click on <Reader> to display the Reader window:
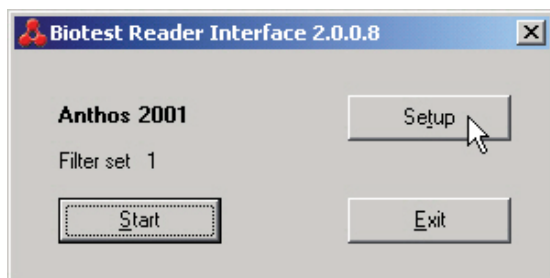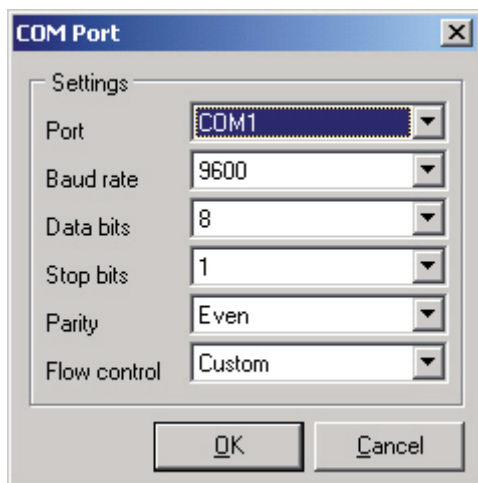

- Select <Setup> to access the Setup menu.
- Select your reader from the reader list:

- You can now enter the required filter and output file settings:

- Another button will take you to the COM settings:

- Save and quit the COM settings by pressing <OK>
- Save and quit the reader configuration by pressing <OK>

> ### Attention:
> Please note the Reader recommendations in chapter System requirements!

5.2 Pipettor configuration

Before the system accepts pipettor data, the HLA Typing Software must be configured in such a way that paths, plate name and plate layout are in line with the result details produced by the pipettor. The current pipettor tests are included in the software installation. In case you have a test which is not available, it must be entered in the test list.

> ### Attention:
> **This is usually the task of the Biotest product specialist!** In case you change this configuration without speaking to Biotest, we cannot be held liable for problems regarding the functioning of the pipettor interface! Our Customer Service will be pleased to assist you.

5.2.1 Pipettor settings: Tecan

Select [icon] - <Automation platform> to display the dialog for pipettor settings. This is where you can enter the required settings:
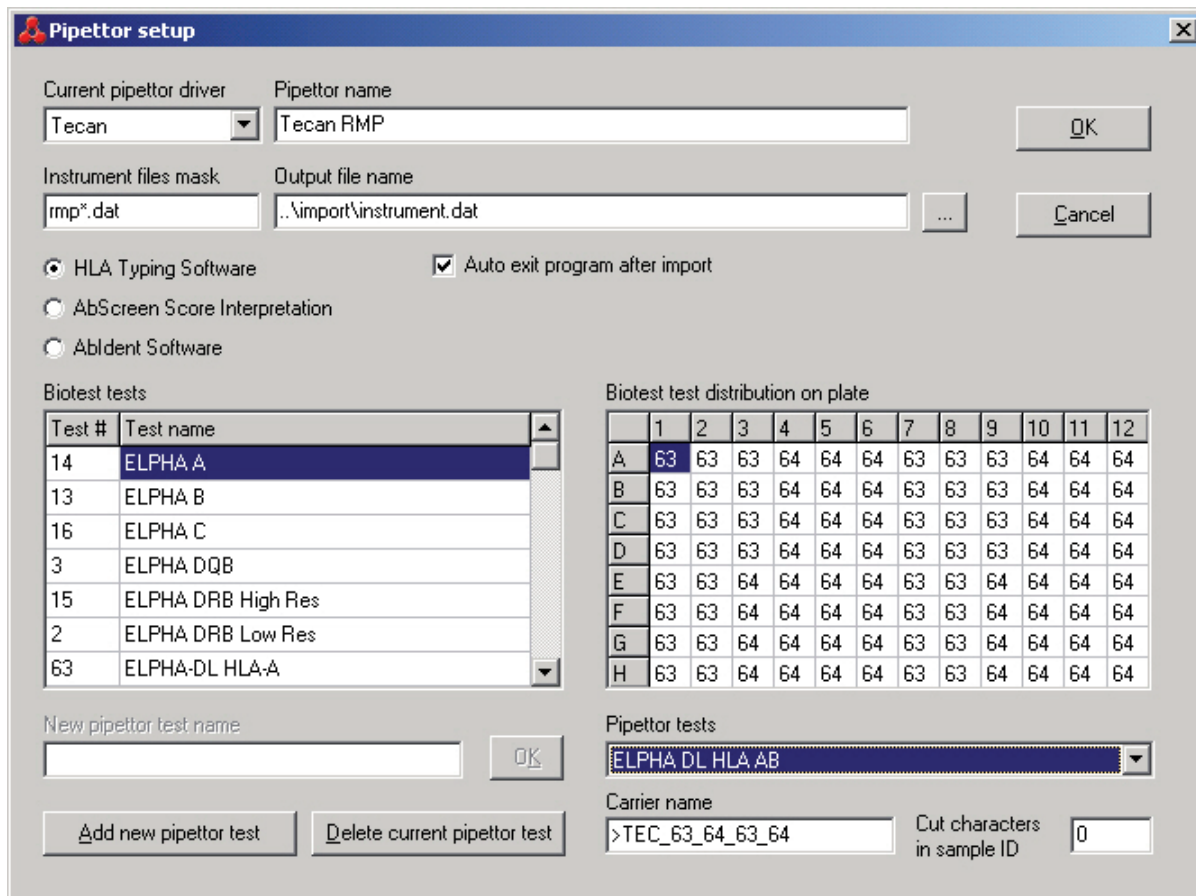
Current pipettor driver: In the Standard Version this is Tecan or Quickstep, whereas the Professional Version allows for more instruments.

Pipettor name: Enter the pipettor name.

Instruments file mask: Tecan: rmp*.dat

    Quickstep: *.txt

Output file name: This file is generated by the software. It is expected in the import directory and must be named "instrument.dat".

Selection menu HLA/AbScreen/AbIdent:

The pipetter interface is used by several Biotest programs. Here, the **HLA Typing software** needs to be selected!

Automatic program end after import:

After importing the data and after confirming the import protocol you return directly to the main menu. The import mask will not be displayed again, it is not necessary to click on <exit>.

5.2.1.1 Create a test

The tests used in your laboratory are usually created by your product specialist during installation. In case you have to create a test after all, please proceed as follows:

- Press <Add new pipettor test>

- Assign a new name (=assay name in the pipettor file), press <OK>

- Properly name the carrier (see Definition of carriers)

- In the MTP window, select a range for the test. Make sure to occupy all A-H wells.

- In the "Biotest Tests" window, double-click on the test to be pipetted in the highlighted area of the plate.

- In case different tests are pipetted onto one plate, highlight the next area on MTP and define the next test.

- If needed, enter at the bottom right how many digits should be removed at the end of the sample ID. The trimming of characters in the sample ID is important for tests with two amplifications such as for example the DRB High Res Test. For this test, a suffix for the corresponding amplification is added to the sample ID in the pipettor files. By removing this position, samples 18G and 18T, as an example, are combined to form sample ID 18. If, in the pipettor file, sample 4711 of an HLA-AB test bears the suffix a for HLA-A and the suffix b for HLA-B, then removing one character causes samples ID 4711a and 4711b to be combined to form sample 4711.

- Finished? Press <OK> at the top right to save your entries.

5.2.1.2 Delete a test

- Select a test from the <Pipettor tests> list.

- Press <Delete current pipettor test> to obtain the following prompt:
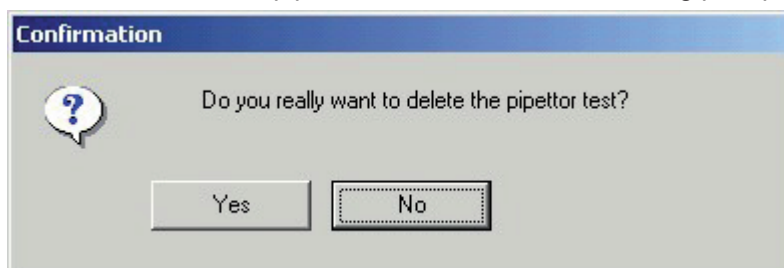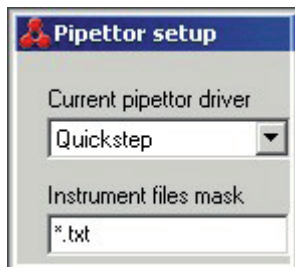

- Press <Yes> to remove the test.

5.2.2 Pipettor settings: Quickstep

With the exception of two details, Quickstep settings are identical with the Tecan settings:

- The driver is named "Quickstep", the corresponding file is named *.txt

- The carrier names starts with >QS

5.3 Information on data security

The HLA Typing Software uses a relational databank (Interbase 6.x by standard) in which all pieces of information generated while working with this software are stored, especially the following data:

- Patient data
- Reader and pipettor raw data
- Typing results
- Lot documentation
- User documentation

This database independently supervises its own integrity and rejects prohibited actions. However, this does not exclude damages resulting from external impacts (e.g. hardware defects)!

Loss of or damage to the databank results in the irretrievable loss of important information!

The IT department responsible for the laboratory is therefore obliged to ensure regular backups to safeguard the database.

> **Standard path and file of the database:**
>
> **C:\program files\Biotest\HLAtyping_xxxx\Database\hlatyping.gdb**

5.4 Information on data protection

> By means of the User Management, the HLA Typing Software offers the option to protect sensitive data (patient data) against unlawful access. Furthermore, the databank is logically protected against unlawful access.
>
> However, it is the user's responsibility to ensure that this option is actually used for this purpose. Thus, for example, passwords must be handled with due care!

5.5   Software prompts / What to do?

Like any program, the HLA Typing Software comprises numerous prompts, warnings or error messages that will be displayed on numerous occasions. In theory, these should be self-explanatory. Since we know, however, that they never are self-explanatory in practice, all the prompts are listed below together with a suggestion on what to do.

In the online version, underlined key words refer to the corresponding entry in the help file.

The following messages may appear	What it means / What you should do
This window contains data which is not saved yet. Should it be closed anyway?	Forgot 💾? Press <No>, save, then close. In case you deliberately do NOT wish to save a change, you may of course close the window by pressing <Yes>.
Please first close the patient form! Please first close the reaction form! Please first close the input form! Please first close the typing form!	In order to avoid "collisions" of the individual software modules, you may not open more than one mask (=window / working area) at a time in which interrelated data could be changed (such as reaction entry and typing, as typing depends on the reactions).
Please close all sub windows of the application!	The selected action (e.g. activation of test lots) can only be carried out while no other window/program part is running.
Patient already exists!	Create patient: last name, first name and date of birth are identical with an existing patient.
Missing last name!	Create patient: No last name was entered.
Date of birth is not valid!	Create patient: Create a patient: date of birth must be entered as DD.MM.YYYY
Plate name should not be empty!	Create test: no plate name was entered or generated.
Missing plate name!	Please enter a different plate name. You can avoid this error by using the option <Create>.
Missing sample number!	Create test: no sample ID was entered. Enter or scan a new sample ID
Carrier in use and can't be deleted!	As soon as a carrier was used for a determination, it can no longer be deleted.
Too few dummy positions (#) for automatic plate name	This error message can also appear when you manually assign a plate name. Reason: incorrect default setting for carrier name.
This name already exists!	Lab Management: You tried to assign one name twice. Enter a different denomination for this lab profile.
Standard lab can not be deleted!	You tried to delete the<Standard> Lab profile. If you do not like the name <Standard>, you may rename it.
Missing lab name!	Lab Management: You defined a new profile but did not name it
Max. 5 false reactions are allowed!	Lab Management: You entered a value that is too high by mistake. As you can always increase the number of false reactions for an individual typing, we recommend that you enter "0" here.
Frequency is not a valid percent value!	Lab Management, cutoff for frequent alleles. In theory this is a number between 0,00 and 100,00. Default setting is 0,01%. Maybe you entered a period instead of a comma?

The following messages may appear	What it means / What you should do
Lab in use, can not be deleted!	Lab Management. As soon as you have worked with a lab profile, it can no longer be deleted, as important information required to produce a result would be lost.
Missing entry in first run!	Manual entry of reactions: only the second run was entered for a double test run.
Missing carrier name!	You defined a new carrier but failed to name it.
At least one test must be assigned!	You defined a new carrier, but failed to assign a test to it.
Test too large!	Define Carrier: There are not enough spare wells left on the plate for the selected test.
Carrier name already exists!	You must assign the carrier a different name.
No allele combination was selected	Default setting "must"; you clicked on <Release> without first selecting an allelecombination.
At least one allele combination should be selected	Default setting "should"; you clicked on <Release> without first selecting an allelecombination. Press <Yes> to return to the Typing Dialog, or press <No> to release
No NMDP codes loaded	You tried to select "NMDP" as output format in the Typing Dialog before importing the NMDP-List.
Selected file is not a patient file!	Import patients: the file may be named *.txt, but the content is incorrect. If you are sure you selected the right file: Verify the file format (IT department and Biotest)!
Patient in use and can't be deleted!	You tried to delete a patient from the patient list who was already assigned a sample.
Sample *4711* has already a patient. Patient *Smith* not read.	During Patient Import, you tried to import a new patient under an existing sample ID.
At least one status must be selected, otherwise the search result list is empty!	Search - Filter: Check at least one box for sample status.
From-date must be before to-date!	Search - Filter:You entered an invalid time period.
You don't have sufficient rights. Please contact your administrator!	You tried to do something for which you are not authorized by the Administrator. He can grant you the missing rights under User Management.
Missing sample name!	Entry in the "Import Pipettor Data" protocol: The sample ID(s) were missing upon the import of pipettor data.
File C:\Programs\Biotest\HLAtyping_20\Import\instrument.dat could not be found. Action canceled.	Incorrect path of output file in the Pipettor or Reader settings. It must be "..\Import\instrument.dat".
Carrier >*QS_13_14* not found. Plate not created.	Entry in the "Import Pipettor Data" protocol: Create the requested carrier via Pipettor Setup!
Plate *12345* already processed. Plate not read	Entry in the "Import Pipettor data" protocol: As soon as the plate was typed, raw data can no longer be changed or re-imported.
No lot selected!	Activate the used lot(s) via ![icon] !
No lot selected for desired test!	Activate the used lot(s) via ![icon] !

The following messages may appear	What it means / What you should do
Please send this error together with today's log file	The error that occurred must be dealt with by Biotest. - Please write down the exact error message so that you can forward it to Biotest. - Furthermore, please send the file C:\Biotest\HLAtyping_20\Log*aktual date*\HLATYPING.log to Biotest
Wrong version of database. Expected database version 2.0	You tried to open the database of an older version using HLA Typing 2.0. First, you need to convert the database before it can be processed with HLA Typing 2.0.
Results with false positions can not be flagged!	In order to be able to mark the selected result, you need to manually correct the faulty position(s) in the bar chart of the typing dialog and re-type the sample.
Sample currently accessed by User *xxx*!	You tried to access a sample in the network operating system that is being processed by another user. This is prevented in order to avoid conflicts that may arise if the same mask is processed at the same time.
For XML export please enter a valid export profile name, because the XML export works together with the regular export file!	You have chosen "XML-Export" in the export mask. You need to enter an export profile in the "profile name" field.
Profile does not exist or does not match report type:	The "profile name" field is empty or the selected profile has the wrong format. Enter the appropriate profile under "profile name".

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