BioPharma Finder 4.0 QF1 Release Notes

These release notes briefly list new features in the Thermo BioPharma Finder™ 4.0 application (build 4.0.68.0), a mass informatics platform for protein characterization of biotherapeutics. Also included are known issues in the 4.0 release of the application.

Contents

For information on installing the BioPharma Finder software, refer to the DVD insert. For information on configuring and using the BioPharma Finder 4.0 application, refer to the user guide available as a PDF file or the Help.

Features

Key features in the BioPharma Finder 4.0 application are workflow-driven experiment creation, method processing, and result review.

Oligonucleotide Analysis

Oligonucleotide Analysis is new to BioPharma Finder 4.0. Features in the Oligonucleotide Analysis workflow include the following:

- Performs a complete characterization of nucleotide-based pharmaceuticals.
- The Sequence Manager supports DNA and RNA for creation of oligonucleotide sequences.
- Users can create customized building blocks for these sequence components: base, backbone linker, 2’ ribose, 3’ terminal, and 5’ terminal.
- The Oligonucleotide Sequence Editor provides a simple user interface that allows for maximum editing of all key components including editing sequences with customized building blocks.
- Confirmation of oligonucleotide sequences with a novel MS2 prediction algorithm, providing extra confidence in your oligonucleotide sequence.
- Comparative analysis of multiple samples, which provides an ideal workflow for bioanalysis.
- Automatic identification and annotation using MS2 data from both HCD and CID fragmentation modes.
- New peak detection algorithm that allows for monitoring of expected impurities and the detection of unexpected impurities or metabolites.
- MS2 confirmation of failure sequences and the site-specific localization of modifications.
- Confirmation of expected and unexpected modifications.

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Peptide Mapping Analysis

Features in the Peptide Mapping Analysis workflow include the following:

- Confirmation of amino acid sequences with a novel MS2 prediction algorithm, providing extra confidence in your peptide sequence assignments.
- Identification of the site and type of expected and unknown post-transitional modifications (PTMs), providing a relative amount of modification in the sample.
- Disulfide bond mapping.
- Detection of low-level impurities and sequence variants.
- Sequence alterations in stress samples, including the deamidation or oxidation level.
- Error-tolerant searches for unexpected modifications.
- De novo sequence searches for unknown components.

Note The BioPharma Finder 4.0 application also includes algorithm improvements and basic bug fixes for the Peptide Mapping Analysis workflow.

Intact Mass Analysis

Features in the Intact Mass Analysis workflow include the following:

- Mass confirmation of target sequences including both proteins and oligonucleotides.
- Confident deconvoluted molecular weight of proteins in both acidic and native conditions.
- Batch-to-batch analysis for sample comparison.
- Novel sliding window algorithm to improve detection on low-abundant species.
- Two deconvolution algorithms. The Xtract algorithm supports high-resolution data (isotopically resolved data), and the ReSpect algorithm supports low-resolution data (isotopically unresolved data).
- Target protein sequence matching, which identifies n-linked glycosylations and other common modifications using the intact mass.
- Identification of Antibody Drug Conjugates (ADC) using the sliding window algorithm.
- Default processing method for oligonucleotides.
- Added support for raw data files from a TSQ series mass spectrometer including a default processing method that supports the following Thermo Scientific mass spectrometers: the ion trap mass spectrometers, the ISQ™ EC single quadrupole mass spectrometer, and the TSQ series of triple quadrupole mass spectrometers.
- A protein or oligonucleotide sequence is not required to annotate a deconvoluted mass. The user can create a sequence using only its mass or chemical formula.
- Improved mass accuracy for the deconvolution of modified oligonucleotides from isotopically resolved data using the new sequence-specific isotope table, and the rapid measurement of the intact molecular weight of biotherapeutics for structural confirmation and characterization.

Top Down Analysis

Features in the Top Down Analysis workflow include the following:

- A simple workflow for sequencing intact protein molecules using ProSightBP™ as the core algorithms.
- Ability to compare multiple raw data files with combined interactive fragmentation coverage maps.
- Support for multiple modes of fragmentation: CID, HCD, ETD, EThcD, and UVPD, enabling maximum protein coverage.

System Requirements

These are the minimum and recommended hardware and software configurations required for BioPharma Finder 4.0 operation.

System	Minimum requirements	Recommend requirements
Hardware	• Intel™ Core™ i7-4770 CPU@3.40 GHz • 8 GB registered RAM • 100 GB storage hard drive – ST1000DM -003 SCSI disk device • DVD/CD-ROM drives • Resolution display 1280 ×1024 (SXGA)	• Quad core Intel Xeon™ CPU (E5-1630v3 3.7 GHz 10MB 2133 4C) • 32 GB DDR4-2133 (4 ×8 GB) registered RAM • 2 TB storage hard drive (SATA, 7200 rpm)—512 GB solid state boot drive (SATA) • DVD-RW optical drive • Resolution display 1920 ×1080
Software	• Microsoft™ Windows™ 10 (English) (64-bit) • Microsoft .NET 4.7.2 • Microsoft Office 2010 • Adobe™ Acrobat™ Reader™ DC	• Microsoft Windows 10 (English) (64-bit) • Microsoft .NET 4.7.2 • Microsoft Office 2016 • Adobe Acrobat Pro DC

License Activation

Use the Thermo Scientific Product Licensing wizard to activate (or deactivate) the BioPharma Finder application. This wizard offers three different licensing options:

- Full features (Supports all workflows—Peptide Mapping Analysis, Oligonucleotide Analysis, Intact Mass Analysis, Top Down Analysis).
- Various options for licensing the individual workflows.

Activation of these features is dependent on the product purchased and is controlled by the license activation key. To add an additional features to the software, contact your customer service representative.

Before you transfer the license to another computer, you must deactivate the existing BioPharma Finder application and then transfer the license key. If you are upgrading from previous versions of Thermo PepFinder™ or Thermo Protein Deconvolution, you must obtain a new license key for the BioPharma Finder application.

❖ To activate (or deactivate) the BioPharma Finder application

1. Open the Product Licensing wizard as follows:
   a. Open the BioPharma Finder application.
   b. Choose **File > About BioPharma Finder** to display the License Activation wizard.
   c. Click **Activate** (or **Deactivate**) to start the activation or deactivation process, as applicable.
2. Locate the activation code as follows:
   a. Log in to your account at thermo.flexnetoperations.com.
   b. In the left navigation pane, under Software & Services, click **Order History**.
   c. From the list of ordered products, click the order number.

      The order number is in the Thermo Fisher Scientific "Your Order is Ready" email message. The Order Details table provides the activation code in the last column.
3. Continue through the Product Licensing wizard to activate the license using the activation code.

Installation and Upgrade

Follow these instructions to install the BioPharma Finder 4.0 software. You must be a system administrator on the installation computer to install the software. You may license the application as either an administrator or as a standard user.

During the upgrade of a previous version of BioPharma Finder, two main software folders, C:\ProgramData\ThermoScientific\Databases and C:\ProgramData\ThermoScientific\BioPharma, are automatically backed up.

Copies of the files are placed in the following location using this notation:

C:\ProgramData\ThermoScientific\BioPharma*legacy application version number*_backup_*DateAndTime*

When the software is successfully installed, you can delete the backup files or move them to another archive location to save space on the processing computer.

❖ To install BioPharma Finder 4.0 software

1. Close all opened Thermo Scientific™ applications.
2. Insert the BioPharma Finder 4.0 DVD into the DVD/CD-ROM drive.

   The autorun program automatically launches the installer wizard. If the wizard does not start, navigate back to the DVD in Windows Explorer and double-click **BioPharmaFinderSetup.exe**.

   The Welcome to the Thermo BioPharma Finder Suite Installer page opens.
3. Click the links to view the installation instructions, release notes, validation certificate, example data, and documents. Then click **Next**.
4. View the entire license agreement as needed and select the check box to accept the licensing terms.
5. Click **Install**.

   The wizard automatically checks the minimum system requirements. If there are missing items, a summary report opens with the appropriate links to download and install the required applications.

   If you are upgrading from legacy software, the installer does the following:

   - Detects legacy software (BioPharma Finder or Protein Deconvolution), uninstalls the legacy software, and upgrades the data. To proceed, click **Yes**.
   - Automatically backs up your legacy results onto the computer and upgrades these results to be compatible with the new software version.
6. To review the IQ report after installation is completed, click the corresponding link. Then click **Finish**.

   If the Windows Security Alert dialog box appears, click **Allow Access**.

You can now start the BioPharma Finder application from the desktop icon or Start menu and activate a license. If you have a demo version of the BioPharma Finder application, use the 60-day trial license. If you purchased the BioPharma Finder application, set a permanent license using the activation code provided through your account.

Xcalibur Security Patch

The BioPharma Finder installer includes a recently distributed security patch for the Xcalibur™ data system. This patch is applied automatically, requiring no user interaction. If the Foundation platform is not installed, the patch will have no effect. For more information about the patch, consult the following website:

https://www.thermofisher.com/software-update

Note You must reapply the Xcalibur/Foundation update if you install, upgrade, or reinstall the Foundation platform.

❖ **To reapply the Xcalibur/Foundation update**

1. Locate the command prompt (cmd.exe) on your processing computer, and then right-click and choose **Run as Administrator**.

   The Windows command prompt opens with Administrator permissions.

2. Navigate to the directory where you unzipped the update files, and then press the ENTER key.

   Note For example, if you unzipped the files to the C:\Update folder, type **cd c:\Update**, and then press the ENTER key.

3. Type **ThermoXcaliburFoundationSU.exe /uninstall /quiet** and press ENTER.
4. Type **ThermoXcaliburFoundationSU.exe /install /passive** and press ENTER.

   The Xcalibur/Foundation Security Update window opens, and then closes when the installation is complete

Resolved Issues

Table 1 lists defects that were resolved or are no longer relevant in the BioPharma Finder 4.0 application. The table excludes Help issues and cosmetic fixes. In some cases, the abstract has been amended or extended from the original to better describe the reported issue. Both an engineering fix and follow-up testing (verified by our product evaluation department) have resolved each of these issues.

Note The table is sorted by software section in ascending oder, and then by the item ID in descending order.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, and 4.0 (Sheet 1 of 4)

Item ID	Software section	Abstract
81326	Installation	During an upgrade from BioPharma Finder 3.0 to 3.1, if there is not enough disk space and the user selects Ignore, the installer still tries to create a backup and installation fails.
81000	Installation	On a few Windows 7 machines, when the BioPharma Finder installer is run, the installer gets stuck at the Initializing step.
42104	Intact Mass Analysis	Mass Std Dev and PPM Std Dev are present in the report but are not present in the Results table or the export for ReSpect sliding window.
23543	Intact Mass Analysis	With the 64-bit ReSpect DLL delivered with BioPharma Finder 1.0, the intensity is very different and missing some low-resolution data.
5298	Intact Mass Analysis	Adding a sample reference to an Xtract sliding window and then saving and running a method does not complete and throws an internal exception.
5297	Intact Mass Analysis	Save reference for Xtract sliding windows shows MS scan numbers as –1–1 in the table and Show Details for Sample Reference.
5145	Intact Mass Analysis	Modification text does not update when switching between peaks in the zoomed-in state.
5025	Intact Mass Analysis	Run queue becomes corrupted. Experiment type does not match Method type—system hangs in processing.
4999	Intact Mass Analysis	On selecting a result row after zooming and reseting the scale, the chromatogram shows the RT range from the previously loaded raw data file.
4754	Intact Mass Analysis	There should be a reasonable default value for Sequence Matching Mass Tolerance with Da as the unit.
4637	Intact Mass Analysis	Source spectrum is intermittently missing on a specific file only.
4449	Intact Mass Analysis	When copying and pasting from the source spectrum, the blue dots are offset from the peaks, which is unexpected.
4362	Intact Mass Analysis	The XIC for standard Xtract and ReSpect is being represented incorrectly.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, and 4.0 (Sheet 2 of 4)

Item ID	Software section	Abstract
4319	Intact Mass Analysis	After the jobs are done, the top jobs (for example, the just-finished jobs) should be shown.
4234	Intact Mass Analysis	There is a user interface style sheet inconsistency among the different tabs in Protein Deconvolution 4.0.
4179	Intact Mass Analysis	There is no averaged spectrum when using the following raw data file from an ion trap mass spectrometer: 9mix_Lyc_monolith.raw.
4169	Intact Mass Analysis	Zooming out to full scale for MS spectrum does not hide the scrollbar.
4158	Intact Mass Analysis	You can export top-level results only for ReSpect sequence matching; last row shows as an expandable row like Export All.
3532	Intact Mass Analysis	Report > ReSpect/Xtract Mass tables – The order of matching sequence + modification is not consistent when compared to the deconvolved spectrum and component table in the Results view.
3388	Intact Mass Analysis	"Reset Method" does not work for Chromatogram parameters.
3238	Intact Mass Analysis	Reporting > Source Spectrum – The scan filter for the source spectrum is displayed incorrectly.
3087	Intact Mass Analysis	It takes 72 minutes to create 2400 rows using Add Queue. The requirement states 8 minutes.
2259	Intact Mass Analysis	Parameters > Chromatogram page – If invalid values are entered for the Chromatogram *m/z* range, it does not show the tooltip about the valid values.
78060	Peptide Mapping Analysis	Peptide Mapping > Save as Displayed – Missing Column "Level" causing data overlapping in results grid after exporting to Save As Displayed.
63263	Peptide Mapping Analysis	Peptide Mapping > ID type is incorrect. Workaround: Select the MS2 tab and check if the spectrum is displayed.
62577	Peptide Mapping Analysis	Peptide Mapping – After placing an experiment on run queue, Home page still has method checked.
62396	Peptide Mapping Analysis	Peptide Mapping > ETD/CID select ETD over higher quality CID.
62395	Peptide Mapping Analysis	Peptide Mapping > Large experiment is only using one file for MS2.
54723	Peptide Mapping Analysis	Arrangement of tabs – Seen differently than normal right after processing.
52383	Peptide Mapping Analysis	Peptide Mapping > Process and Review – Glycans might not be included in the theoretical mass value.
52381	Peptide Mapping Analysis	Peptide Mapping > Process and Review – Theoretical mass does not include oxidation for gas phase oxidation.
52380	Peptide Mapping Analysis	Peptide Mapping Analysis > Process and Review – Theoretical mass does not have the correct value for dimer peptides.
42105	Peptide Mapping Analysis	Double-click results to open in intact queue and load results, but this feature is not enabled in Peptide Mapping Analysis.
40794	Peptide Mapping Analysis	When MS2/Full window is changed to floating by dragging the window and then changed back to "Dockable," MS2/Full data is not displayed any more.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, and 4.0 (Sheet 3 of 4)

Item ID	Software section	Abstract
40758	Peptide Mapping Analysis	MSFileReader is not installed when running the installer in repair mode. Workaround: Do not use repair option in BioPharma Finder 3.0 installer. Instead, remove and reinstall.
40426	Peptide Mapping Analysis	When a Peptide Mapping Analysis experiment is deleted from the load results tab, the mapping tab is not removed. Workaround: Exit the application, and then restart the application.
40081	Peptide Mapping Analysis	Protein coverage results found in the results table under the shading chromatogram on the mapping might not agree with the coverage results on the Protein Coverage Map. This can occur for both default setting and user-defined coverage. This issue will be addressed in a future release.
38707	Peptide Mapping Analysis	Peptide Mapping Analysis > Large experiment is only using one file for MS2.
38505	Peptide Mapping Analysis	In Peptide Mapping Analysis, the MS ID Type might be incorrectly labeled. Workaround: Review the results by clicking on the component and looking to see if an MS2 spectrum appears in the MS2 tab. If multiple files are present, expand the table to the raw file level and review each raw file for MS2 spectra.
38396	Peptide Mapping Analysis	Peptide Mapping Analysis for single file experiment - for some components, ID type is displayed as Full, even though MS2 spectra and fragment coverage map is present.
38277	Peptide Mapping Analysis	Refresh issue with loading protein sequence after reprocessing the data—None of the tabs are selected.
35247	Peptide Mapping Analysis	Limitation in the component table for displaying peptides with 7 or more modifications.
24538	Peptide Mapping Analysis	Sometimes a peptide might not be highlighted on the Protein Sequence tab.
20965	Peptide Mapping Analysis	The Peptide Sequence Coverage Map does not paste into MS word correctly. Workaround: Use the Windows snipping tool or the print screen command to capture the image.
20475	Peptide Mapping Analysis	Glycosylated peptides are not displayed in the results table when you use the default parameter settings because their confidence score is less than 80% if you search for them using variable modifications instead of the N-glycan database. Workaround: Lower the confidence score to 0% to observe this type of variable modification or use the N-glycan database.
17270	Peptide Mapping Analysis	All MS/MS Ion runs do not show the Modification Summary report.
17143	Peptide Mapping Analysis	Disulfide + Sodium Adduct - High Negative Delta mass for MS2 ID rows.
17030	Peptide Mapping Analysis	Gas phase–NH3Loss – Seems like we are using the wrong mass for the calculation, as the Delta Mass is greater than expected.
17015	Peptide Mapping Analysis	Isomerization for same peptide shows up as two different modification masses - shows large delta mass ppm.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, and 4.0 (Sheet 4 of 4)

Item ID	Software section	Abstract
15925	Peptide Mapping Analysis	Add glycan list to the default list of variable modifications for the side chain. This feature will be redesigned in a future release, but a workaround exists. Workaround: User can add common glycans as the variable modification, instead of using N-gly as CHO or Human, so the annotation is more specific.
14263	Peptide Mapping Analysis	When the Protein Coverage Map is copied and pasted to Office 2007, amino acid is not displayed properly.
11740	Peptide Mapping Analysis	Toggling between Fragmentation types and back to original shows predicted spectrum with different scaling and labels. Error in Mass Analyzer: – Scaling might not be that important, but users need the result values to be correct. MS/MS values are confirmatory only.
9296	Peptide Mapping Analysis	The Fragment Coverage Map is shown for components with ID type as Full MS Error in Mass Analyzer. Improvement has been made but more can be made.
9206	Peptide Mapping Analysis	Memory usage is not optimized during various operations - loading result or switching to mapping tab.
62580	Protein Sequence	MSQC – Loading a non-correct MSQC file can cause an exception dialog.

Known Issues

Suggested recovery actions

- For some issues, restarting the application is the appropriate recovery action.
- As a fix, we generally do not recommend reinstalling the software or the operating system, which more commonly occurs after you install a new hard drive.
- After installing the software on some processing computers, we are seeing an issue with viewing the IQ report using the link. If this occurs, you can find the IQ report in the C:\Program Files\Thermo\IQ Reports folder.

Feature requests and other removed items

- We do not include issues where there is insufficient information logged to successfully reproduce the reported problem.
- We do not list feature requests as software issues, regardless of the reported significance or severity of the request. Product managers evaluate logged feature requests for future releases.
- We report only discrepancies in the documented software as known issues.

Terminology

Severity	Interpretation
Critical	A problem that renders the system unusable because either an entire function is unusable and no workaround exists, or use of the current system compromises data integrity or results in data loss. Catastrophic problems also include significant and non-obvious quantitative errors, and all human and instrument safety issues.
High	A serious issue that does not affect data integrity (meaning data loss, corruption of data, or the wrong answer), but affects the customer's ability to use the product as designed. It can be a failure, design issue, or documentation error or omission. A workaround might or might not exist.
Medium	A minor error or poor behavior of a product feature. There is probably a workaround.
Low	An issue that has a limited effect on customer usage of the product; for defects with visibility so low that a customer might never see it; or for ease of use issues or other items not causing any performance degradation.

Risk	Interpretation
High	Occurrence is likely to happen and can compromise operation.
Medium	Occurrence is uncommon, but if it occurs, can compromise operation.
Low	Issue is minor; however, the software might operate differently from a user's expectations. A workaround is often available.
No Risk	This issue causes no problems but is commonly an inconsistency or a 4- Low issue.

Known defects

Table 2 contains known defects in the software, categorized by software section, with a brief abstract and information related to each defect's severity and risk. The Item ID is the internal number assigned to each issue. Product management assesses risk, which can differ significantly from the reported severity.

Table 2. Known defects (Sheet 1 of 7)

Severity	Abstract	Risk	Item ID
High	Oligonucleotide Analysis only supports one variable modification on an oligonucleotide sequence.	High	117286
High	Top Down Analysis – Intact deconvolution spectrum might not update correctly when changing between peaks in the Results table. Workaround: Load another result, then load this result again. For intact deconvolution, select the empty peak first.	High	63112
High	When you remote desktop to a Windows 10 machine and select Load Result or Open Result, a blank screen appears instead of the results on the Process and Review page. Workaround: Close the application, restart the application, and then select Load Result or Open Result to display the results on the Process and Review page.	High	42050
High	Memory usage is not optimized during various operations such as loading results or switching to the mapping tab.	High	38744
High	The protein sequence information might not be displayed correctly in the load results table and the identification parameters when upgrading a legacy Protein Deconvolution 4.0 result. Workaround: To reprocess the results in BioPharma Finder 3.0, use the same protein sequence (added manually) and then save the results.	High	37244
High	Duplicate copies of a chromatogram and deconvolution and source spectra (from the same raw data file) are created for a multiconsensus experiment when the raw file contains more than one component that passes the multiconsensus merge parameters. This might appear as a bug; however, if you view the raw file information, the individual component information is displayed for review.	High	32986
High	When three chains are added to a FASTA file, components are missing the "matched sequences." This issue is as designed; when three chains are added to the same sequence, the target mass of the protein is higher than the component. As a result, none of the sequence is matching. This issue has been documented in Protein Deconvolution 4.0. Workaround: Import each chain as a separate FASTA file, and add these sequences to the method. A sequence match gives the expected result. In a future release, the algorithm will be updated so that users can add all chains in the same sequence.	High	14421

Table 2. Known defects (Sheet 2 of 7)

Severity	Abstract	Risk	Item ID
High	Missing retention time – The design was changed in Protein Deconvolution 4.0, and this error surfaced as a side error. To fix it requires redesigning the algorithm. Workaround: Close the application, restart the application, and then select Load Result or Open Result to display the results on the Process and Review page.	High	10137
High	Copied images from BioPharma Finder to Microsoft Word or PowerPoint™ that are then saved as PDF images might be corrupted. The Save as PDF command in Word and PowerPoint requires installing Acrobat Pro, which would then display the images correctly in a PDF file.	High	9716
High	The Auto ReSpect feature cannot find the expected components.	High	3281
High	Performance of "finalizing results" is slow.	High	2235
Medium	Oligonucleotide Analysis – For Predicted Oligo MS/MS (kinetic model), when a sequence is added in all lowercase letters, no error message is displayed to let the user know that the correct format is all capital letters or triplet code format.	Medium	123294
Medium	During the installation, if a previous version of BioPharma Finder is installed but has never been launched, the BioPharma Finder 4.0 upgrade installation will fail. Workaround: Before installing BioPharma Finder 4.0, make sure that the previous version of the application has been opened at least once.	Medium	123001
Medium	Peptide Mapping Analysis parameters, beginning and ending peak width, may be 0.00 when processing an upgraded result from previous versions of BioPharma Finder.	Medium	122165
Medium	Oligonucleotide Sequence Editor – Gives an error when the formula contains any of the elements with a quantity greater than 100 000 (for example C101,000H20,000)	Medium	119790
Medium	Installer – IQ report link is not working on a few PC/VM – Adobe is installed. Workaround: User can find the IQ report in the following location C:\Program Files\Thermo\IQ Reports.	Medium	119656
Medium	Oligonucleotide Analysis > Process and Review page – The 3' terminal is not highlighted completely on the Oligonucleotide Sequence page.	Medium	117056
Medium	Installer – During installation, the mongodb access dialog box does not appear. ❖ **To complete the installation** 1. While the installer is still running and the 1920 error dialog box is displayed, go to the following folder: C:\Program Files\Thermo\BioPharma Finder 2. Right-click ThermoFisher.BioPharma.DBUpgradeUtility.exe, and choose **Run as Administrator**. 3. In the error dialog box, click **Retry**. The BioPharma Finder installation completes successfully.	Medium	81387
Medium	Peptide Mapping Analysis – Theoretical Monoisotopic Mass is slightly different for Targeted versus non-Targeted experiments.	Medium	80599

Table 2. Known defects (Sheet 3 of 7)

Severity	Abstract	Risk	Item ID
Medium	Peptide Mapping Analysis targeted analysis – Modification summary relative abundance calculations will be not used to defined peptides when more than one modification is on same peptide, it is excluded from numerator.	Medium	80050
Medium	Targeted Peptide Mapping > Modification Summary – % abundance values for modifications that use unique peptides in the calculation could be incorrect.	Medium	79541
Medium	Non targeted/Targeted > Multiple (and Single) File Experiment – Predicted MS2 does not work for some peptides when MS2 spectra are searched.	Medium	77170
Medium	Top Down Analysis – When you delete the sequence that you added from the Home page, the proteoform is not present after processing. Workaround: If the sequence is used in an experiment that is being processed or is in a submitted state, do not delete it from the Global Sequence Reference table.	Medium	63260
Medium	Top Down Analysis Xtract parameters for intact deconvolution – *m/z* range does not correspond with the range on the source spectrum's scan filter header when Intact Deconvolution is unchecked after selecting an RT range. Workaround: Manually change the *m/z* range in Parameters > Intact Deconvolution tab and save the method.	Medium	63022
Medium	Peptide Mapping Analysis – The best fragmentation MS2 is now selected, but the predicted MS2 spectrum is not the correct fragmentation type. Workaround: Manually select the correct fragmentation method in the Predicted Peptide MS/MS dialog box.	Medium	62682
Medium	Top Down Analysis – ProSightBP table is not sorted by relative abundance on initially clicking a proteoform. Workaround: Sort manually on Relative Abundance.	Medium	62214
Medium	Intact: When the queue is paused and BioPharma Finder is upgraded to 3.0, the application crashes after prompting you to start the queue. Workaround: Process all data experiments in the queue before upgrading to the later version.	Medium	61937
Medium	Licensing: In offline deactivation, the response file for “Deactivation.req” is called “Activation.xml”. Workaround: Edit the default name and name it Deactivation.req.	Medium	61014
Medium	Intact > Process and Review: XIC disappears in Auto Peak Detection experiment when reviewing data. Workaround: Reload the result to view the XIC.	Medium	60726
Medium	For MSQC, when copying peptide sequences into the sequence box with “> name,” the information does not show in the table.	Medium	60347
Medium	Predicted Time – Not always the same for processing the same experiment for Modification summary.	Medium	52946
Medium	Intact > Sliding Window - multiple raw files - match Mass error Percent CV - for single raw file should be zero.	Medium	52888
Medium	Peptide Mapping Analysis > Process and Review – Theoretical mass does not include K+ in the mass value and glycans with K+ also.	Medium	52382

Table 2. Known defects (Sheet 4 of 7)

Severity	Abstract	Risk	Item ID
Medium	Peptide Mapping Analysis > Process and Review – Peptide ID has (m) mass but the monoisotopic experimental (observed) is 0.000	Medium	52372
Medium	(UXLib 83877) Licensing – In the license activation dialog box, canceling a permanent activation and clicking Back to select Trial license activation generates an error.	Medium	51905
Medium	QB files for intact Default Native Above 1 million - cannot set RT time to include both RT values.	Medium	49511
Medium	Mass Std Dev and PPM Std Dev are present in the report but not present in the Results table or export for ReSpect sliding window.	Medium	42104
Medium	With a remote desktop to a Windows 10 machine, by selecting Load Results or Open Results, you see a blank screen instead of seeing the result on the Process and Review page. Workaround: Close and restart the application, and then select Load Results or Open Results to display results on the Process and Review page.	Medium	42050
Medium	Application error/crash – When launching a second instance of the application from a different user on the same machine.	Medium	41418
Medium	When you save results after recalculating the average DAR for selected check boxes, the results and drug load are zero for rows not checked. Workaround: Uncheck all rows and then click Recalculate. The drug load values appear for all rows with drug load.	Medium	41362
Medium	Use of restricted time that is greater than actual chromatogram time causes chromatogram and source spectrum to be empty. Workaround: Adjust restricted time to fit into the actual chromatogram window.	Medium	40735
Medium	When a Peptide Mapping Analysis experiment is deleted from the Load Results tab, the Mapping tab is not removed. Workaround: Exit and then restart the application.	Medium	40426
Medium	Single-scan raw data files exported from Qual Browser can cause the source spectrum to be blank when switching from sliding window to average over RT deconvolution. Workaround: Create a method with a sliding window deconvolution that is within the RT range of the file.	Medium	40422
Medium	Protein coverage results found in the Results table under the shaded chromatogram on the map might not agree with the coverage results on the protein coverage map. This can occur for both default settings and user-defined coverage. This issue will be addressed in a future release.	Medium	40081
Medium	(Upgrading from BioPharma Finder 1.0 SP1 to 3.0) The RT range parameter has a different meaning from past releases. For custom methods, it is set to 0 to 0, instead of the value set in the time limit parameter. Workaround: Change the RT range manually.	Medium	39721
Medium	When exporting a multiconsensus experiment and there is a component with a raw data file containing multiple peaks, only the first component is exported. Workaround: Export all components, all levels.	Medium	39426
Medium	Software does not fully support display on 4K monitors.	Medium	38718

Table 2. Known defects (Sheet 5 of 7)

Severity	Abstract	Risk	Item ID
Medium	Peptide Mapping Analysis > ETD/CID – Select ETD over higher-quality CID.	Medium	38708
Medium	In Peptide Mapping Analysis, the MS ID Type might be incorrectly labeled. Workaround: Review the results by clicking the component and looking for MS2 spectra on the MS2 tab. If multiple files are present, expand the table to the raw data file level and review each raw file for MS2 spectra.	Medium	38505
Medium	If the raw data file folder path and raw data file name are greater than 256 characters, the number of components detected in the queue is listed as 0. However, the experiment still processes correctly, even though the value is listed as 0. Workaround: The value is displayed correctly in the load results table.	Medium	38426
Medium	Peptide Mapping Analysis – Modification summary relative abundance calculations: When more than one modification is on the same peptide, it is excluded from numerator.	Medium	38385
Medium	Peptide Mapping Analysis can have an issue with multiple labels for the same Glycan in some MS2 spectra.	Medium	38377
Medium	Peptide Mapping Analysis – Monoisotopic Mass is slightly different for Targeted verses non-Targeted experiments.	Medium	38376
Medium	Canceling Peptide Mapping Analysis can crash the application; it seems to be related to clicking the button. Workaround: If the application crashes when canceling, reopen it to continue processing.	Medium	35934
Medium	There is a limitation in the component table for displaying peptides with seven or more modifications.	Medium	35247
Medium	For multiconsensus Average DAR experiments, if a raw data file does not contain the component being used for the Average DAR calculation, the table will display an empty spaces instead of the raw file name.	Medium	35097
Medium	The drug load override does not work when the component you want to override is an unchecked row and other rows are checked. Workaround: Uncheck all of the components in the main table. Select the component you would like to change the drug load value of, and then check the override check box.	Medium	34990
Medium	N-term and C-term modification are not included on the DAR list of modifications; therefore, they cannot be used for assigning drug load values in this release.	Medium	31909
Medium	Drug load values are only assigned to components with identifications.	Medium	30767
Medium	If a processing method has an error, the software still prompts the user to save the method. Workaround: Do not save methods with errors.	Medium	30357
Medium	If multiple resolutions are used during data acquisition, the application requires two different processing methods that use the appropriate resolution values to obtain the best results.	Medium	24386
Medium	The peptide sequence coverage map does not copy into MS word correctly. Workaround: Use the Windows Snipping Tool to capture the image, or do a screen copy.	Medium	20965

Table 2. Known defects (Sheet 6 of 7)

Severity	Abstract	Risk	Item ID
Medium	All MS/MS scan data does not show the Modification Summary report.	Medium	17270
Medium	Disulfide + Sodium Adduct – High Negative Delta mass for MS2 ID rows.	Medium	17143
Medium	Gas phase-NH3Loss – Seems as if we are using the wrong mass for calculation—the delta mass is larger than expected.	Medium	17030
Medium	Isomerization for the same peptide shows up as two different modification masses—showing a large delta mass ppm.	Medium	17015
Medium	Highlighted peptide sequences on the Protein Sequence tab in the Peptide Mapping Analysis workflow might not highlight disulfide bond peptides correctly all the time.	Medium	16720
Medium	(UXLib 14705) When you have a remote desktop to a machine with a BioPharma Finder trial license, intact protein is not enabled.	Medium	14462
Medium	Peptide Mapping Analysis – The chain mass is not updated when linking disulfide bonds in the Protein Sequence Editor. Workaround: When a search is performed, only the target protein mass is used for searching; therefore, this issue will not cause problems in your results because the application does not use individual chain mass information.	Medium	14419
Medium	When the Protein Coverage map is copied to Office 2007, the amino acid is not displayed properly.	Medium	14263
Medium	The Mapping tab for results is missing for duplicate disulfide chain—shows on the Process and Review page.	Medium	14079
Medium	With an upgrade from an earlier version of Protein Deconvolution to BioPharma Finder with a permanent license key, the experiment type and load results are deactivated until you restart the application.	Medium	13612
Medium	An apex RT should be within its RT range.	Medium	11958
Medium	The resolution displayed on the experimental HCD spectra might be incorrect.	Medium	11778
Medium	The later loaded raw file should not overwrite the previously loaded data.	Medium	5910
Medium	Unexpected Exception-RunQueueViewModel.StatusHandler encountered for a large run queue with the PepFinder application (tryptic digest) file-nativeLYSCETDCID2.raw.	Medium	5291
Medium	The user can set different time limits for processing a sliding window and chromatogram. During processing, the chromatogram window is shown.	Medium	4565
Medium	The RT Range for a sliding window can be zero for start and finish, and in auto mode, you do not get the suboptimal warning in the run queue message.	Medium	4258
Medium	The resolution for mixed data of FTMS Full MS and ITMS Full MS is not correct.	Medium	1918
Low	The exported Modification Summary with contents is empty when viewed using Open Office.	Low	117636
Low	Peptide Mapping Analysis Workbook – RT (Min) - the communicator bar red error message does not go away even after fixing it. User has to click on another row.	Low	75306
Low	Peptide Mapping Analysis – Performance- Trend MS Area is missing the raw data file labels on the *x* axis for a 100 file experiment.	Low	73403
Low	Top Down Analysis – Selecting a method or typing the experiment name triggers the Clear Settings dialog box when Home tab is clicked.	Low	61013

Table 2. Known defects (Sheet 7 of 7)

Severity	Abstract	Risk	Item ID
Low	Peptide Mapping Analysis – Refresh issue- on Modification Summary page upon Manual integration.	Low	53410
Low	File order is reversed in Results table.	Low	53190
Low	Top Down Analysis – UI items are not properly aligned on the Identification tab; PPM label is truncated. Workaround: This issue is specific to a certain VGA card only.	Low	51752
Low	Top Down Analysis – UI items not Properly aligned on Identification tab, PPM label is truncated	Low	38738
Low	Top Down Analysis – After you select a processing method or name the experiment, clicking the Home tab opens the "This action will clear the settings" prompt.	Low	38712
Low	MSQC – Selecting peptide or protein shows a table of amino acids - N-term is indexed as 1.	Low	38710
Low	Peptide Mapping Analysis – After placing an experiment on run queue, the Home page still has method checked.	Low	38709
Low	Peptide Mapping Analysis – Clearing the filter for a column does not set back to original filter type.	Low	38384
Low	In the summary table found on the parameters save method page, the report parameters are listed and enabled for multi-consensus experiments. Reporting is not a feature for multi-consensus or DAR enabled experiments, and reports will only be produced for single file experiments.	Low	36231
Low	Multi-consensus merging parameters are not made unavailable for single file experiments.	Low	34626
Low	In this release, the application performs the deconvolution process every time the user reprocesses the experiment even if no deconvolution parameters are changed. This feature will be redesigned in a future release to improve performance.	Low	34061
Low	MS Dimer Predicted Spectrum does not show up correctly in the sequence dialog box (assume that MS/MS predicted spectrum is incorrect as well).	Low	12896

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