



User guide

Omixon HLA Twin RUO
Version 4.0.0

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2 Revision and Change History

Version	Approval date	Author	Summary of changes	Approved by
3.0.0	 29 Jun 2018	Adél Juhász Ágnes Pásztor	Introduced ABO- and MIC-related modifications in genotyping and result display. Removed the word "HLA" where ABO or MIC could be meant as well. Miscellaneous minor corrections in the text.	Adél Juhász Ágnes Pásztor
3.1.0	 31 Aug 2018	Petra Hoch	Company Information section was added. Minor corrections in phrasing and formatting.	Adél Juhász
3.1.1	 08 Nov 2018	Krisztina Rigó Petra Hoch	Performance measurements updated for Holotype HLA v1 and added for Holotype HLA v2. Minor corrections in phrasing and formatting.	Adél Juhász
3.1.2	 13 Nov 2018	Adél Juhász	Added IMGT database support definition to support period description. Minor corrections in references to the Handbook.	Krisztina Rigó
3.1.3	 13 Feb 2019	Adél Juhász	Added Twin genotyping description including SG execution logic Modified temporary folder setting recommendations for server setup	Krisztina Rigó Mónika Hulita
4.0.0	 06 Aug 2019	Adél Juhász	Updated Quick Start Guide with: <ul style="list-style-type: none"> New result table structure Locus level markups New placement of the assignment history function Collapse/Expand table functionality Event Log Typer Manager Bottom information panel on Dashboard Removed Omixon HLA Server section Refactored the Installation Guide section by adding: <ul style="list-style-type: none"> Available configurations Desktop Installation Standalone Server Installation First use guide: <ul style="list-style-type: none"> Creating the first user Connecting to the server 	Marton Pogany
4.0.0	 09 Aug 2019	Adél Juhász	Moved System Requirements page from Introduction to Installation Guide and updated it with actual values Added pages to Installation Guide: <ul style="list-style-type: none"> Introduction Client installation Data migration 	Marton Pogany



3 Introduction

3.1 Company information

This product is manufactured by Omixon Biocomputing Ltd.

Address:

H-1117 Budapest
Fehérvári út 50-52.
Hungary, EU

Website: <http://www.omixon.com>

Technical contact: support@omixon.com¹

Sales contact: sales@omixon.com²

3.2 General information

Omixon HLA Twin RUO provides two independent algorithms for genotyping next generation sequencing data: Statistical Genotyping (SG) and Consensus Genotyping (CG). The algorithms were co-developed with the Omixon Holotype HLA sequencing assay. The two algorithms can be run simultaneously and results can be examined in a single table. Alongside this high-level overview table, detailed statistics and quality control measures are provided for each sample.

Omixon HLA Twin RUO is for Research Use Only. Not for use in diagnostic procedures.

Omixon HLA Twin offers time based licensing, which allows unlimited genotyping in a given period of time. Please contact sales@omixon.com³ for a quote. A license valid for 90 days is included in the evaluation version.

Each software version is supported for 13 months from its release. Note that while bug fixes will be implemented for all editions of the software during the support period, validation of new IMGT databases will only be performed for CE editions. It is strongly advised to upgrade to the newest software version before end of support.

3.3 Sequencing technologies

Omixon HLA Twin supports sequencing data from these major sequencing technologies:

- Illumina
- Roche 454
- Ion Torrent

3.4 Principle of method

3.4.1 Consensus Genotyping (CG) algorithm

The consensus genotyping algorithm is a de novo assembly based method. The assembler method is receiving data prefiltered to genes based on the IMGT database. The output of the assembly is one or more contigs, each contig consists of one or more phased regions. The generated consensus sequences are compared to the allele sequences in the IMGT/HLA database and the allele pair or pairs with minimal key-exon, other exon and non-exon mismatch counts are reported. The consensus genotyping algorithm reports full (4-field) resolution genotyping results.

3.4.2 Statistical Genotyping (SG) algorithm

The statistical genotyping algorithm is an alignment based method. Reads and read pairs are aligned to all exonic sequences defined in the IMGT database then assigned to alleles with the highest alignment score. Alleles are pre-filtered and paired. Allele pairs are compared and

¹ <mailto:support@omixon.com>

² <mailto:sales@omixon.com>

³ <mailto:sales@omixon.com>



ordered based on the combined amount of supporting reads in the pair. All allele pairs that are considered equally good results based on the comparison results are reported. The statistical genotyping algorithm reports exon-based (3-field) resolution genotyping results.

3.4.3 Twin Genotyping

Twin genotyping is a combination of the CG and SG algorithms described above. When performing Twin genotyping, the CG algorithm is run for all targeted loci. Subsequently the SG algorithm is run for loci with CG results fulfilling a set of predefined conditions. In addition to the user defined execution conditions the SG algorithm is programmed to always run for loci with novel alleles and never for the locus HLA-DRB3.

3.5 Validation methods and performance characteristics

The performance statistics presented below were generated using Omixon HLA Twin version 3.1.1 and IMGT database version 3.31.0_5. Performance measures were calculated using the method described by Ng et al. (1993)¹. Genotyping results were compared to available reference genotyping information on a two-field level resolution.

3.5.1 Holotype HLA v1

Altogether 416 samples (originating from 197 reference cell lines) were analyzed. Sequencing data was generated using Holotype HLA version 1.

Measure	HLA-A	HLA-B	HLA-C	HLA-DPB1	HLA-DQA1	HLA-DQB1	HLA-DRB1	Total
Sensitivity	99.52%	98.56%	98.68%	99.04%	99.52%	95.55%	98.32%	98.45%
Specificity	99.98%	99.97%	99.95%	99.96%	99.95%	99.80%	99.96%	99.95%
Precision	99.52%	98.56%	98.68%	99.04%	99.52%	95.55%	98.32%	98.45%
Negative Predictive Value	99.98%	99.97%	99.95%	99.96%	99.95%	99.80%	99.96%	99.95%
Type Correctly Classified	99.97%	99.94%	99.91%	99.92%	99.91%	99.61%	99.92%	99.90%

3.5.2 Holotype HLA v2

Altogether 176 samples were analyzed. Sequencing data was generated using Holotype HLA version 2.

Measure	HLA-A	HLA-B	HLA-C	HLA-DPA1	HLA-DPB1	HLA-DQA1	HLA-DQB1	HLA-DRB1	HLA-DRB3	HLA-DRB4	HLA-DRB5	Total
Sensitivity	100.00%	98.58%	97.73%	99.71%	98.86%	95.71%	96.88%	99.43%	98.21%	89.71%	98.28%	97.58%
Specificity	100.00%	99.98%	99.93%	99.97%	99.96%	99.76%	99.84%	99.99%	99.64%	96.57%	99.43%	99.90%
Precision	100.00%	98.58%	97.73%	99.71%	98.86%	95.71%	96.88%	99.43%	98.21%	89.71%	98.28%	97.58%
Negative Predictive Value	100.00%	99.98%	99.93%	99.97%	99.96%	99.76%	99.84%	99.99%	99.64%	96.57%	99.43%	99.90%
Type Correctly Classified	100.00%	99.96%	99.87%	99.94%	99.92%	99.55%	99.69%	99.98%	99.40%	94.85%	99.14%	99.82%



3.6 Release notes

For the list of new features and bug fixes see the section *Release Notes* at <https://www.omixon.com/support-and-resources/hla-twin/>

3.7 References

¹Ng J, Nurlay CK, Baxter-Lowe LA, Chepak M, Cappe PA, Hagland J, KaKuraya D, Manes D, Rosner G, Schmeckpaper B, Yang SY, Dupont B and Hartzman RJ (1993), Large-scale oligonucleotide typing for HLA-DRB1/3/4 and HLA-DQB1 is highly accurate, specific, and reliable. *Tissue Antigens*, 42: 473–479.



4 Quick start guide

4.1 Log in

After initializing the run of the HLA software, the user must log in to the application.
Enter user name and password to the fields and click login. At first login, a superuser is created.

4.2 Genotyping dashboard

After logging in to the software, the Genotyping dashboard will be visible. This is the home dashboard of the software. All genotyping functions are available from here.

The dashboard consists of the following subscreens:

- Information Panel: this contains all the main functions and some high-level information about the current folder and selected files. It also shows information about the current user and active IMGT database and provides some navigation functions.
- File Browser: this part of the screen can be used for navigation between all accessible folders.
- Bottom Panel:

The Information Panel is located on the top of the screen. It has 3 different sections:

- The top part shows:
 - the ID of the current user,
 - the memory usage widget panel,
 - the status panel of the process manager,
 - the welcome tutorial button,
 - the logout button,
 - and the exit button.
- The middle part shows:
 - the navigation buttons: Back, Forward, Up and Home (Home takes you back to the Genotyping dashboard.)
 - the available information about the used IMGT database right from the navigation buttons
 - the bookmark and context specific help buttons on the right side of the screen
- The lower part presents a series of buttons that enables you to choose between the main functions of this dashboard:
 - the typing and data analysis options to submit genotyping
 - the typing and data analysis options to visualize results
 - the file browser functions to navigate between samples and folders
 - the Typer Manager for deploying and undeploying typer nodes in distributed server configurations
 - Application settings

The main section of the display is the File Browser where you can navigate by clicking on drives and folder names - just like in a regular file browser. Use the browser to navigate to the folder where your genotyping samples are stored. Each sample file is marked with a small DNA sign and has its own unique name identical to the name that was generated by the sample sheet. For paired reads, the software automatically pairs files based on the file names and only the "R1" FASTQ file is displayed in the file browser to decrease redundancy and help navigation. By hovering the mouse over the sample file, you can see the size of the individual FASTQ files.

After a sample is analysed, a separate file, the genotyping result file will be displayed in the file browser. The result file has .htr extension. By default, all result files are placed automatically into the same folder where the sample data is. Each analysis file is marked with a small table sign. The name of the analysis file consists of the sample name and a timestamp that belongs to the time when the analysis was submitted. By hovering the mouse over or selecting the analysis file, you can see all available information about the analysis in the bottom information panel. When looking at an .htr file, on the very right you can see the high level quality summary of the typing results. Results are annotated using a "Traffic light" system. Similarly to a traffic light, three different colors are used with different meanings. Unlike in a real traffic light, "mixed colors" are available.

The genotyping functions are disabled - buttons grayed out - as long as there are no samples displayed on the screen. As soon as you locate a FASTQ file (or any other supported format) - the genotyping buttons become active.

To submit an analysis, follow the Analysis section.

You can find detailed information about this screen and all available functions in the *Genotyping Dashboard* section of the *Omixon Handbook*.

4.3 Analysis

When at least one sample is located, you have several options to start genotyping.

4.3.1 Simple Genotyping - recommended for Holotype samples

Genotyping with the default parameters can be initiated by a single click on the "Analyse" button displayed in each row for each sample. You can type multiple samples with the Holotype protocol by selecting them with mouse click and the Ctrl or the Shift button and pressing the Simple Genotyping button in the top menu. You can check that the typing is running in the Process manager displayed in the top right corner. You can find detailed information about this and other related functions, such as genotyping with custom parameters and re-analyzing samples in the *Genotyping Dashboard* section.

4.3.2 Results

As the progress reaches 100% in the *Typer Scheduler*, a new result file will appear in the file browser. In case multiple samples are typed at once a result for each will be presented as soon as it's ready - you can start viewing the first results while the rest is still in progress. The result files display a Traffic light result for quick overview and you can display further details by clicking the "View" button at the end of each row. To display multiple results use the Ctrl or Shift button to select them and then the "View results" button in the top menu. When working with analysis results in Omixon HLA software please be aware that primer sequences do not affect the results since they are trimmed before the analysis. You can find detailed information about interpreting the results in the *Genotyping Analysis Result* and *Genotyping Sample Result* sections.

4.4 Genotyping Analysis result

As described in the Results section, you can visualize your results by highlighting one or multiple samples and clicking to the "View results" button. This will navigate you to the next section of HLA Twin: The Genotyping analysis results.

This screen consists of three main parts:

- Information panel: the structure of this panel is largely identical to the Genotyping dashboard Information Panel (see above for details)
- Function panel: function buttons for filtering, assigning, approving etc.
- Result table: an overview table displaying the analysis results

The Function panel has the following buttons:

- Sample details and browse alignment
- Display setup buttons
- Assignment buttons
- Export table
- Further options to comment sample/approve sample/cancel the approval of a sample/ show Linkage Disequilibrium







In the Results Table of the Genotyping analysis results, you can see a high-level overview of your results for each locus of each sample.

The table has the following columns:






- Sample
 - Contains the name of the .htr file that is generated based on the name of the sample and the timestamp that refers to the time when the analysis was submitted.
 - If one sample has been analyzed multiple times, the displaying of the samples follows the order of the analysis. You can use the timestamp to track different analysis times.
 - In the top right corner you find the clock shaped Assignment history icon and the approval state indicator icon
- Separate columns for the analyzed loci:
 - Result alleles are displayed in two rows signaling the two chromosomes
 - A variety of locus and allele level markups are displayed in these columns

In the topmost row for each locus, the locus specific markups are displayed. These include:


- Quality control traffic lights:
These lights are based on the locus level quality control measures and can be one of the following:

- (green) - PASSED: the locus passed all QC tests,
- (yellow/green) - INFO: one or more QC tests produced lower than average results,
- (yellow) - INSPECT: one or more QC tests produced concerning results, manual inspection of the results needed,
- (red/yellow) - INVESTIGATE: one or more QC tests showed low result quality, manual inspection and possibly reanalysis is needed,
- (red) - FAILED: one or more QC tests showed very low result quality, manual inspection is needed to determine the cause and the locus or sample likely needs re-sequencing or re-typed by alternative methods.
- Zigosity markups: Heterozygous loci have the  markup while homozygous loci are marked by . Hemizygous loci are marked with . In case a locus is hemizygous only one allele is displayed and the other cell is left empty. In case the zigosity of a locus can't be determined based on the data available, it is marked with .
- Novelty markups: loci with alleles containing exonic (or exonic and intronic) novelties are marked with , while loci with novel alleles containing only intronic novelties are marked with .

Also allele results can have a variety of markups, including:

- Best match and assignment state: On the very left of the displayed allele result you can see the small "tick" icon indicating whether or not the allele result is a "Best matching allele". The icon is blue for best matching alleles and grey for remainder allele candidates. You can assign the allele result by simply clicking the tick mark - the sign will become green, indicating that the result is assigned.
- Concordance traffic lights:
The concordance traffic light system has the following outputs:
 - (green): results of SG and CG are fully concordant (at the 3rd field),
 - (yellow): results of SG and CG are concordant up to 4-digits (2nd field),
 - (red/yellow): results of SG and CG are concordant up to 2-digits (1st field),
 - (red): results of SG and CG are discordant.
- Note, that concordance traffic lights are only presented for best matching alleles and only if the result was produced with the Twin genotyping algorithm and the Statistical algorithm ran for the specific locus.
- Homozygosity: Alleles displayed with the blue font are homozygous.
- Rare alleles are marked with an *exclamation point* icon .
- Novel alleles containing exonic (or exonic and intronic) novelties are marked with , while novel alleles containing only intronic novelties are marked with .
- Imbalanced alleles are displayed with *italic* font.
- Allele extensions: Alleles with extended allele sequence are marked with a *plus sign* .
- Low amplification: If a minor allele with well-known low amplification is present in the imbalanced minor allele list, the allele is marked with . In this case validation of the homozygous result using an alternate genotyping method (e.g. SSO) is strongly suggested.

By hovering the mouse over the different parts of the table a tooltip will be displayed containing further available information on the sections.

 **Note**
If more than 50 best matching results can be found on a locus, LD will not be calculated. If you press the Show LD details button, no information will be displayed.

From the Genotyping Analysis result dashboard, you can enter the Genotyping Sample Result or the Genome Browser directly. In the Genotyping Sample Results you can observe the detailed quality metrics of the analyzed sample. To enter here, highlight the sample you wish to see and click on the "Sample Details" button on the bottom row of the Top section. In the Genome Browser you are able to visualize the detailed results for each of the typed loci. To enter here, highlight the sample you wish to see and click on the "Browse Alignment" button on the bottom row of the Top section. For further information, see the Genotyping Analysis result section of the Omixon Handbook.

4.4.1 Troubleshooting missing results

When no alleles could be reported for a targeted gene, a markup describing the possible reason for the missing allele call is shown. For additional information, hover over the info icon next to the markup and read the tooltip. The following cases can be reported:

For non DRB3/4/5 loci:

- *Not targeted* - Meaning that the locus was not targeted in the specific analysis. This markup is a placeholder for loci which were targeted in other analyses displayed in the table.
- *No data present* - No data present means that the locus has dropped out during sequencing and should be re-sequenced.
- *Insufficient or low quality data* - There is insufficient data or the data is of low quality in the sample. Quality control results should be checked for more detail.

For DRB3/4/5:

- *Not targeted* - Meaning that the locus was not targeted in the specific analysis. This markup is a placeholder for loci which were targeted in other analyses displayed in the table.
- *Allele not expected* - There is no allele expected at this locus based on known linkage disequilibrium with HLA-DRB1 and HLA-DQB1.
- *Expected allele not found* - This markup means that based on known linkage disequilibrium information, data was expected for the locus/allele but was not found.
- *Unexpected allele found* - Data was found for a locus/allele, which was not expected based on known linkage disequilibrium information.
- *Insufficient or low quality data* - There is insufficient data or the data is of low quality in the sample. Quality control results should be checked for more detail.

When no alleles are reported for a targeted gene it is suggested to rerun the sample in question using a higher number of reads. (The number of processed reads can be set in the *Advanced Genotyping wizard*.) The reasons behind the missing allele level results can be that the coverage does not reach the minimum threshold on the allele or on the exons, or the coverage depth is too small. Processing more reads can help making the signals that support the correct alleles stronger.

4.5 Genotyping Sample result

In the Genotyping Sample result screen, you can inspect the details of the genotyping results, the quality metrics and the data statistics for each locus of a selected sample.

This screen can be divided into four main sections:

- Information panel - note that the structure of this panel is largely identical to the Genotyping dashboard Information Panel (see above for details)
- Function panel: function buttons for filtering, assigning, approving etc.
- Result table: the contents of the result table are identical to that of the table on the Genotyping Analysis result screen, however in this screen the table is displayed in collapsed mode in order to leave more space for the Details Panel.
- Details Panel: displaying the genotyping result, quality metrics and data statistics

The Function panel has the following buttons:

- Opening the browser
- Detailed genotyping information
- Customizing displayed results
- Assigning alleles
- Commenting

The collapsed result table shows the first best matching allele pair for each locus. If there are multiple best matching allele results, the level of ambiguity is indicated by coloring the affected fields red in the allele name, while leaving matching fields black.

In the Details Panel you can choose from three different tabs:

- Genotype
 - In the Genotype section, you can observe the genotype that is selected by the software.
 - You can add/remove alleles manually
- Quality control
 - Several quality control measures are calculated for every locus. Each measure for each locus is marked with a traffic light system.
 - The Quality control table has one column for all of the metrics and separate columns for each of the displayed loci.
 - The "Overall" row indicates the overall result for each of the individual loci based on the traffic light system.

- Each metric has its own row in the table. Right next to the name of the metric, a small "i" mark is displayed. By hovering the mouse over the "i" mark, a pop-up window will be displayed, containing more detailed description of the selected metric.
- For each of the metrics, you can see the traffic light, the value of the metric and a small "i" mark with the information about the specific thresholds of the metric. By hovering the mouse over the "i" mark, a pop-up window will be displayed, containing more detailed information about the thresholds of the selected metric.
- Data Statistics
 - Overview section - Read counts and proportions are available for several different steps of the analysis.
 - Allele imbalance section - This figure shows the per-region allelic imbalance for all the genes.
 - Fragment size section - This histogram shows the fragment size distribution of paired reads.
 - Read quality section - On this graph, the base quality per 5 bases is shown for the processed reads. Read positions are on the x-axis while on the y-axis quality values are shown.

Different loci can be selected on the left side of the bottom section.

For the selected loci, you can enter to the genome browser by clicking to the "Browse Alignment", "Browse Allele 1", "Browse Allele 2" buttons.

For further information, please see the Genotyping Sample result section of the Omixon Handbook.

4.6 Gene Browser

The Gene Browser allows visual inspection of genomics data. Multiple allele candidates can be browsed together.

With default settings, the following tracks are available in the browser:

- *Position track* - Shows the coordinates for all visible tracks. Numbering starts from one.
- *Phasing track group*:
 - Phasing track* - This track contains annotations for continuously phased regions (aka Phasing regions).
 - Variants track* - Shows the number of overlapping read pairs between two consecutive heterozygous positions (i.e. two position where the two consensus sequences differ from each other). The 'Straight' label shows the number of reads for each consensus that supports the phasing shown in the browser, while the 'Cross' label shows the number of supporting reads for the other possible phasing of the two positions.
- *Consensus sequence 1* - The generated consensus sequence for one of the chromosomes.
- *Coverage depth for consensus 1* - Shows the depth of coverage for every position of the consensus sequence 1 *assembly*.
- *Consensus sequence 2* - The generated consensus sequence for the other chromosome.
- *Coverage depth for consensus 2* - Shows the depth of coverage for every position of the consensus sequence 2 *assembly*.
- *Allele 1 sequence* - Nucleotide sequence of the allele that matches the first consensus the best.
- *Region annotation for allele 1* - Annotations for exons, introns and UTRs are shown for allele 1.
- *Coverage depth track for allele 1* - Shows the depth of coverage for every position of the allele 1 *alignment*.
- *Allele 2 sequence* - Nucleotide sequence of the allele that matches the second consensus the best.
- *Region annotation for allele 2* - Annotations for exons, introns and UTRs are shown for allele 2.
- *Coverage depth track for allele 2* - Shows the depth of coverage for every position of the allele 2 *alignment*.

For novel alleles, two reference tracks are shown: the reference sequence of the novel allele (*Novel ref*) and the reference sequence of the closely related allele (*Rel ref*) from which the novel allele was derived.

Note that consensus sequences and the corresponding short reads can be viewed in the browser, even when no allele match pairs are found.

Additional tracks:

- *Noise track* - Shows systematic noise filtered out during consensus assembly. The noise consensus contains the major nucleotide for every position.
- *Amino acid track* - Shows the amino acid sequence for all allele and consensus sequences, including novel alleles, colored based on amino acid hydrophobicity.

By default, detailed coverage tracks are displayed for the allele alignments, alongside region annotations. The coverage track has a built-in base statistics visualization support: for bases in reads different from the actual consensus/reference base the corresponding coverage depth is shown with the associated nucleotide base color proportionally.

Additional modes for short read tracks

Other than the default *coverage depth mode*, the following alternative short read visualization modes are available for the short read track:

- *Short read mode* - Shows short reads displayed in a stranded fashion, so that forward strand reads (pink) and reverse strand reads (yellow) can be easily distinguished within the display.
- *Fragment mode* - Paired visualization mode that shows the corresponding forward and reverse reads in pairs in the same line. Overlapping sections between read pairs are marked with blue, while non-overlapping reads are connected with a thin line.



In both of the above modes, the short reads track can be *collapsed* which gives a summary view of the short reads (and does not allow each read to be inspected in detail).

4.7 Settings dashboard

Reachable from the *Genotyping dashboard* using the *Application settings* button, the *Settings dashboard* displays an overview of the settings in the tool, allows access to administration features and display configurations. Some general information about the current version of the software and the current user is also available on this dashboard.

4.8 General information

There are three blocks of information on the Settings Dashboard:

- Omixon HLA edition: this part contains the name and version of the software, the build identifier with a dedicated copy to clipboard button and some contact and copyright information.
- User info: this part contains the login name, first and last name of the current user.
- License info: this part shows the number of available credits and the expiration date of the license.

4.9 Sidebar

The left sidebar contains the following function sets:

4.9.1 General

In this function group you can set where analysis data and result files are stored, create and manage protocols, set targeted genes for analysis and select the assay version to be used for analysis. For details about protocols see the *Analysis Protocols* help page.

4.9.2 Database

With the *Install New Database* function, you can set up one or multiple versions of the IMGT database used for genotyping. With the *Select Active Database* function, you can specify the active version of the database. Genotyping will always be initiated using the active version. You can set whether or not to use database extensions in the *Configure Database Extensions* menu.

4.9.3 Administration

With the *User management* option, you can create, edit and remove users. With the *Display Hardware Key* option, you can display an alphanumeric identifier for your computer which can be used for generating a license for that specific machine. The *Upload Licence* option can be used for manually importing a license file into the software.

4.9.4 Automation

This function group allows you to configure automatic analysis on server-client configurations.

4.9.5 Export Settings

Here you can configure LIMS export.

4.9.6 Screen Settings

In this function group you can change the display configurations for the Gene Browser and result screens. Note, that these changes will modify the default behavior and appearance of the software. If you only want to temporarily change browser settings the *Display settings* option on the browser screen should be used. You can also modify the default filters of the Genotyping result screens. Be aware, that if you unselect a locus in this wizard, results for that locus won't be shown, regardless of the typing results. For both configuration sets,



you can set all the parameters back to the default values using the *Restore defaults* function. For details about these settings, please see the following help pages: *Analysis Result Screens* and *Gene Browser*.



5 Installation guide

5.1 Introduction

5.1.1 General information

This is an excerpt from the *Software Installation Guide*. If you couldn't find the information you were looking for in this document, please consult the extended *Software Installation Guide*. For further information and assistance, please contact us at support@omixon.com.⁴

5.1.2 Updating from HLA Twin 3.1.3 or below

Please note that the update process is different than usual. To ensure a safe update without any data loss, please take the time to read the Installation and Configuration chapter that is relevant to you.

5.2 Available Configurations

5.2.1 General information

This chapter explains the three possible configurations HLA Twin can be used in. Each of them is suitable for laboratories with different throughput.

This User Guide contains instructions for installing the Desktop and the Standalone Server as well as the Client. For detailed information on installing the Distributed Server please consult the extended *Software Installation Guide*.

5.2.2 Desktop

- Suitable for smaller laboratories
- One user can be logged in at a time
- One sample can be analyzed at a time

The software runs on one computer, the users have to share the same computer to work with the software. HLA Twin has its own user management system, so it does not matter who is logged in in Windows, the user can work under their own identity in HLA Twin (this is important for audit, workflow and commenting features). If the same software is installed on another computer, the two pieces of software are unable to communicate, so the mentioned user information will be unavailable. We advise against it.

5.2.3 Server (standalone)

- Suitable for medium-throughput laboratories
- **Multiple users can work at the same time**
- One sample can be analyzed at a time

The HLA Twin Server (standalone):

- runs sample analyses
- prepares the information for the HLA Twin Client
- holds all user data

The HLA Twin Client

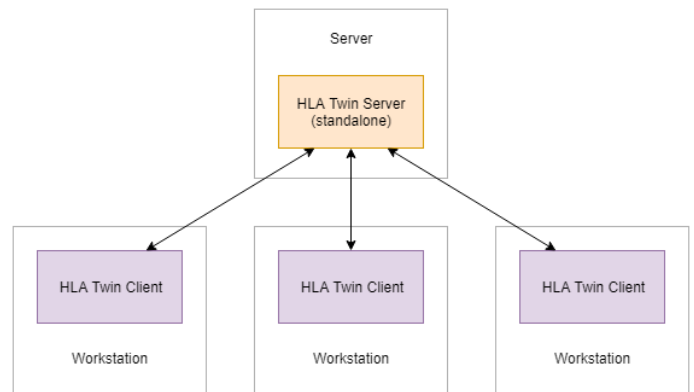
- controls the HLA Twin Server

⁴ <mailto:support@omixon.com>.



- shows what the HLA Twin Server sends to it
- is "an empty shell"

Multiple HLA Twin Client software can connect to the HLA Twin Server at the same time.
The license is bound to the HLA Twin Server so the number of HLA Twin Clients is not limited.



5.2.4 Server (distributed)

- Suitable for high-throughput laboratories
- Multiple users can work at the same time
- **Multiple samples can be analyzed at the same time (depending on the number of Typers)**

The HLA Twin Server (distributed):

- **does not** run sample analyses
- controls the HLA Twin Typer instances
- prepares the information for the HLA Twin Client
- holds all user data

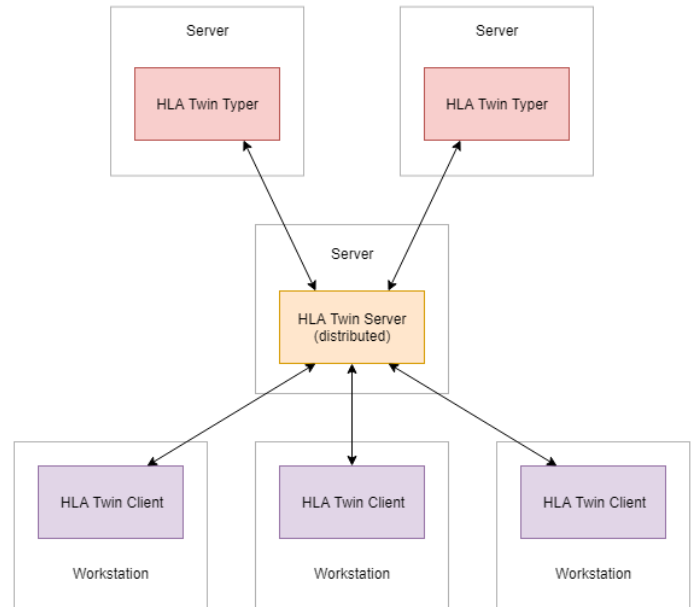
The HLA Twin Typer:

- runs sample analyses
- sends the analysis results to the HLA Twin Server

The HLA Twin Client

- controls the HLA Twin Server
- shows what the HLA Twin Server sends to it
- is "an empty shell"

Multiple HLA Twin Typers can be connected to one HLA Twin Server. An HLA Twin Server and an HLA Twin Typer instance can run on the same server.



5.3 System requirements

5.3.1 HLA Twin Desktop

- **CPU:** 64bit CPU with at least 4 physical cores (8 threads or vCPUs)
- **OS:** Any 64bit operating system
- **RAM:** At least 12 GB for the software but 16 GB is recommended
- **Video:** OpenGL 2.0 compatible video card

5.3.2 HLA Twin Client

- **CPU:** 64bit CPU with at least 2 physical cores (4 is recommended)
- **OS:** Any 64bit operating system
- **RAM:** At least 4 GB for the software but 6 GB is recommended
- **Video:** OpenGL 2.0 compatible video card
- **Network:** At least a 100/1000 Mbps connection

5.3.3 HLA Twin Server (standalone)

- **CPU:** 64bit CPU with at least 4 physical cores (8 threads or vCPUs)
- **OS:** Any 64bit operating system (OSX not supported)
- **RAM:** At least 18 GB for the software but 26.5 GB is recommended
- **Network:** At least a 100/1000 Mbps connection



5.3.4 HLA Twin Server (distributed)

- **CPU:** 64bit CPU with at least 4 physical cores (8 threads or vCPUs)
- **OS:** Any 64bit operating system (OSX not supported)
- **RAM:** At least 6 GB for the software but 8 GB is recommended
- **Network:** At least a 100/1000 Mbps connection

5.3.5 HLA Twin Typer (distributed)

- **CPU:** 64bit CPU with at least 4 physical cores (8 threads or vCPUs)
- **OS:** Any 64bit operating system
- **RAM:** At least 16 GB for the software but 22 GB is recommended
- **Network:** At least a 100/1000 Mbps connection

5.3.6 Storage space

Storage space requirements depend on the size of the samples and need to be calculated with regards to legal requirements for storing the data, minimum level of backup and redundancy, as well as on the expected annual volume. Omixon can assist with calculating the storage space requirements, please contact support@omixon.com⁵ if you need any help.

5.4 Desktop installation

5.4.1 Updating from HLA Twin 3.1.3 or below

You will not be able to update your previous version of HLA Twin 3.1.3 Desktop as you could in previous versions. Also, the installer will not allow you to install HLA Twin 4.0.0 in the same folder where an older version was installed.

The internal database from your old installation needs to be migrated in order **to keep your user data and audit information**. The migration is part of the installation process (step 8). For further details, please see Database migration.

After a successful installation and migration, you can uninstall previous versions of HLA Twin Desktop from your computer.

5.4.2 Installing HLA Twin Desktop

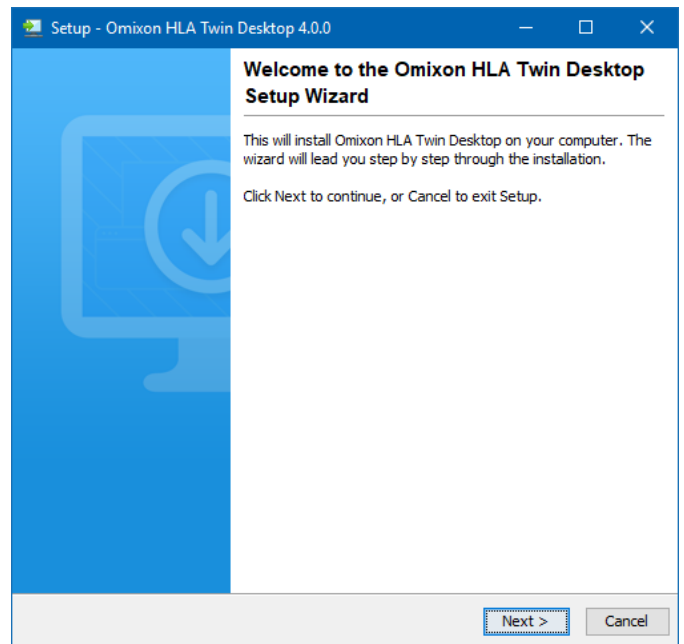
1. This step depends on the operating system you are using.

- **Windows users:** Open the installer (omixon_hla_twin_XXX_windows-x64_with_jre-**desktop**.exe)
- **Linux users:** Open a terminal window, get permissions to the installer (chmod +x omixon_hla_twin_XXX_unix_with_jre-**desktop**.sh) then run the installer.
- **OSX users:** Open the installer (omixon_hla_twin_XXX_macos_with_jre-**desktop**.dmg) (if you are using OSX 10.14.6 Mojave or above, you might get an error message. If so,

⁵ <mailto:support@omixon.com>

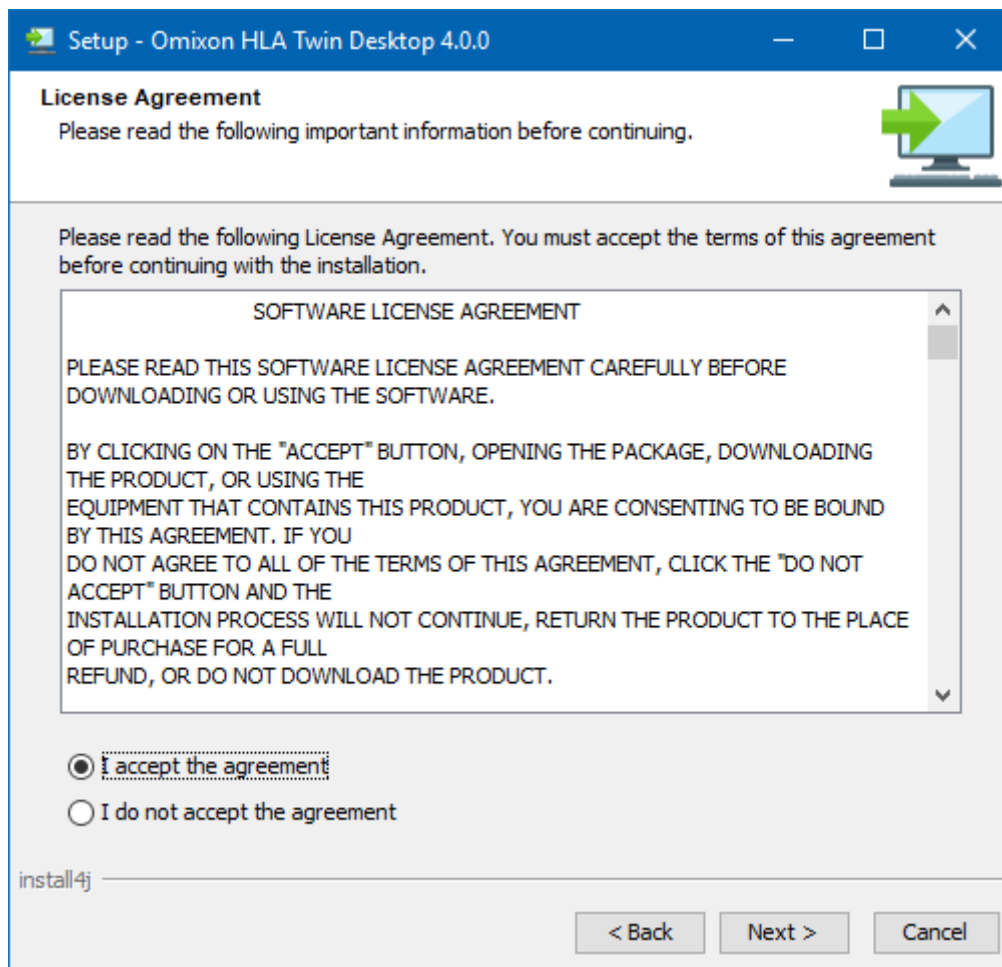


please contact us at support@omixon.com⁶⁾



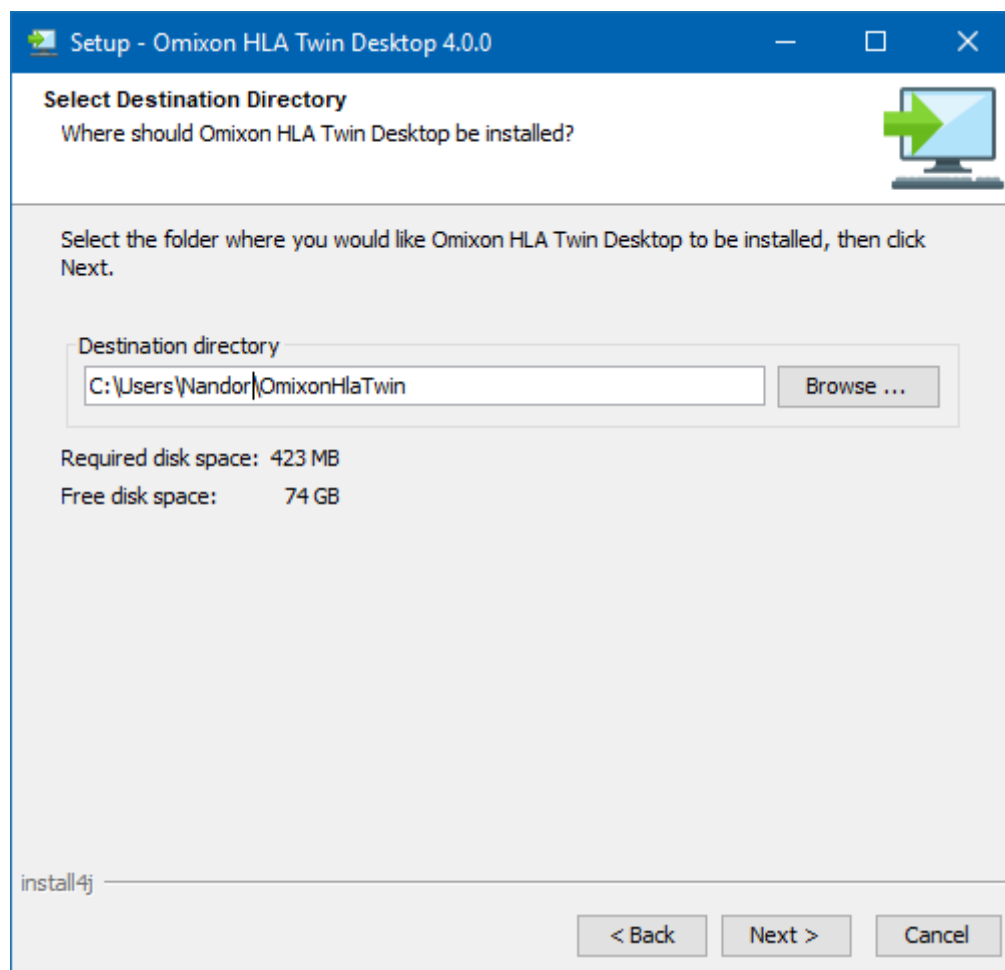
⁶ <mailto:support@omixon.com>

1. Accept the license agreement

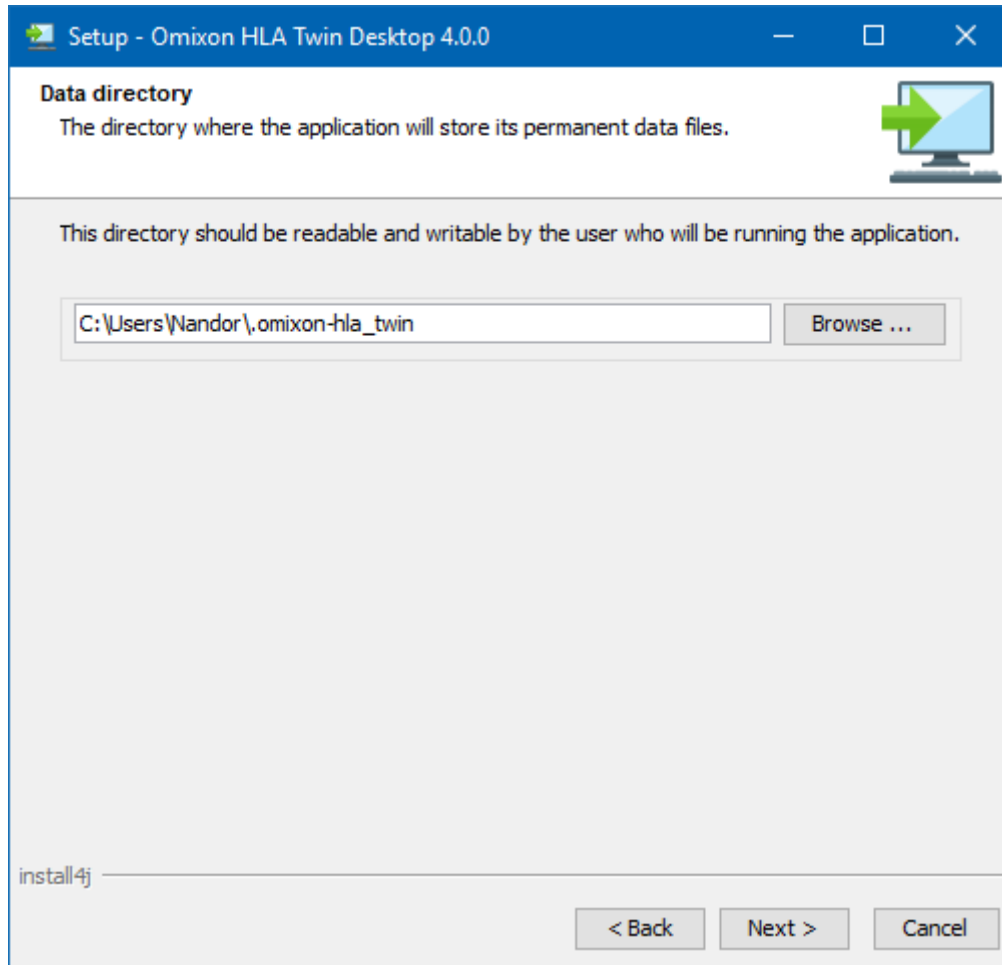


2. Select an installation folder.

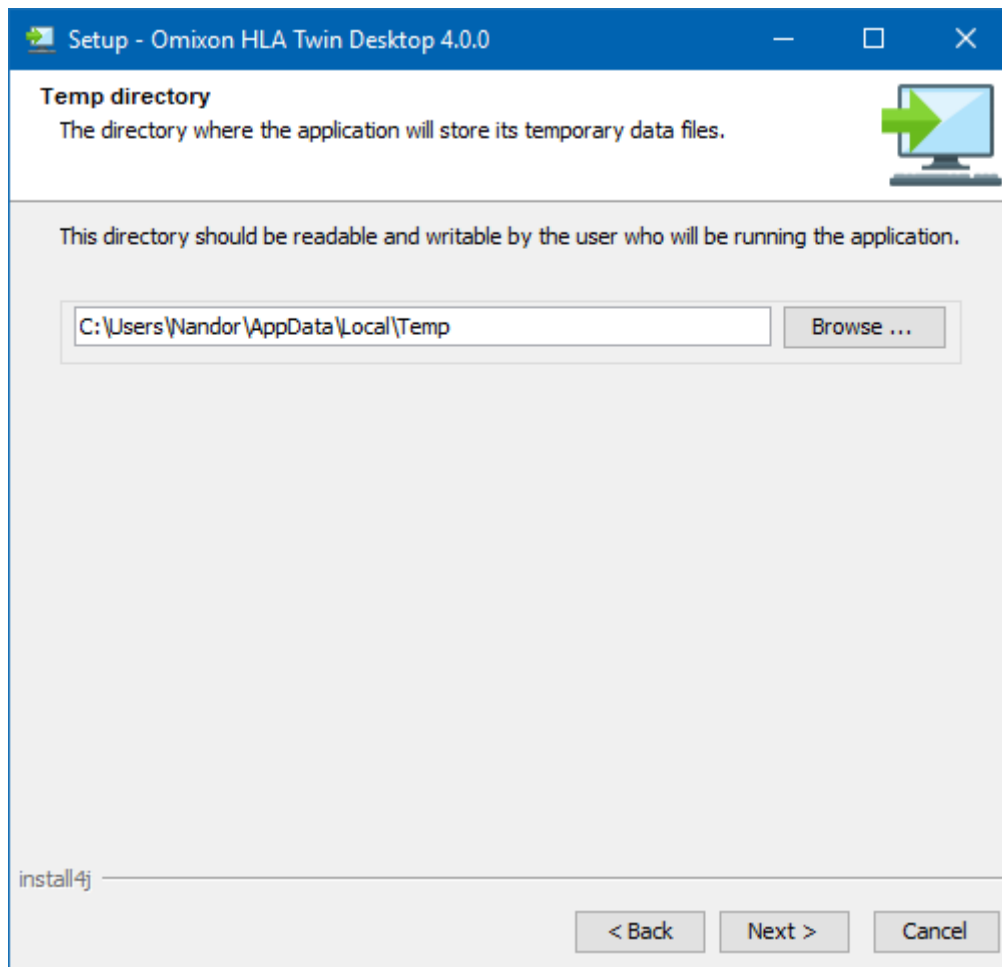
Windows users, please keep in mind that you might want to change the destination directory so other users in Windows can access the software (the same applies to the other installation folders in the next steps as well).



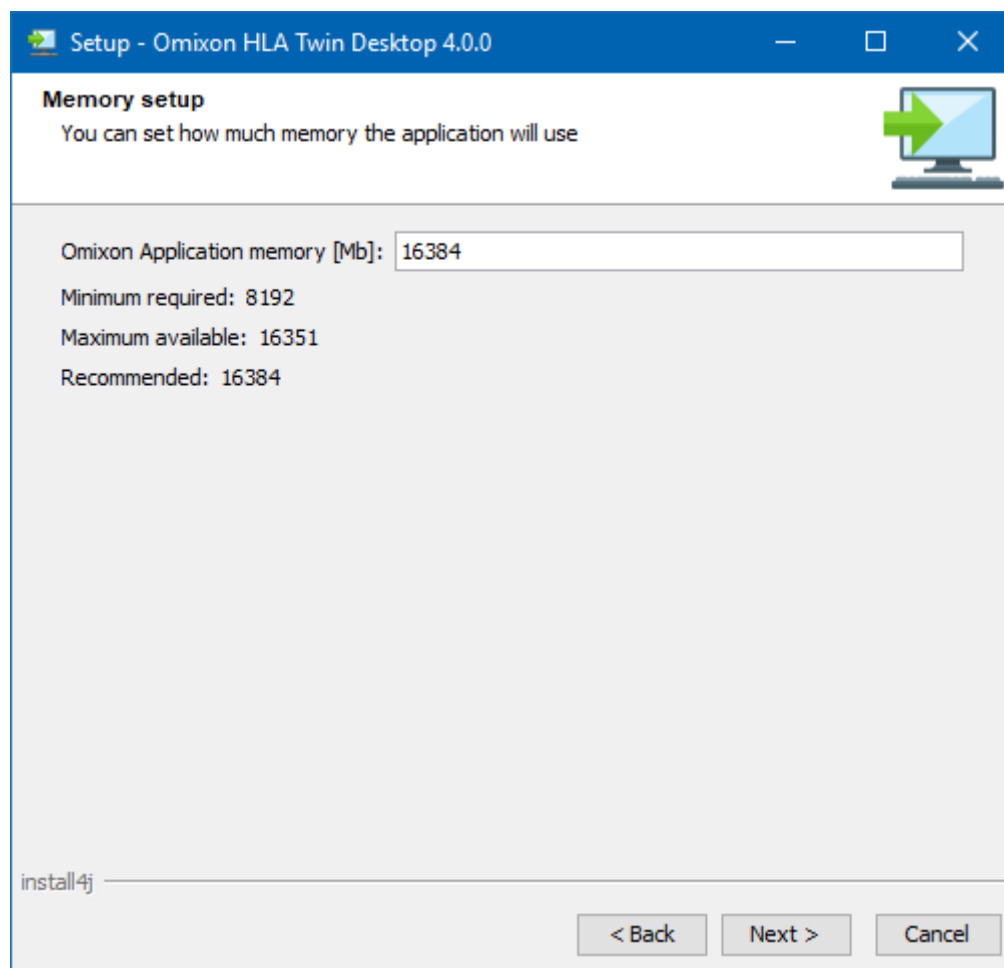
3. Select a folder for the software's internal database containing user data, reference databases, and audit information.



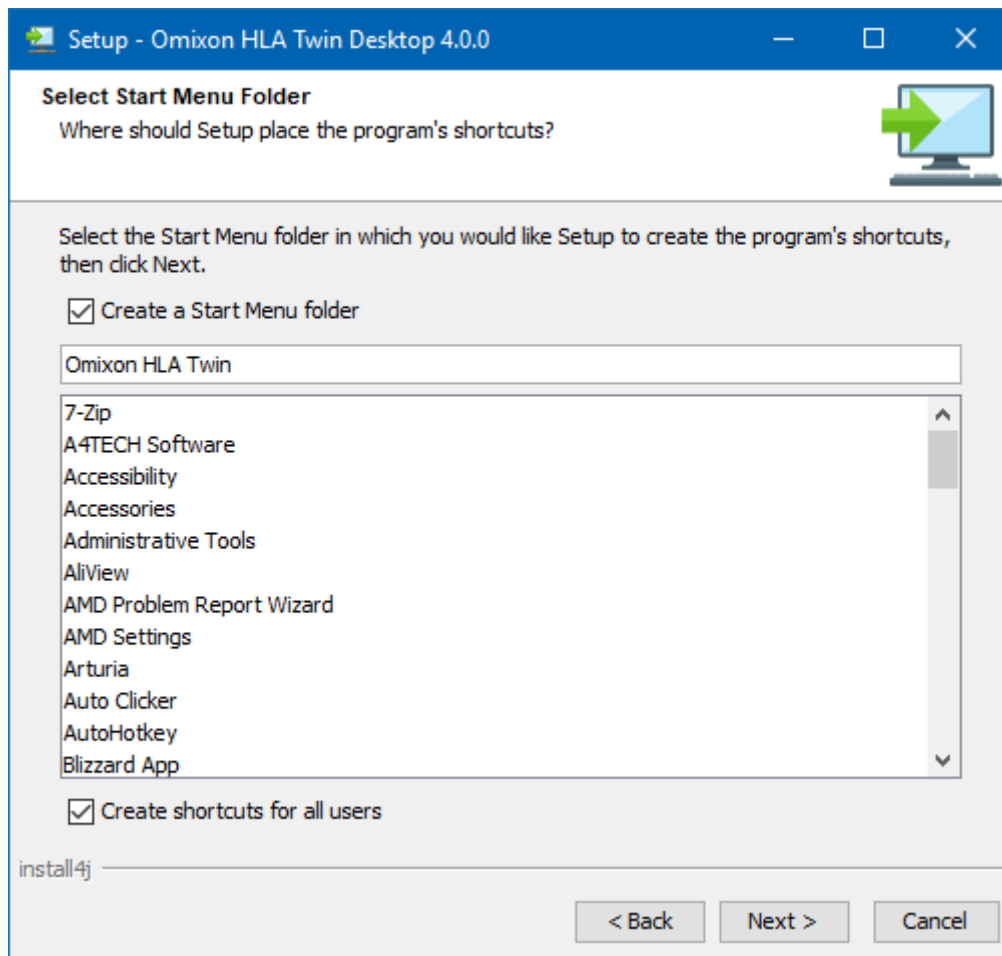
4. Select a folder for temporary files



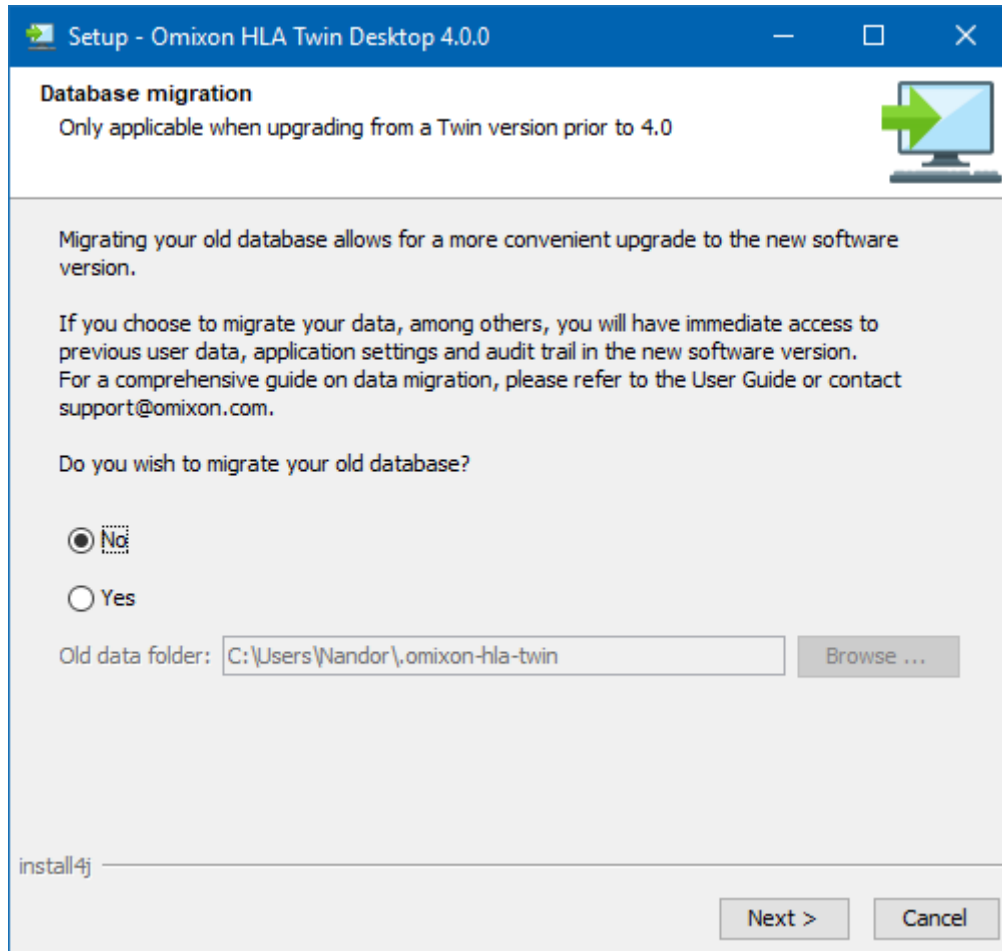
5. Configure the memory settings.



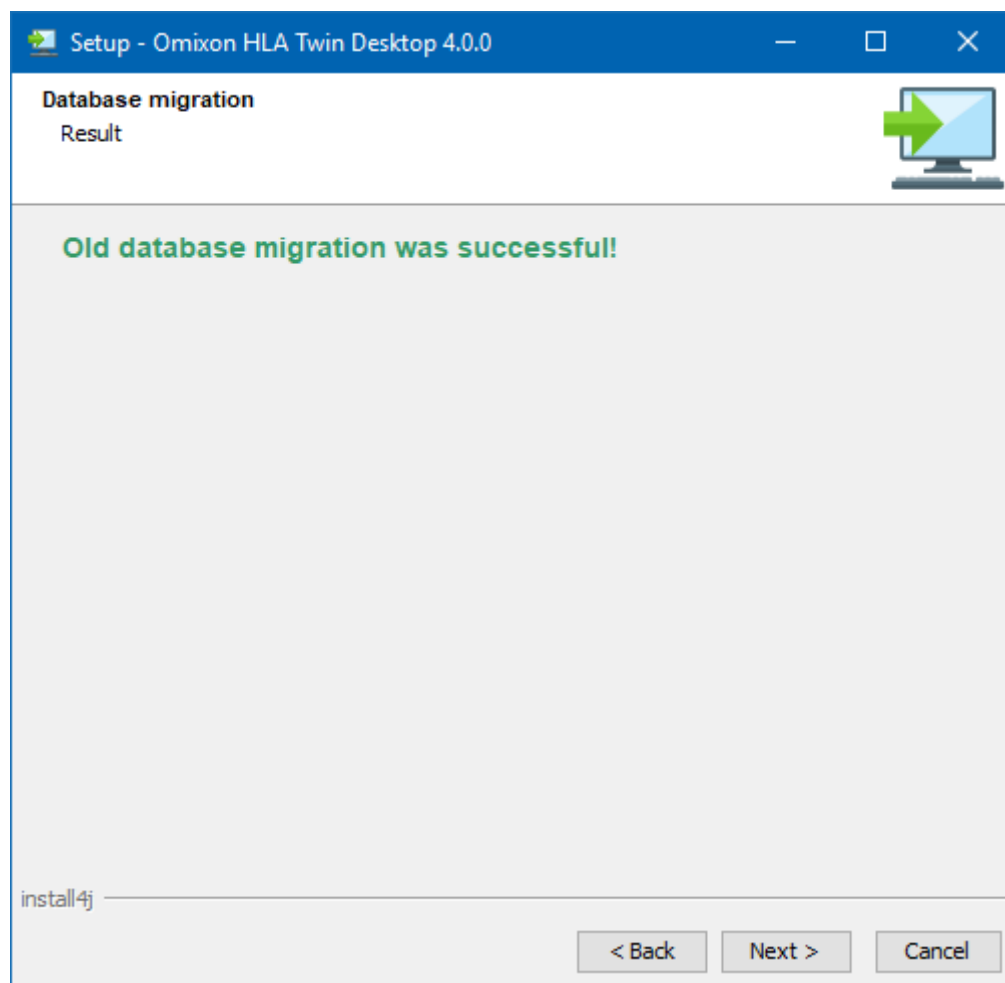
6. Select Start Menu folder



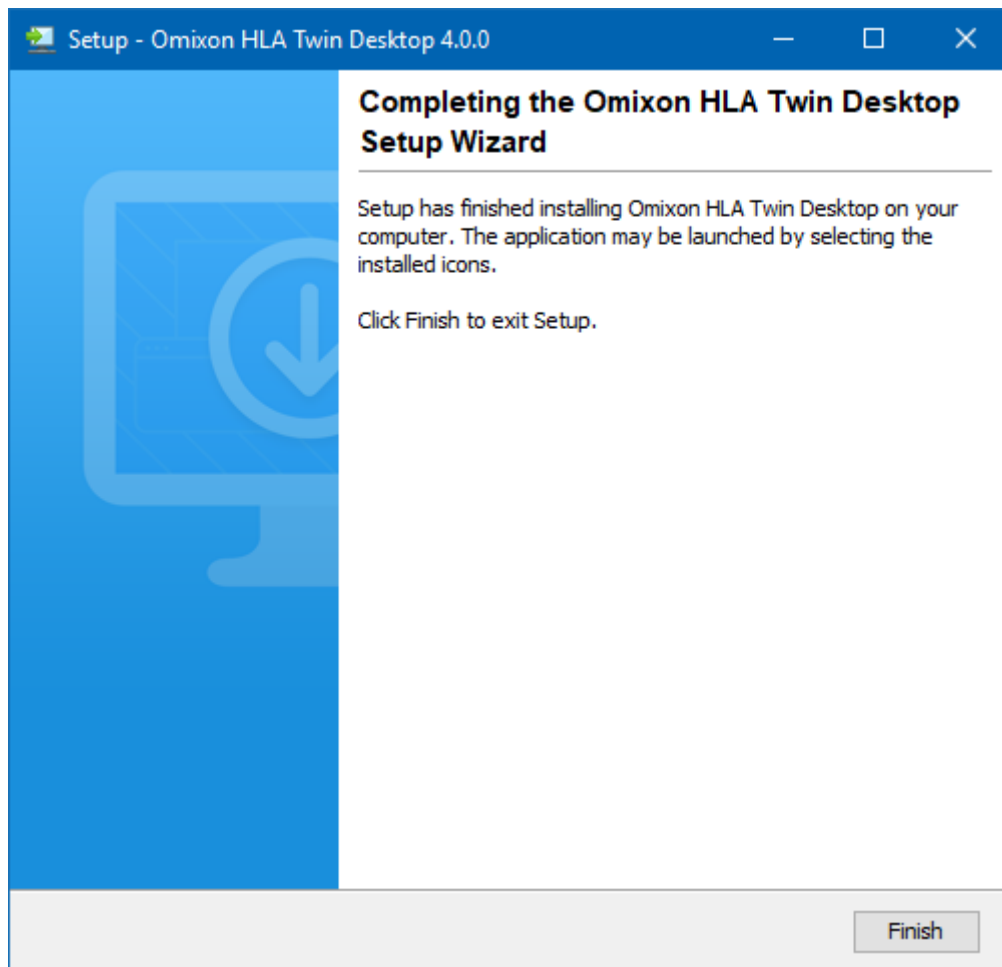
7. After the installation finishes, the installer gives you the option to migrate your old database.
- **If you are a new user:** select "No" and click on next
 - **If you are updating from HLA Twin version 3.1.3 or below:** please consider migrating the old database to keep your audit information. For further details, please see Database migration.



If you selected yes, the following message will be prompted after a successful migration.



8. Click Finish



5.5 Standalone server installation

5.5.1 Updating from HLA Twin 3.1.3 or below

You will not be able to update your previous version of HLA Twin 3.1.3 Server as you could in previous versions. Also, the installer will not allow you to install HLA Twin 4.0.0 in the same folder where an older version was installed.

The internal database from your old installation needs to be migrated in order **to keep your user data and audit information**. The migration is part of the installation process (step 11). For further details, please see Database migration.

After a successful installation and migration, you can uninstall previous versions of HLA Twin Server from your computer.

Please keep in mind that HLA Twin Client 4.0.0 is only compatible with HLA Twin Server 4.0.0.

There is **no HLA Twin Typer Server NG** service in the new version of HLA Twin Server, one service will handle the analyses and the Clients.

5.5.2 Notes before installation

Networking: HLA Twin Server will communicate with HLA Twin Clients on ports 4380 and 4381 by default, so please make sure to allow them on your firewall.

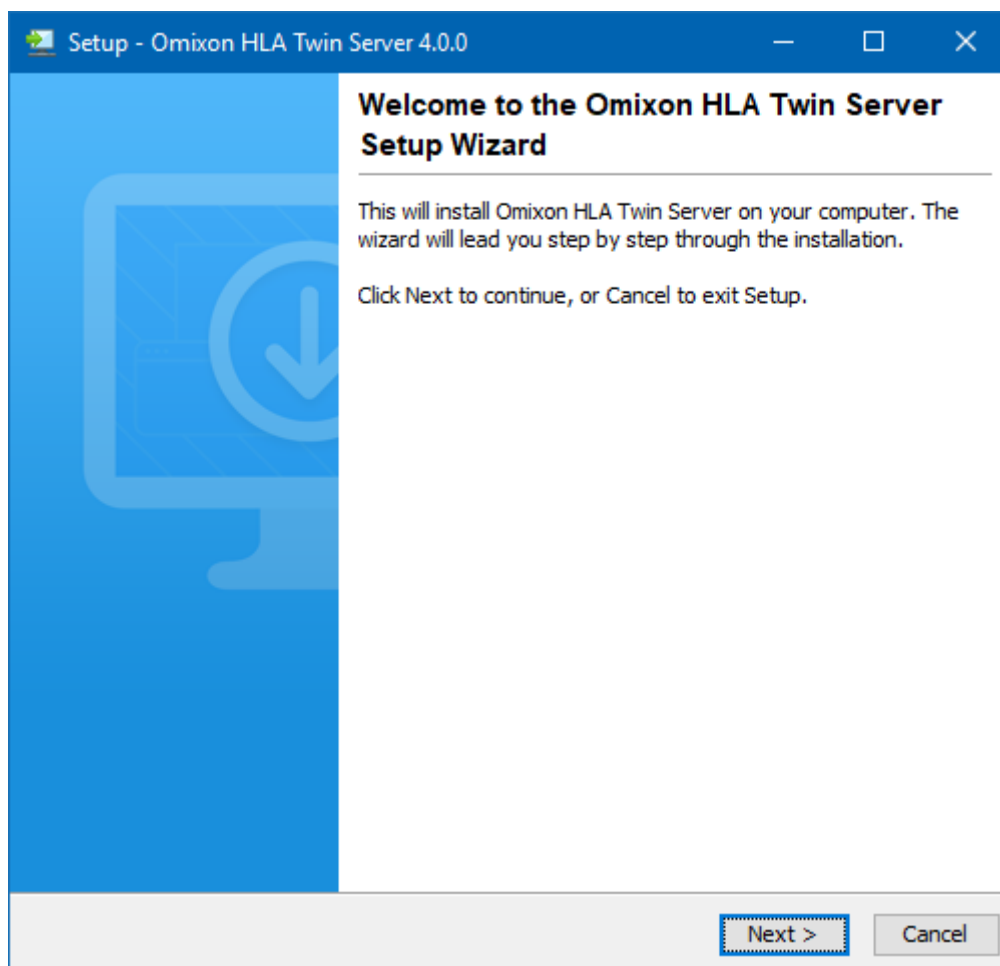
Databases: High throughput labs might benefit from using an external, MySQL-compatible database for HLA Twin Server's database. If you would like to use an external database, please configure it prior to the installation. Details can be found in Setting up an external database.

Windows Service: The HLA Twin Server will run as the Omixon HLA Twin NG Server service in Windows, which is set to automatic startup by default.

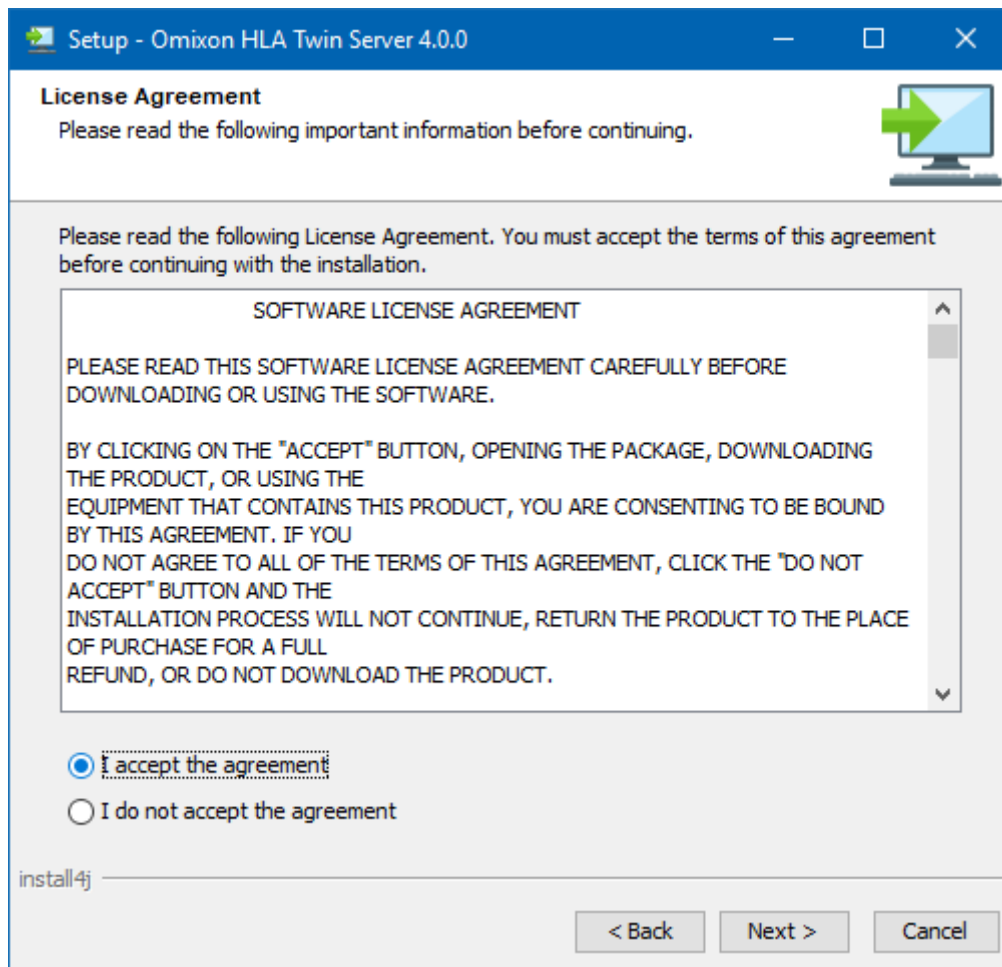
5.5.3 Installing HLA Twin Server

1. This step depends on the operating system you are using.

- **Windows users:** Open the installer (omixon_hla_twin_XXX_windows-x64_with_jre-**serverclient**.exe)
- **Linux users:** Open a terminal window, get permissions to the installer (chmod +x omixon_hla_twin_XXX_unix_with_jre-**serverclient**.sh) then run the installer.

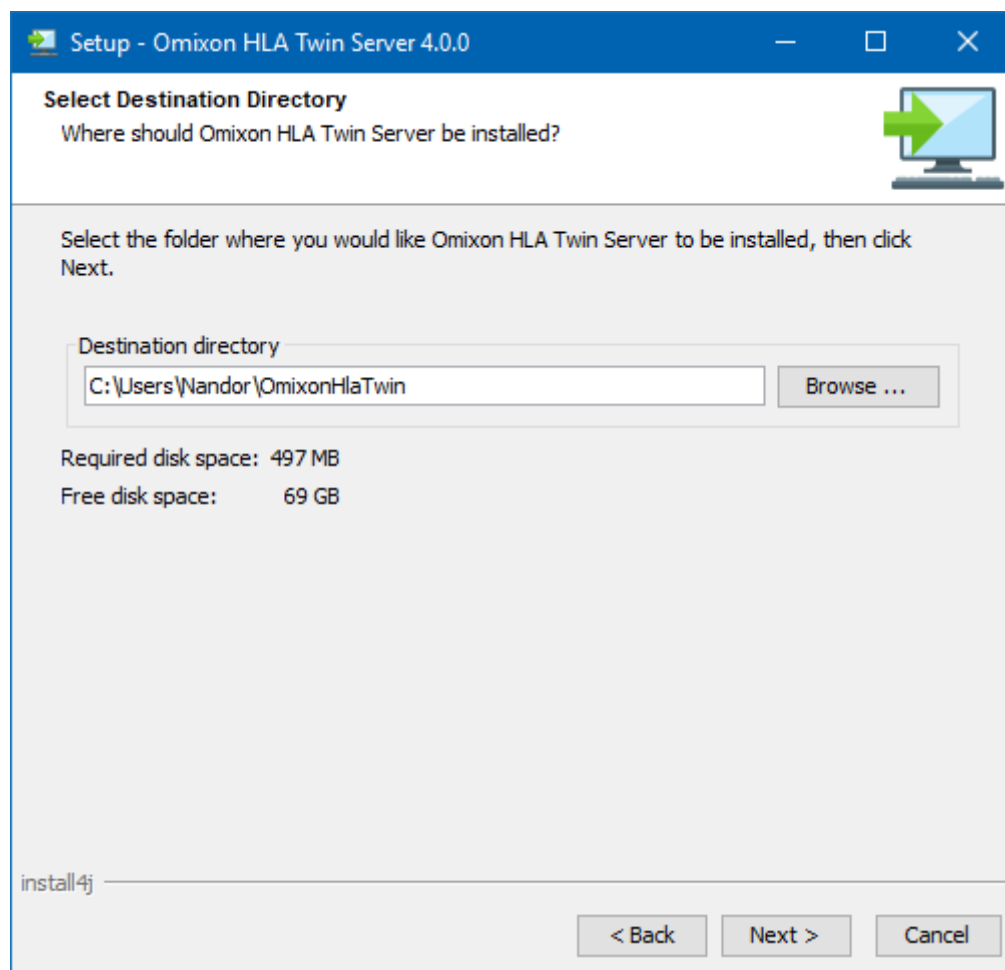


2. Accept the license agreement

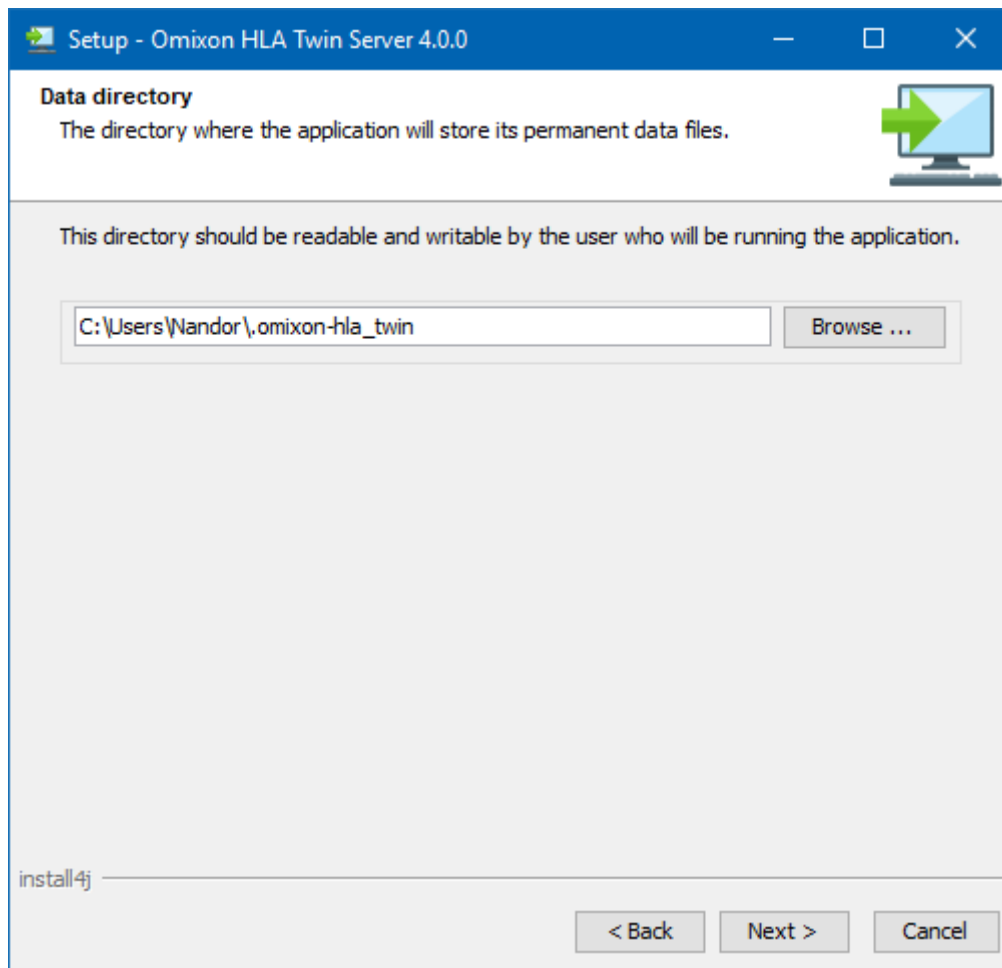


3. Select an installation folder.

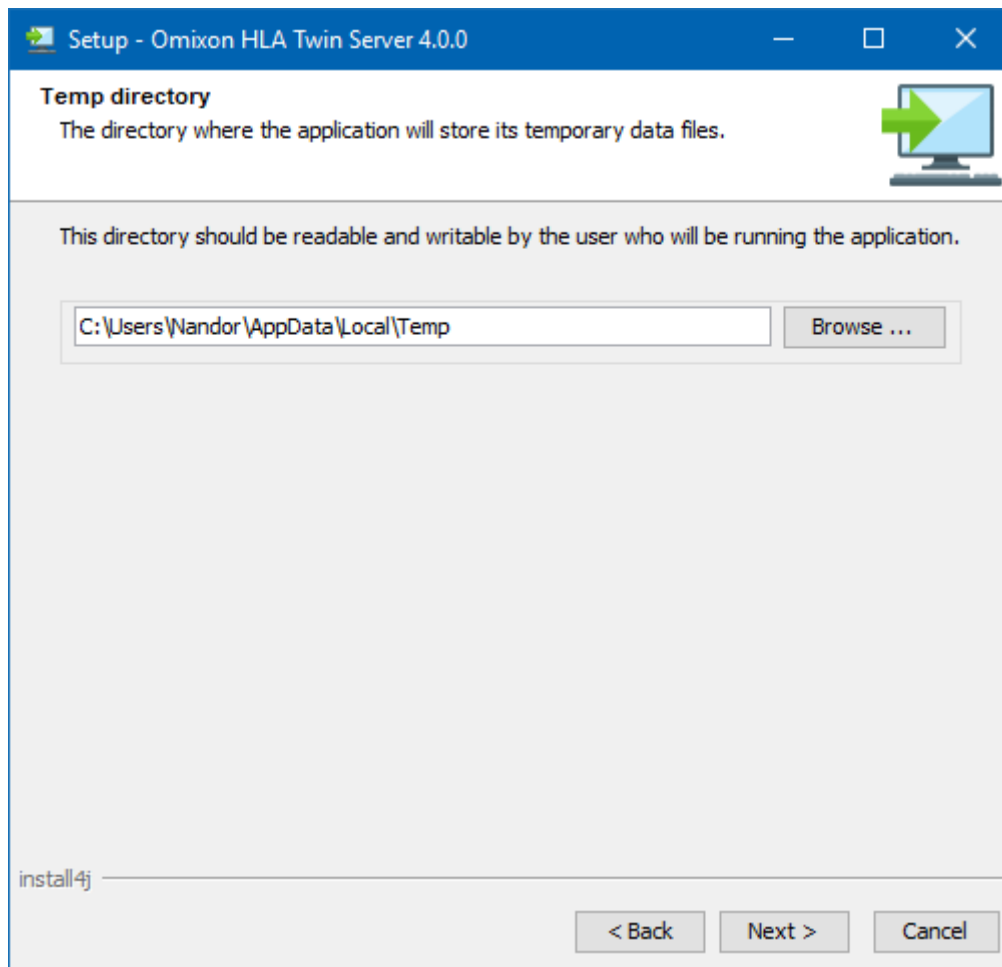
Windows users, please keep in mind that you might want to change the destination directory so other users in Windows can access the software (the same applies to the other installation folders in the next steps as well).



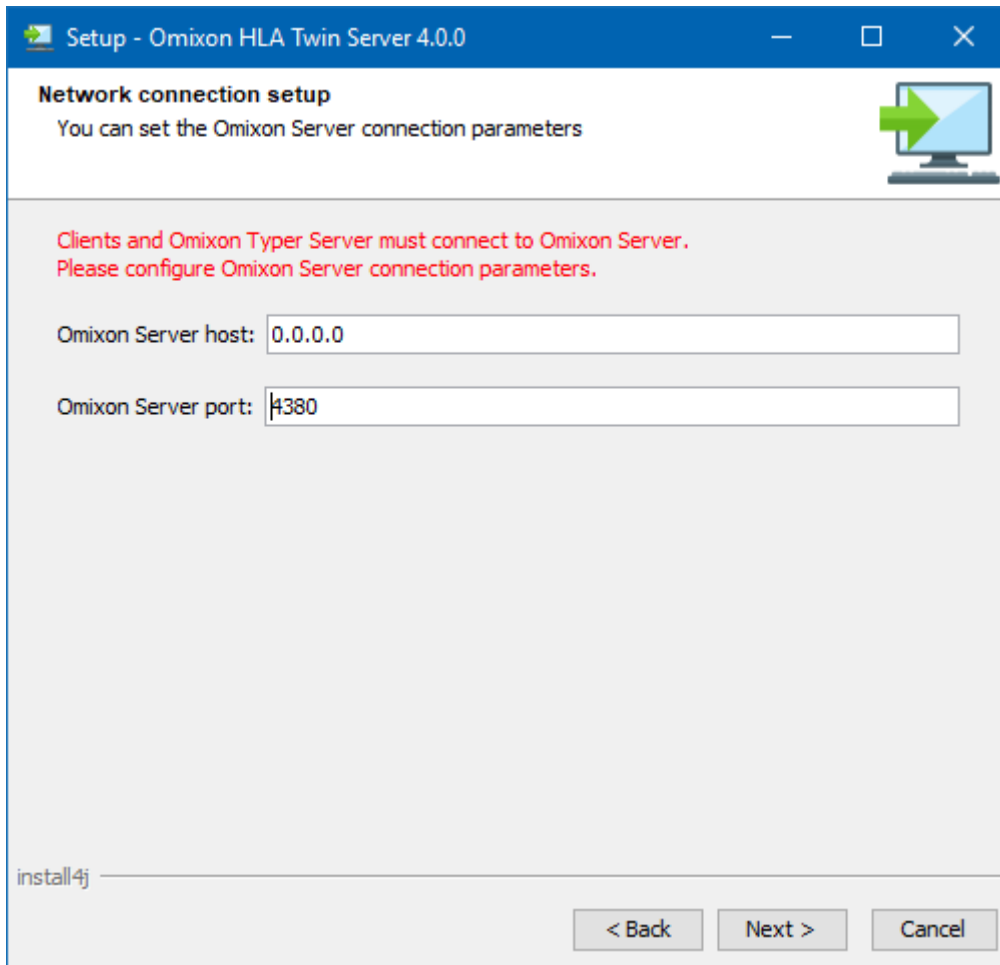
4. Select a folder for the software's internal database containing user data, reference databases, and audit information.



5. Select a folder for temporary files



6. Configure the IP address and port number that the HLA Twin Server will use for communication (local IP)



7. Select the type of database you want HLA Twin Server to use for storing user data, reference databases, and audit information.
- **Internal:** Suitable for low-throughput labs. The software will generate its own database, no further configuration is required
 - **External:** Suitable for high-throughput labs. The software is able to interface with an external, MySQL-compatible database instead of the internal one. Please note that you will need to configure the database first, information on that can be found in Setting up an external database.

Setup - Omixon HLA Twin Server 4.0.0

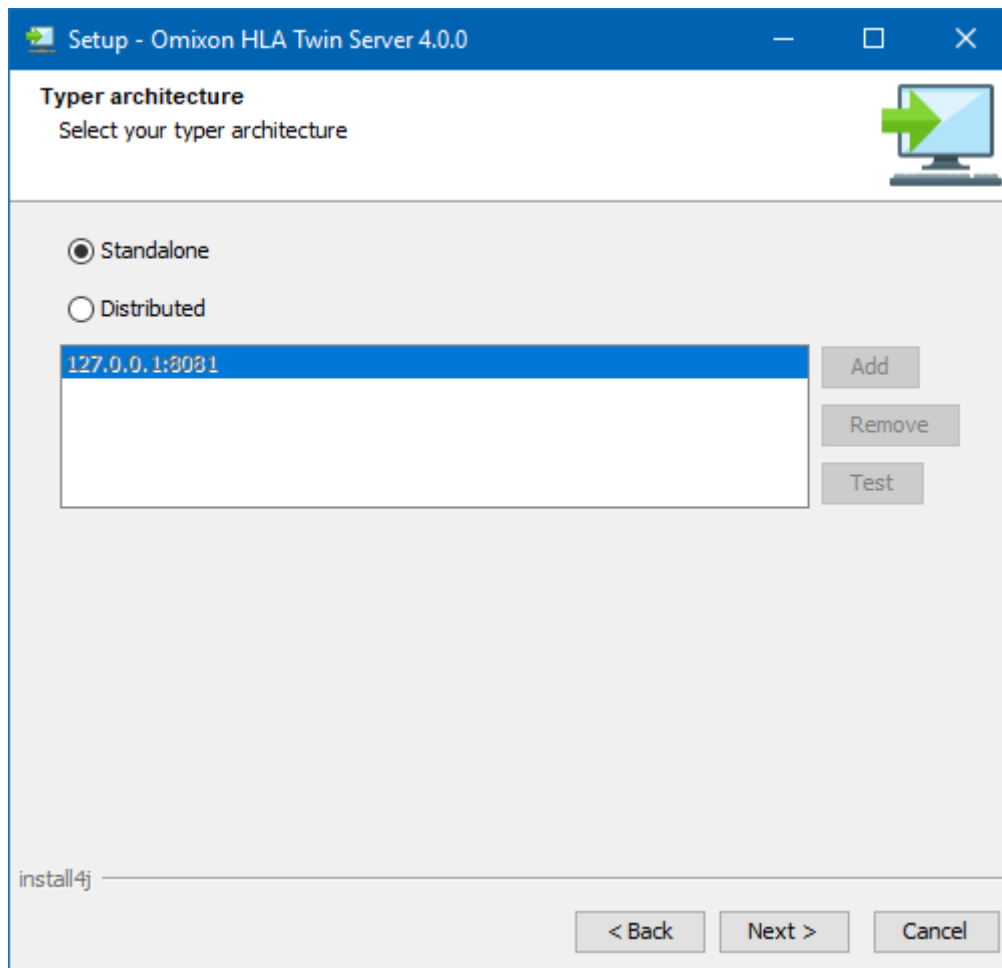
Persistence provider
Select your persistence provider

☒ Internal (H2)
☐ External (MySQL)

Host:
Port:

install4j

8. Select the standalone architecture (for the distributed configuration with multiple HLA Twin Typers on separate servers, please follow the Server (distributed) chapter)



Setup - Omixon HLA Twin Server 4.0.0

Typer architecture
Select your typer architecture

☒ Standalone
☐ Distributed

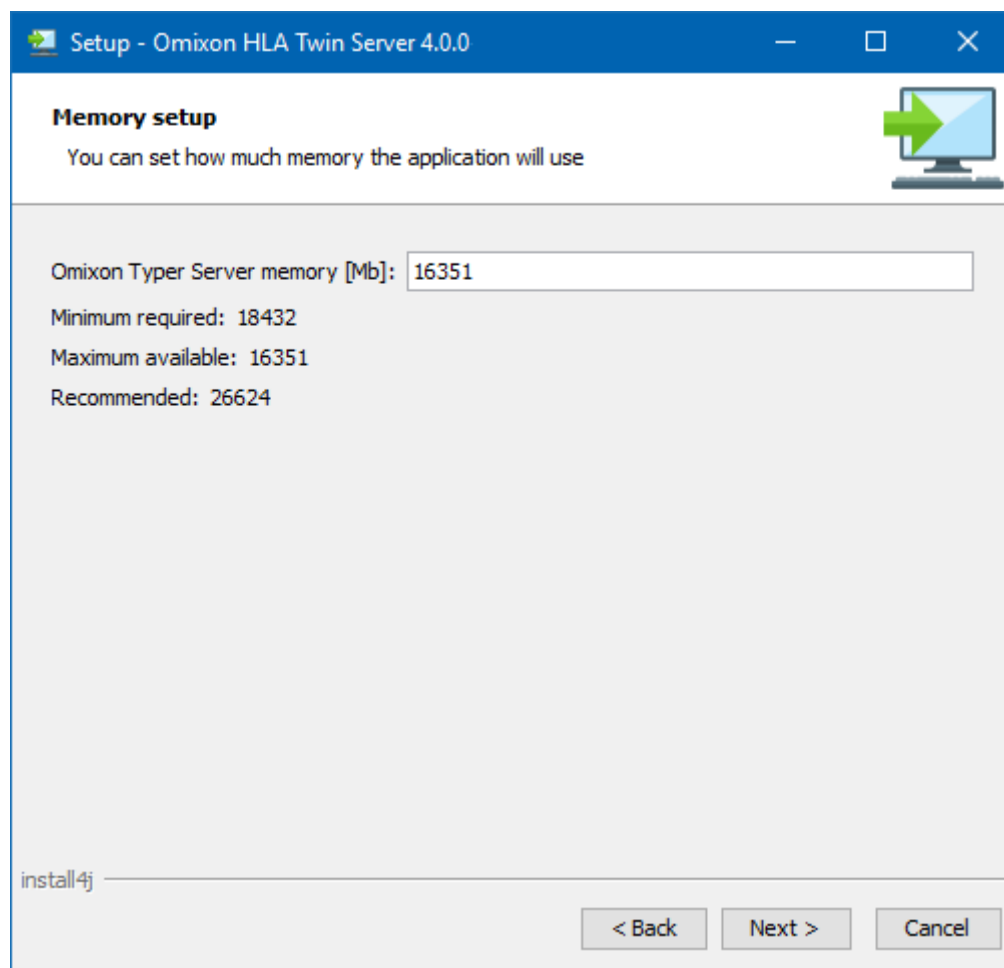
127.0.0.1:3031

Add
Remove
Test

install4j

< Back Next > Cancel

9. Configure the memory settings



Setup - Omixon HLA Twin Server 4.0.0

Memory setup

You can set how much memory the application will use

Omixon Typer Server memory [Mb]: 16351

Minimum required: 18432

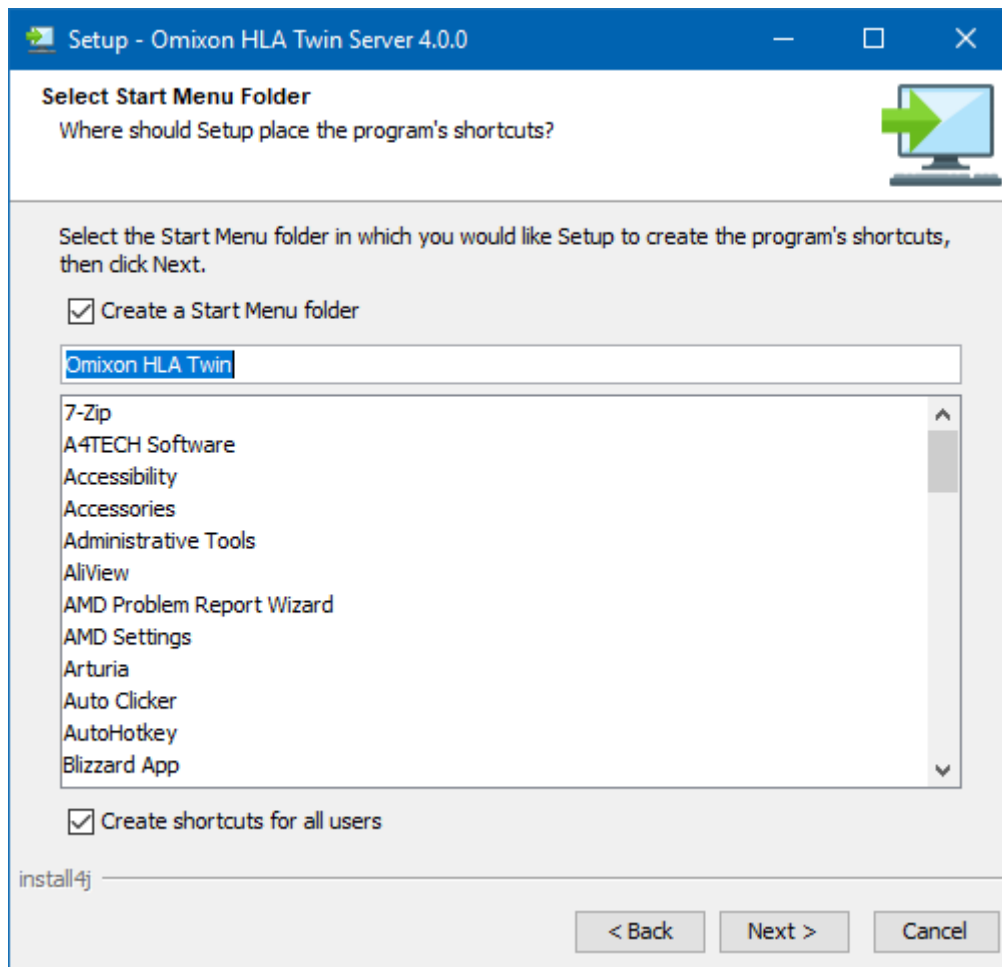
Maximum available: 16351

Recommended: 26624

install4j

< Back Next > Cancel

10. Select Start Menu folder




11. After the installation finishes, the installer gives you the option to migrate your old database.

- **If you are a new user:** select "No" and click on next
- **If you are updating from HLA Twin version 3.1.3 or below:** please consider migrating the old database to keep your audit information. For further details, please see Database migration.

Setup - Omixon HLA Twin Server 4.0.0

Database migration
Only applicable when upgrading from a Twin version prior to 4.0



Migrating your old database allows for a more convenient upgrade to the new software version.

If you choose to migrate your data, among others, you will have immediate access to previous user data, application settings and audit trail in the new software version. For a comprehensive guide on data migration, please refer to the User Guide or contact support@omixon.com.

Do you wish to migrate your old database?

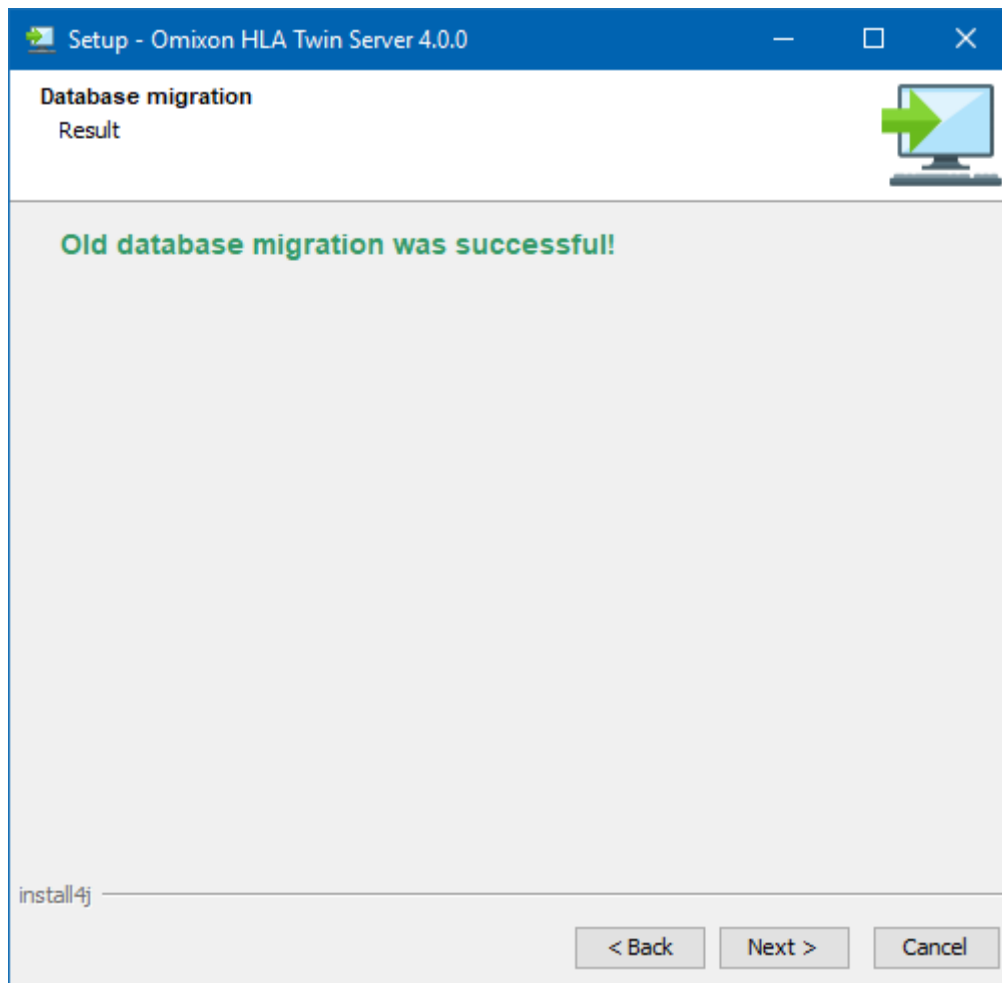
☒ No

☐ Yes

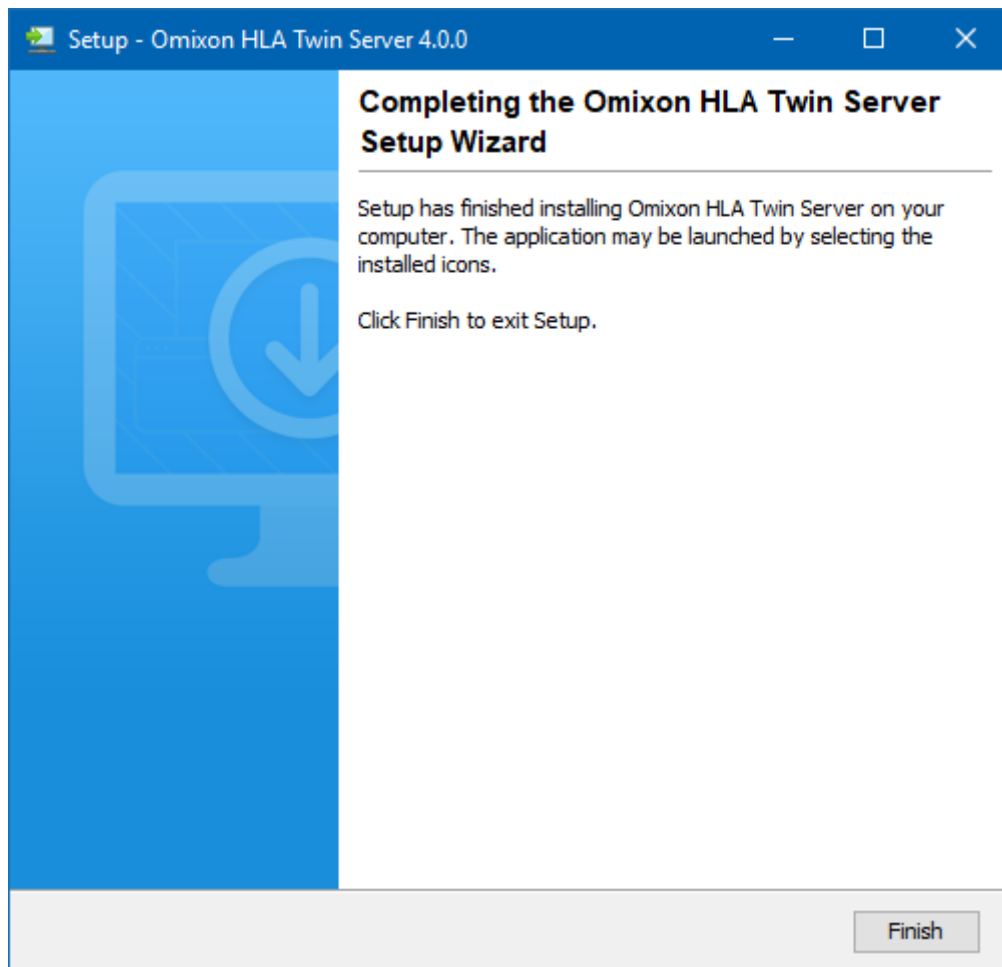
Old data folder:

install4j

If you selected yes, the following message will be prompted after a successful migration.



12. Click Finish





5.6 Client installation

5.6.1 Updating from HLA Twin 3.1.3 or below

You will not be able to update your previous version of HLA Twin 3.1.3 Client as you could in previous versions. Also, the installer will not allow you to install HLA Twin 4.0.0 in the same folder where an older version was installed.

After a successful installation and migration, you can uninstall previous versions of HLA Twin Client from your computer. Please keep in mind that HLA Twin Client 4.0.0 is only compatible with HLA Twin Server 4.0.0.

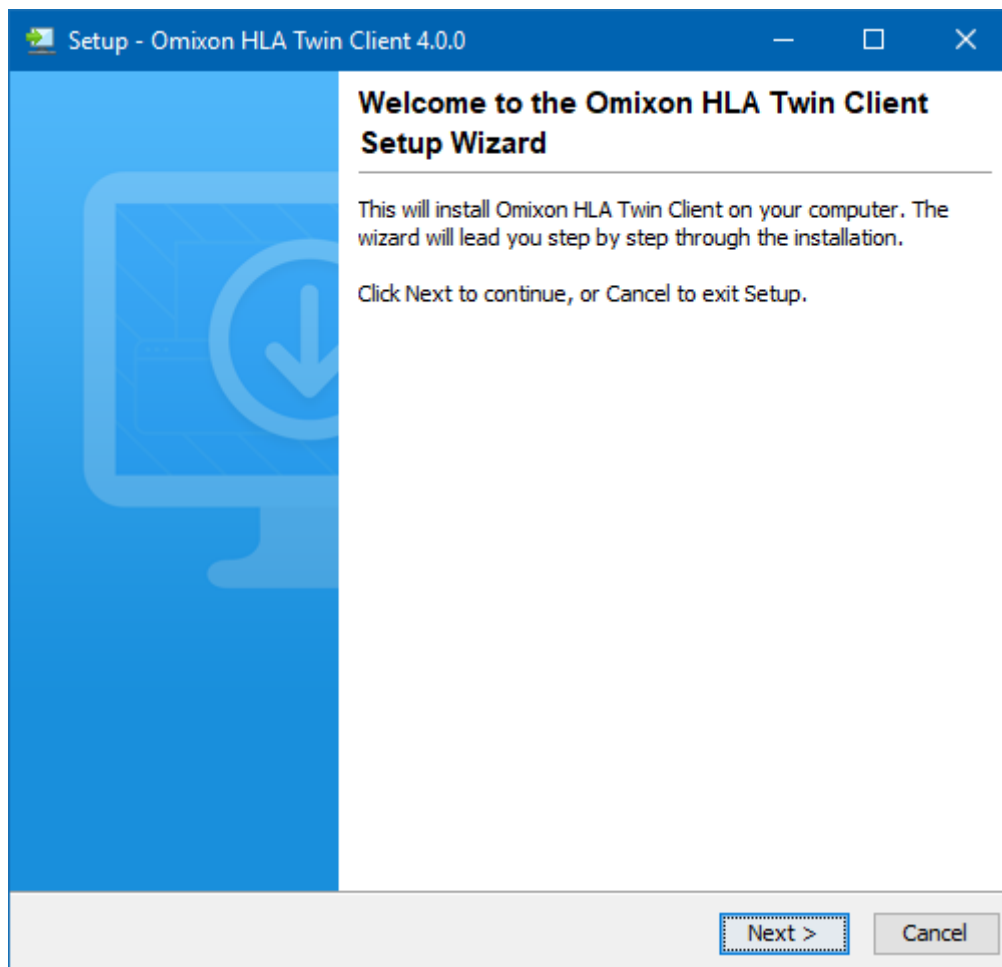
5.6.2 Notes before installation

Networking: HLA Twin Server will communicate with HLA Twin Clients on ports 4380 and 4381 by default, so please make sure to allow them on your firewall.

5.6.3 Installing HLA Twin Client

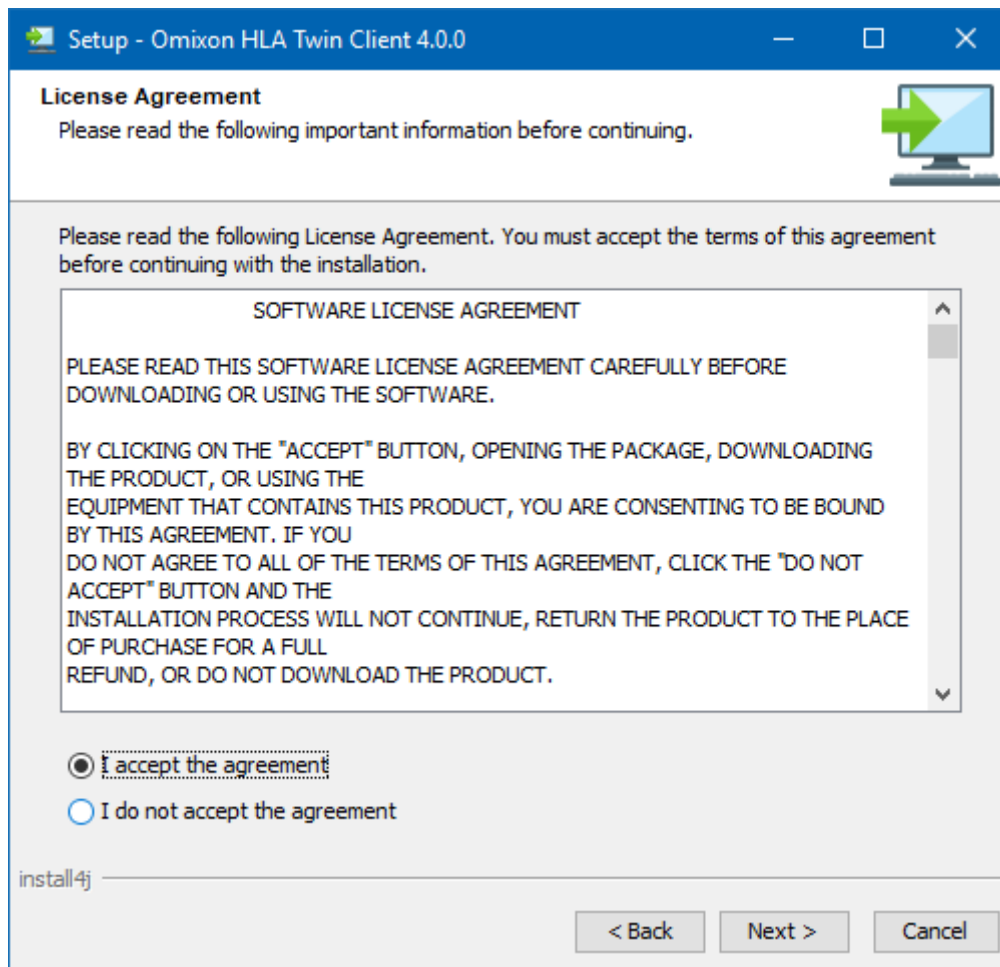
1. This step depends on the operating system you are running.

- **Windows users:** Open the installer (omixon_hla_twin_XXX_windows-x64_with_jre-**client**.exe)
- **Linux users:** Open a terminal window, get permissions to the installer (chmod +x omixon_hla_twin_XXX_unix_with_jre-**client**.sh) then run the installer.
- **OSX users:** Open the installer (omixon_hla_twin_XXX_macos_with_jre-**client**.dmg) (if you are using OSX 10.14.6 Mojave or above, you might get an error message. If so, please contact us at support@omixon.com⁷)



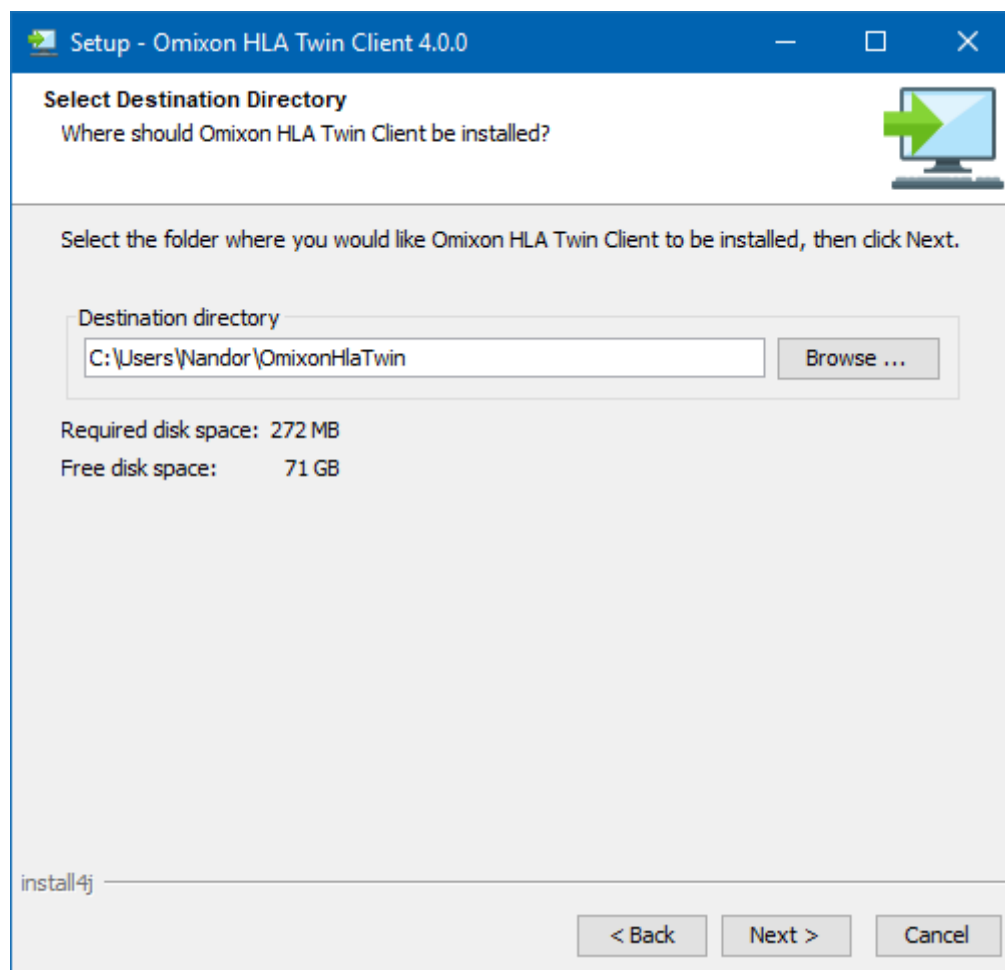
⁷ <mailto:support@omixon.com>

2. Accept the license agreement

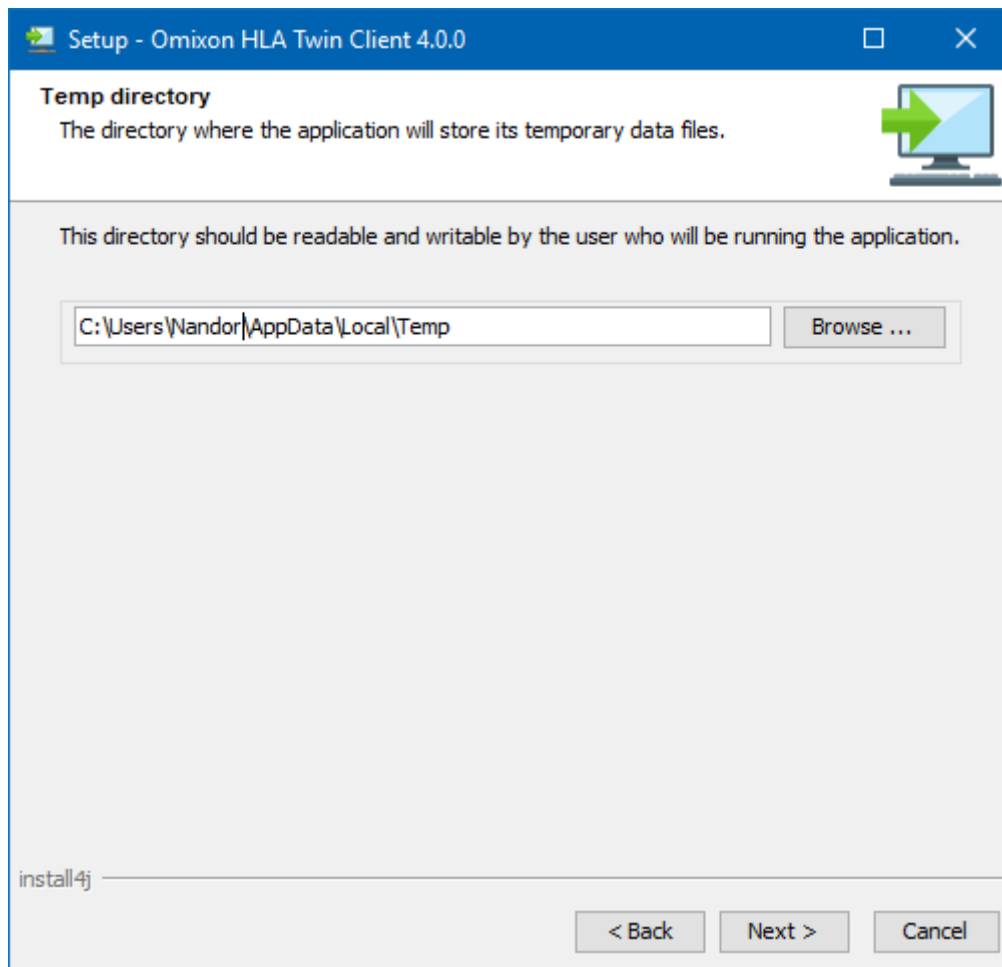


3. Select an installation folder.

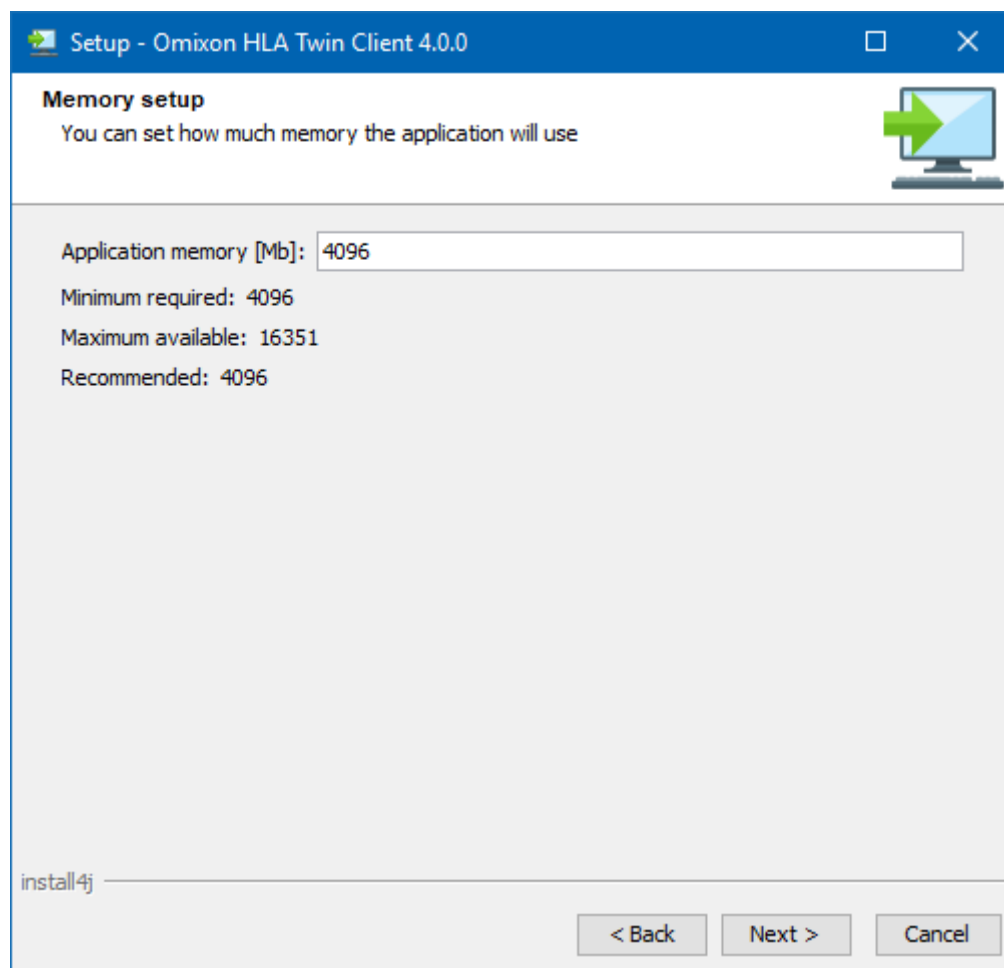
Windows users, please keep in mind that you might want to change the destination directory so other users in Windows can access the software (the same applies to the other installation folders in the next steps as well).



4. Select a folder for temporary files



5. Configure the memory settings



Setup - Omixon HLA Twin Client 4.0.0

Memory setup
You can set how much memory the application will use

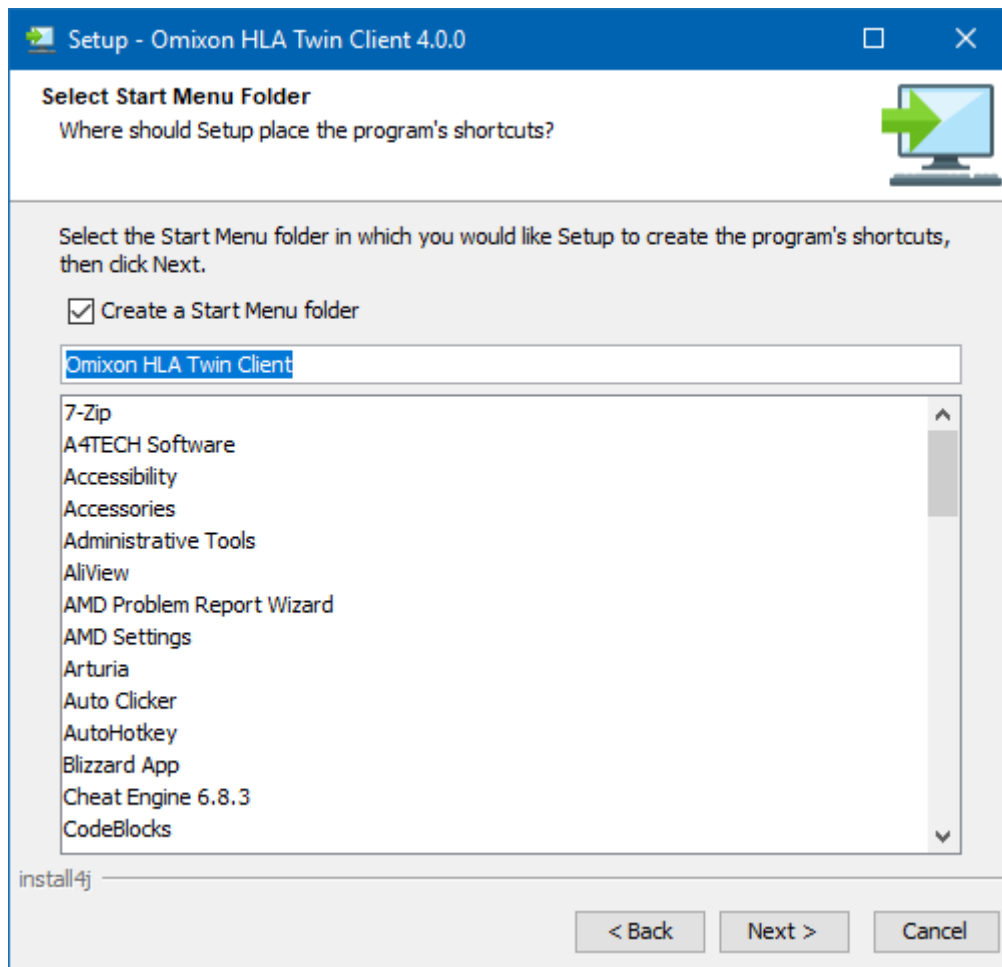
Application memory [Mb]: 4096

Minimum required: 4096
Maximum available: 16351
Recommended: 4096

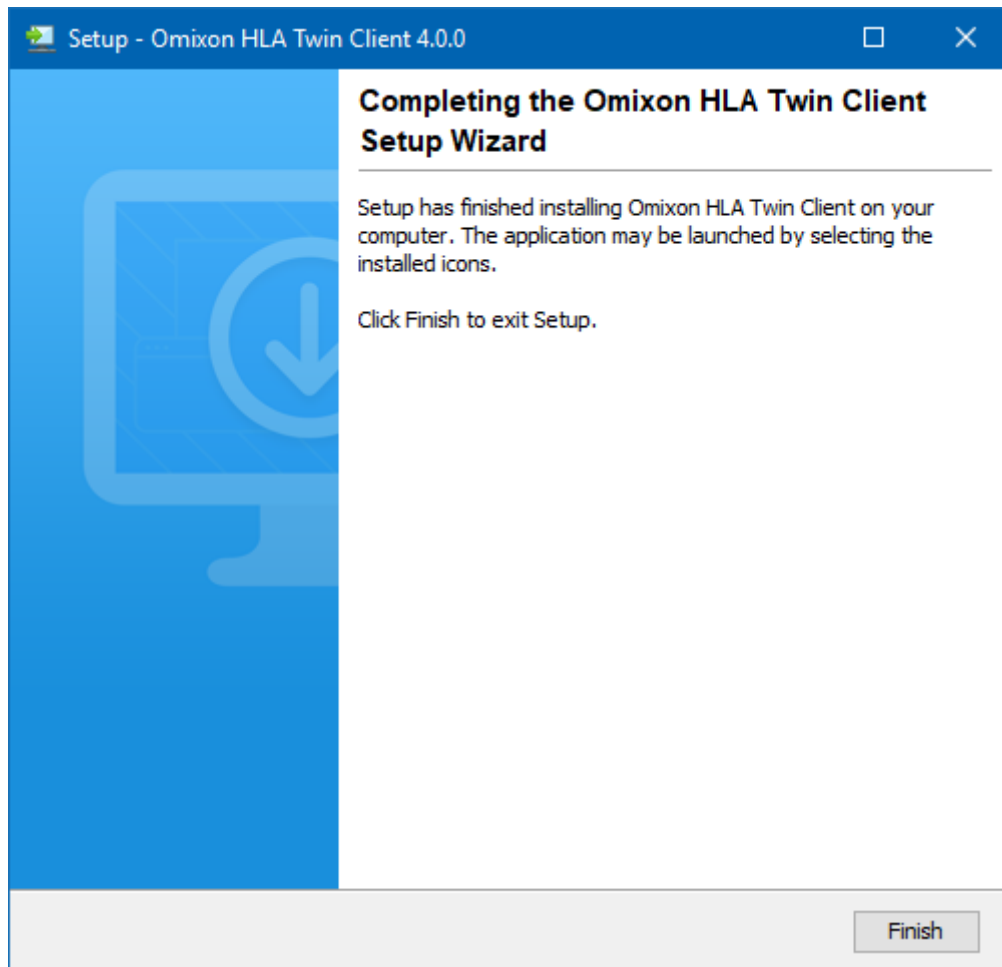
install-4j

< Back Next > Cancel

6. Select Start Menu folder



7. After the installation finishes, click on Finish



5.7 Database migration

This chapter is for users who plan to update from HLA Twin version 3.1.3.

5.7.1 Overview

The format of the internal database in HLA Twin 4.0.0 was changed for a more robust and efficient one (H2). This was necessary in order to provide a better user experience in the software.

Database migration is the process of transforming the data from your old HLA Twin database into the new one. We suggest that you do migrate your old database so the new version of HLA Twin will contain all the information that might be necessary for an audit.

5.7.2 Data to be migrated

The migration will basically transfer all data that is required for an audit. This entails:

- user accounts with their preferences
- global configurations such as automation configuration and scheduling, saved protocols, or the active reference database version
- analyses and their approval workflow information
- tasks regarding exports
- reference database imports

5.7.3 The migration process

The migration process is the last step of the HLA Twin installation. It will ask you to decide whether you would like to migrate your old database, and then it will ask you for the path where the old database is located.

The migration could take up to a few minutes. If you encounter an error, please contact us at support@omixon.com⁸

5.7.4 Old database location

The old database folder is `C:\Users_username_.omixon-hla-twin\` by default on Windows (where `_username_` is the Windows user's name the software is installed under) and `~/omixon-hla-twin` on Linux, or could be on a custom path typically close to the software installation folder.

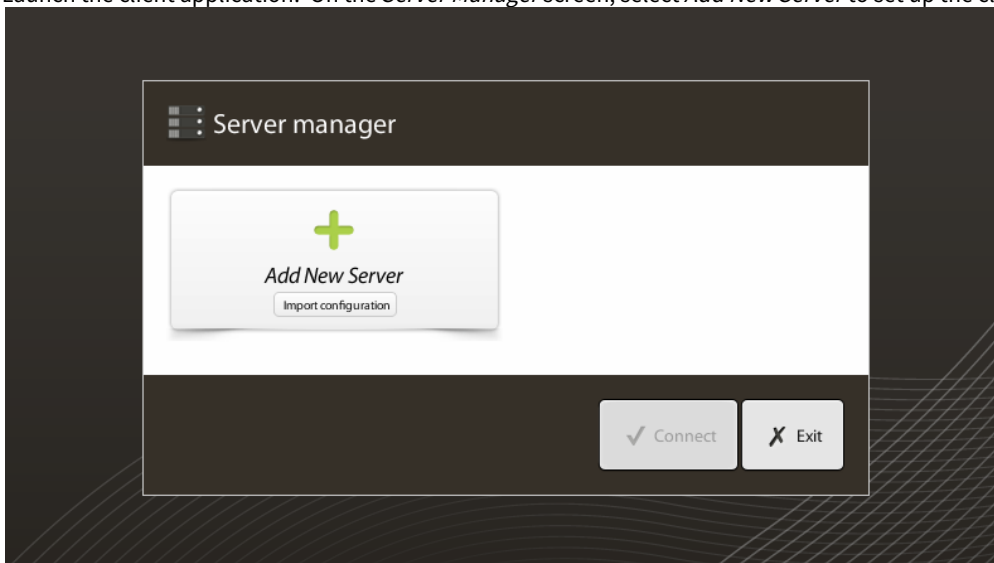
5.8 First use instructions

5.8.1 Connecting to the server

After setting up and starting the server, it is listening to incoming client connection requests.

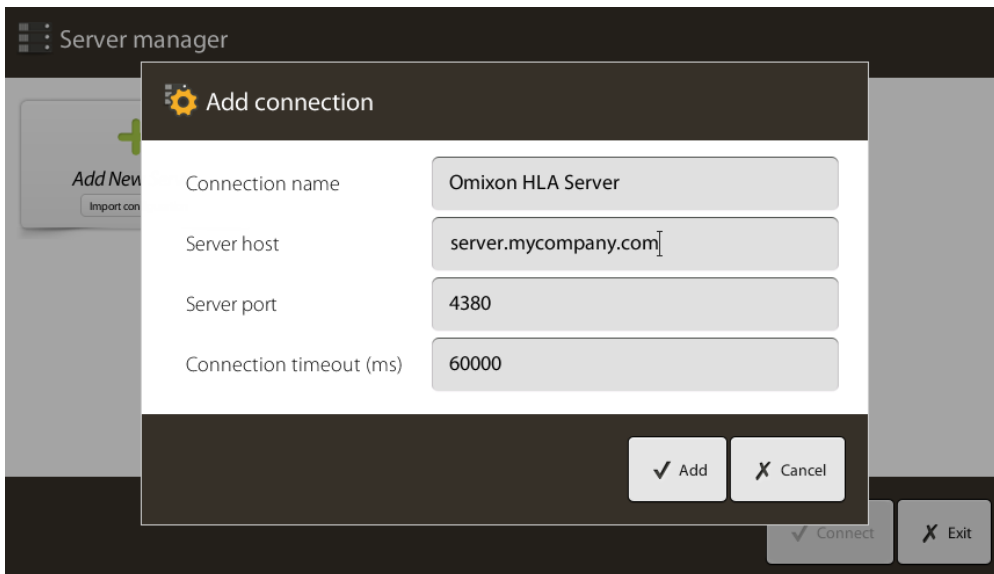
Connecting the client

Launch the client application. On the *Server Manager* screen, select *Add New Server* to set up the client-server connection.



Name your connection and enter exactly the same host and port settings which were set for the server during or after the installation.

⁸ <mailto:support@omixon.com>



Server manager

Add connection

Connection name: Omixon HLA Server

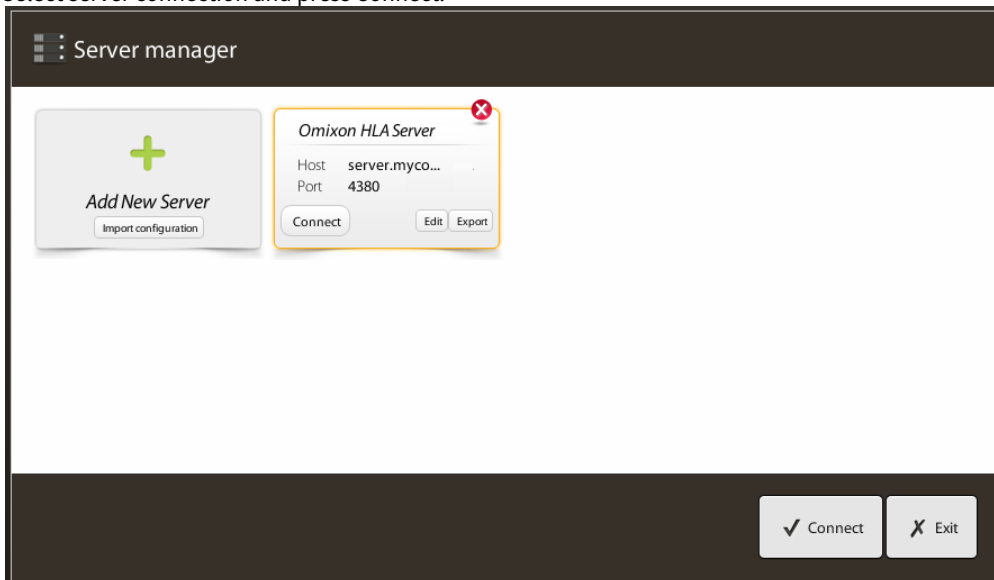
Server host: server.mycompany.com

Server port: 4380

Connection timeout (ms): 60000

✓ Add ✗ Cancel

Select server connection and press *Connect*.



Server manager

Add New Server
Import configuration

Omixon HLA Server
Host: server.myco...
Port: 4380
Connect Edit Export

✓ Connect ✗ Exit

IMPORTANT

Check your firewall settings on the server computer. Set up your firewall to let Omixon HLA Server accept incoming connections. Also make sure that outbound connections are enabled for the Omixon HLA Server in order for connected clients to receive status updates (eg. for displaying task progress information).

Exporting and importing connection configuration

Instead of configuring the connection manually, you can choose to import a configuration file by clicking the *Import configuration* button on the *Add New Server* card in the *Server Manager* dialogue. If you wish to choose this option, ask your System Administrator to provide you with a connection file. Connection settings can be exported to a file by clicking *Export* on the selected connection in the *Server Manager* dialogue.

5.8.2 Creating the first user



When starting the desktop application or connecting to the Omixon Server for the first time, you will be prompted to create the very first application user. The first user to register becomes a *Superuser* by default meaning that he/she has access to the full functionality of the software, including creating further user accounts. It is recommended that the System Administrator registers first to complete the setup. Please consult the *Settings Dashboard/User Management* chapter of the *Omixon Handbook* for further information on user roles and permissions.