BioPharma Finder 5.0 Release Notes

These release notes briefly list new features in the Thermo BioPharma Finder™ 5.0 application (build 5.0.68.8), a mass informatics platform for protein characterization of biotherapeutics. Also included are known issues in the 5.0 release of the application.

Contents

For information on installing the BioPharma Finder software, refer to either the Installation and upgrade section in these Release Notes or the DVD insert. For information on configuring and using the BioPharma Finder 5.0 application, refer to the user guide available as a PDF file or the Help.

Key features

BioPharma Finder 5.0 software provides a simplified comprehensive biotherapeutic attribute characterization with advanced capabilities to increase throughput and confidence for BioPharma workflows with built for purpose data processing, curation, and reporting in a connected environment to streamline and enable collaboration on a global scale.

See these sections:

- New in BioPharma Finder 5.0
- Oligonucleotide Analysis
- Peptide Mapping Analysis
- Host Cell Protein Analysis
- Intact Mass Analysis
- Top Down Analysis

New in BioPharma Finder 5.0

The following are new features in BioPharma Finder 5.0:

- Simplied comprehensive biotherapeutic protein attribute characterization with advanced capabilities to increase throughput and confidence for peptide mapping workflows with built for purpose data processing, curation, and reporting in a connected environment to streamline and enable collaboration on a global scale.
- New capabilities to advance biotherapeutic protein attribute characterization workflows including; Sequence confirmation, Quant of peptides & mods, Identification of disulfide links, Sequence variant analysis, De novo sequencing, O & N glycan identification, Host cell proteins (HCP), Hydrogen Deuterium Exchange (HDX) protection factor plots, Trend analysis, and Multi-attribute method (MAM) method development and
- Dynamically collaborate, compare, track and finalize peptide results and workbooks using versioning history.

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- Comprehensive and easy-to-use built-in peptide mapping reporting functionality, including:
  - New default templates, or, you can design and share your own report templates to publish curated result reports in PDF or .xls file formats.
  - Tailor report content with the report designer functionality including dynamic data tables, column filters, custom calculations, charts and graphs, and images, such as peptide coverage maps.
  - Custom report templates that you can use to implement standardized result reporting protocols
- Access and save results in a single secure location using shared sign-on for the entire workflow for enhanced data integrity and security.
- Connectivity streamlines and enables collaboration on a local and global scale, including.
  - Seamless data processing capabilities by multiple users across any computer connected to the virtual private cloud or on-premise server.
  - An all-encompassing solution for peptide mapping analysis for data processing, review, and reporting.

Note The above features are provided in BPF 5.0 with connectivity between Thermo Scientific HyperBridge™ software and Thermo Chromeleon™ Chromatography Data System (CDS).

- **HyperBridge software**. The HyperBridge software provides centralized and secure data storage for enhanced collaboration and knowledge sharing.
- **Chromeleon Enterprise Chromatography Data System**. Chromeleon Enterprise Chromatography Data System 7.3.1 manages all analytical processes from instrument control, data storage and processing, to generating the final results on CQAs and new peak detection in both development and QC environments. Chromeleon CDS provides ease of administration, ensures continuous update (24/7/365) and meets modern data integrity and regulatory requirements.

Oligonucleotide Analysis

Features in the Oligonucleotide Analysis workflow include the following:

- The identification feature for oligonucleotide analysis has been expanded to include in silico mRNA digestion and mRNA mapping.
- Select from the common RNases or add a custom RNase and the software will identify the mRNA pieces using MS2 or full scan data and provide sequence coverage map.
- Expanded sequence matching for oligonucleotides in the intact mass analysis workflow with the addition of terminal truncation searching capabilities from both the 3’ or the 5’ terminus.
- Improvements have been added for manual validation of the MS2 spectrum in both the peptide mapping and oligonucleotide analysis workflows. The user can view the theoretical fragments, control the fragments displayed on the MS2 spectrum and the sequence coverage map. You can also view the delta mass for the matching. This provides deeper investigation into the matched identification.
- Performs a complete characterization of nucleotide-based pharmaceuticals.
- Sequence manager supports DNA and RNA for creation of oligonucleotide sequences.
- You can create customized building blocks subunits including base, backbone linker, 2’ ribose, 3’ and 5’ terminus.
- Editing sequences with customized building blocks is achieved using a simple user interface allowing for maximum editing of all key components.
- Confirmation of oligonucleotide sequence with a novel MS2 prediction algorithm, providing extra confidence in your oligonucleotide sequence.
- Comparative analysis of multiple samples an ideal workflow for bioanalysis.
- Automatic identification and annotation using MS2 data utilizing both HCD and CID fragmentation modes.
- New peak detection that allows for monitoring of expected impurities but also provides results for detection of unexpected impurities or metabolites.
- MS2 confirmation provides site specific localization of modifications or failure sequence.
- Confirmation of expected and unexpected modifications

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.

Host Cell Protein Analysis

Features in the Host Cell Protein Analysis workflow include the following:

- Host cell protein identification and quantitation is added to the peptide mapping analysis and combines product specific peptide mapping results with host cell protein identification.
- This easy to use workflow starts with a peak list where the software identifies all of the product specific peptides considering all potential modifications (normal peptide mapping), then remaining unmatched peaks with MS2 information are searched using Comet against larger host cell protein databases (for example, CHO, Human, Mouse).The results are then merged.
- The software automatically generates a quantitation report for the host cell proteins and includes the product specific sequence as well. If more than 3 peptides are identified from the protein, the software selects the most abundant per file, reducing the time the user must manually determining the values.

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 TSQ data files including a default method processing method
- A protein or oligonucleotide sequence is not required to annotate a deconvoluted mass. You 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 5.0 operation.

System	Minimum requirements	Recommend requirements
Hardware	• Memory configuration 32 GB RAM • CPU 8 cores • 100 GB storage hard drive • Resolution display 1920 ×1080 (SXGA) • Optional: DVD/CD-ROM drives	• Memory Configuration 64 GB RAM • CPU 8 cores, or a processor with higher cores • 2 TB storage hard drive (solid state boot drive (SATA) for best performance) • Resolution display 1920 ×1080 • Optional: DVD/CD-ROM drives
Software	• Microsoft™ Windows™ 10 (English) (64-bit) • Microsoft .NET 4.8 • Microsoft Office 365 • Adobe™ Acrobat™ Reader™ DC	• Microsoft Windows 10 (English) (64-bit) • Microsoft .NET 4.8 • Microsoft Office 365 • Adobe Acrobat Pro DC

Note BioPharma Finder 5.0 connection with HyperBridge is only supported using Microsoft Windows 10 operating system and will not work with older operating systems.

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 5.0 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.

❖ To install BioPharma Finder 5.0 software

1. Close all active Thermo Scientific™ applications.
2. Insert the BioPharma Finder 5.0 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**.

   Note If you downloaded the installer from Flexera™, click **BioPharmaFinderSetup.exe** to start the installer.

   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 then 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. If you want review the IQ report after the installation is completed, click the corresponding link. Click **Launch** to open the application, or click **Close** to exit the wizard.
7. Start the Thermo BioPharma Finder application from the desktop icon or from the Start menu, and then activate a license as follows:

   - If you have a demo version of the BioPharma Finder application, use the 60-day trial license.

   –or–

   - If you purchased the BioPharma Finder application, set a permanent license using the activation code provided through your account.

❖ To upgrade from BioPharma Finder 3.0 version to BioPharma Finder 5.0 version

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 upgrade from BioPharma Finder 2.0 and previous versions, and upgrade from Protein Deconvolution to BioPharma Finder 5.0 version

The upgrade from these older versions of BioPharma Finder is not directly supported by BioPharma Finder 5.0 version and requires a step upgrade.

When you upgrade from BioPharma Finder 2.0 or previous versions and install BioPharma Finder 5.0 version, the installer shows a message stating this upgrade is not supported. See the installation instructions for details.

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 5.0 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, 4.0QF, 4.1, and 5.0 (Sheet 1 of 4)

Item ID	Software section	Abstract
23543	Intact Analysis	With 64-bit ReSpect dll delivered with BPF1.0, intensity is very different and missing some low-resolution data.
5297	Intact Analysis	Save reference for Xtract sliding shows MS scan numbers as –1–1 in table and Show Details for Sample Reference.
4754	Intact Analysis	There should be a reasonable default value for Sequence Matching Mass Tolerance with Da as the unit.
4158	Intact Analysis	You can export top level results only for ReSpect sequence matching; last row shows as an expandable row like Export All.
5145	Intact Analysis	Modification text does not update when switching between peaks in the zoomed-in state.
5298	Intact 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
4999	Intact Analysis	On selecting a result row after zoom and reset scale, the chromatogram shows RT range from previously loaded raw data file.
5025	Intact Analysis	Run queue becomes corrupted. Experiment type does not match Method type—system hangs in processing.
3532	Intact Analysis	Report - ReSpect/Xtract Masses table: The order of matching sequence + modification is not consistent when compared to the deconvolved spectrum and component table in the results view.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, 4.0QF, 4.1, and 5.0 (Sheet 2 of 4)

Item ID	Software section	Abstract
4319	Intact Analysis	After the jobs are done, the top jobs (for example, the just finished jobs) should be shown.
4234	Intact Analysis	There is a user interface style sheet inconsistency among the different tabs in Protein Deconvolution 4.0.
3087	Intact Analysis	It takes 72 minutes to create 2400 rows using Add Queue. The requirement states 8 minutes.
4449	Intact Analysis	When copying and pasting from the source spectrum, the blue dots are offset from the peaks, which is unexpected.
4637	Intact Analysis	Source spectrum is missing, intermittently on a specific file only.
2259	Intact Analysis	In Parameters > Chromatogram page, if invalid values are entered for the Chromatogram m/z range, it does not show the ToolTip about the valid values.
4179	Intact Analysis	There is no averaged spectrum when using an ion trap data "9mix_Lyc_monolith.raw" file.
3388	Intact Analysis	"Reset Method" does not work for Chromatogram parameters.
4362	Intact Analysis	The XIC for standard Xtract and ReSpect is being represented incorrectly.
40758	Peptide Mapping	MsFileReader is not installed when running the installer in repair mode. Workaround: do not use repair option in BPF 3.0 installer instead remove and reinstall.
9206	Peptide Mapping	Memory is not released during various operations. Algorithms Layer has been fixed and there might be some other workflow where memory might not be released. Deferred to next release, so more improvements can be made.
38277	Peptide Mapping	Refresh issue with loading Protein sequence after reprocessing the data, none of tabs are selected
40794	Peptide Mapping	When MS2/Full window is changed to floating by dragging the window and changed back to "Dockable", MS2/Full data is not displayed any more.
15925	Protein Sequence	Add glycan list to the default list of variable modification 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.
20475	Peptide Mapping	Glycosylated peptides will not be displayed in the results table using default parameters because their confidence score will be 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.
9296	Peptide Mapping	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.
11740	Peptide Mapping	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, users need result values to be correct, and MS/MS values are confirmatory only.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, 4.0QF, 4.1, and 5.0 (Sheet 3 of 4)

Item ID	Software section	Abstract
63263	Peptide Mapping	Peptide Mapping->ID type is incorrect. Workaround - Select the MS2 tab and check if the spectrum is displayed. Workaround - Select the MS2 tab and check if the spectrum is displayed.
38505	Peptide Mapping	In Peptide Mapping the MS ID Type might be incorrectly labeled. Workaround: review the results by clicking on the component and looking to see if an ms2 spectra 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.
35247	Peptide Mapping	Limitation in the component table for displaying peptides with 7 or more modifications.
42105	Peptide Mapping	Double click on results to open in intact queue and load results but this feature is not enabled in Peptide Mapping Analysis
40081	Peptide Mapping	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 address in a future release.
40426	Peptide Mapping	When a Peptide mapping experiment is deleted from the load results tab, mapping tab is not removed. Workaround: exist out of the application and restart application.
17270	Peptide Mapping	All MS/MS Ion runs do not show Modification summary report.
17143	Peptide Mapping	Disulfide + Sodium Adduct - High Negative Delta mass for MS2 ID rows.
17030	Peptide Mapping	Gasphase-NH3Loss - seems like we are using the wrong mass for calculation - Delta Mass large than expected.
17015	Peptide Mapping	Isomerization for same peptide shows up as two different modification masses - shows large delta mass ppm.
14263	Peptide Mapping	When Protein Coverage map is copied and pasted to office 2007, amino acid is not displayed properly.
62395	Peptide Mapping	Peptide mapping->Large experiment -> is only using 1 file for MS2.
62396	Peptide Mapping	peptide mapping->ETD/CID select ETD over higher quality CID
4169	Intact Analysis	Zooming out to full scale for MS spectrum does not hide the scrollbar.
3238	Intact Analysis	Reporting - Source spectrum shows “F:” Assume this is for Filter; do not think we have filters for chromatograms.
62577	Peptide Mapping	Peptide mapping - After placing an experiment on run queue - Home page still has method checked.
62580	Protein Sequence	MSQC: Load a non-correct MSQC file - cause exception dialog.
20965	Peptide Mapping	Peptide sequence coverage map does not paste into MS word correctly. Workaround: use the snipping Windows tools to capture the image or do a screen copy.
24538	Peptide Mapping	Sometime a peptide might not be highlighted on the protein sequence tab.
81000	Installation	On a few Win 7 machine, when BioPharma installer is run, the installer could get stuck at the "Initializing" step.

Table 1. Resolved issues in BioPharma Finder 1.0, 1.0 SP1, 2.0, 3.0, 3.1, 3.2, 4.0QF, 4.1, and 5.0 (Sheet 4 of 4)

Item ID	Software section	Abstract
42104	Intact Analysis	Mass Std Dev and PPM Std Dev present in the report but not present in Results table or the export for ReSpect Sliding Window
38707	Peptide Mapping	Peptide mapping->Large experiment -> is only using 1 file for MS2.
81326	Installation	During upgrade from BF3.0 to 3.1, if there is not enough disk space, if a user selects “Ignore"> it still tries to create a backup and installation fails.
38396	Peptide Mapping	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.
78060	Peptide Mapping	Peptide Mapping: Save as Displayed: Missing Column "Level" causing data overlapping in results grid after exporting to Save As Displayed
54723	Peptide Mapping	Arrangement of tabs - seen differently than normal right after processing.
52377	Peptide Mapping	Peptide Mapping->Process & Review-> Mono Mass Theo. does not include the Na+
52381	Peptide Mapping	Peptide Mapping->Process & Result->Theoretical mass does not include oxidation for gasphaseoxidation.
52383	Peptide Mapping	Peptide Mapping->process & review-> glycans not be included in the theoretical mass value.
52380	Peptide Mapping	Peptide Mapping->Process & review->Theoretical mass does not have the correct value for dimer peptides.

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	Shading plots might not be visible in the reports for experiments with many data files.	High	230105
High	Duplicate copies of a chromatogram, decon and source spectra (from the same raw file) are created for multiconsensus experiment when the raw file contains more than 1 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 will be displayed for review.	High	32986
High	When remote desktop to a win 10 machine, select Load result or open result, it shows a blank screen instead of opening the result in Process and review. Workaround: Close the application, restart the application, then select load result or open result, result is displayed in Process and review.	High	42050
High	Memory usage is not optimized during various operations - loading result or switch to mapping tab.	High	38744
High	The protein sequence information might not be displayed correctly in the load results table and identification parameters when upgrading a legacy Protein Deconvolution 4.0 result. Workaround: to reprocess the results in BioPharma Finder 4.1using the same protein sequence (add manually) and then save the results.	High	37244

Table 2. Known defects (Sheet 2 of 7)

Severity	Abstract	Risk	Item ID
High	Missing retention time. 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, then select load result or open result, result is displayed in Process and review.	High	10137
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 PD 4.0. Workaround: Import each chain as a separate FASTA file and add these sequences to the method. Sequence match gives expected result. In a future release, the algorithm will be updated so that users can add all chains in the same sequence.	High	14421
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 the installation of Acrobat Pro to create a PDF, which would then display the images correctly in a PDF file.	High	9716
High	Performance of "finalizing results" is slow.	High	2235
High	The Auto ReSpect feature cannot find the expected components.	High	3281
High	Top Down - Intact - if no deconvolution for specific peak does not update deconvolution graph - shows different peak. Workaround - Load another result, then load this result again. For intact deconvolution - select the empty peak first.	High	63112
High	Oligo Analysis only supports 1 variable modification on an oligonucleotide sequence	High	117286
Medium	Network issues could cause errors with opening large experimental results when connected to HyperBridge.	Medium	240503
Medium	Theoretical mass of some modifications in the oligonucleotide analysis workflow are not correctly calculated for full MS data.	Medium	185972
Medium	Theoretical Protein/peptide manager; custom protease that cleavage on both C-term and N-term residues will not cleavage at the N-term side correctly.	Medium	179638
Medium	In peptide mapping the "find all ions with MS/MS" tasked using as default in the host cell protein workflow may generate components that have both average and monoisotopic mass equal to zero and contain MS2 spectrum.	Medium	178056
Medium	Performance issues could occur when searching extremely large datasets in the host cell protein workflow. Workaround: Increase the S/N value to 3 or greater and reduce the retention time range to exclude undigested protein that elutes in the high organic.	Medium	150046
Medium	Negative protein terminal variable modifications do not return the correct identification for the host cell protein search.	Medium	164107

Table 2. Known defects (Sheet 3 of 7)

Severity	Abstract	Risk	Item ID
Medium	Application might not respond when user is loading or viewing results for top down experiments with more than 25 proteoforms. Workaround: reduce the total number of proteoforms searched in one experiment by performing multiple experiments with less than 10 proteoforms per experiment.	Medium	177288
Medium	Intact experiments that use Respect is still able to be processed, but queue show as zero components due to the following situation where report name = Raw name + Experiment name + Folder length > 256 characters.	Medium	39291
Medium	For intact experiments, when bioPharma 1.0sp1 is upgraded to BF2.0, for custom methods RT range is set to 0 to 0 instead of the value set in time limit parameter.	Medium	39286
Medium	Peptide mapping analysis can have an issue with multiple labels for same Glycan in some MS2 spectra.	Medium	38377
Medium	QB files for intact Default Native Above 1 million - cannot set RT time to include both RT values.	Medium	49511
Medium	(UXLib 83877) Licensing - in license activation dialog - when cancel from permanent activation and select "back" to select Trial license > activation gives an error.	Medium	51905
Medium	Peptide mapping-> Process & Review-> Peptide ID has (m) mass but the monoisotopic experimental (observed) is 0.000	Medium	52372
Medium	Peptide Mapping-> Process and Review-> theoretical mass does not include K+ in the mass value and glycans with K+ also.	Medium	52382
Medium	Intact - Sliding Window - multiple raw files - match Mass error Percent CV - for single raw file should be zero	Medium	52888
Medium	Predicted Time - not always the same for processing same experiment for Modification summary.	Medium	52946
Medium	Peptide mapping analysis: Modification summary relative abundance calculations: When more than one modification is on same peptide, it is excluded from numerator.	Medium	38385
Medium	Peptide mapping analysis: Monoisotopic Mass - slightly different for Targeted verses non-Targeted experiments.	Medium	38376
Medium	Peptide mapping->ETD/CID select ETD over higher quality CID	Medium	38708
Medium	Software does not fully support display on 4k Monitors	Medium	38718
Medium	Intact deconvolution: drug load values are only assigned to components with identifications.	Medium	30767
Medium	For multiconsensus Average DAR experiments, if a raw file does not contain the component being used for the Average DAR calculation the table will display an empty space instead of the raw file name.	Medium	35097
Medium	If a processing method has an error the software will allow the user to save the method. Workaround: do not save methods with errors.	Medium	30357
Medium	If multiple resolutions are used during the data acquisition the software requires two different processing methods which use the appropriate resolution values to obtain the best results.	Medium	24386

Table 2. Known defects (Sheet 4 of 7)

Severity	Abstract	Risk	Item ID
Medium	If raw file folder path and raw file name are > 256 characters, the number of components detected in the queue will be listed as 0. However, the experiment will process correctly even those the value is listed as 0. Workaround: the value is being displayed correctly in the load results table.	Medium	38426
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	Override drug load does not work if other rows are checked, when the component you want to override is an unchecked row. Workaround: uncheck all the components in the main table. Select the component you would like to change the drug load value and check the override check box.	Medium	34990
Medium	Peptide mapping on hitting abort/cancel can crash application - seems to be related to when button is clicked. Workaround: if application crashes during aborting reopen to continue processing.	Medium	35934
Medium	When multiconsensus experiment is exported, the component with a rawfile containing multiple peaks, only the first component is exported. Workaround is to export all components all levels.	Medium	39426
Medium	Application error/crash - when launching a second instance of app from a different user on the same machine.	Medium	41418
Medium	Disulfide bond is not properly highlighted in Protein sequence tab, if peptide sequence is overlapping, then first part of the sequence is not highlighted.	Medium	16720
Medium	Save results after recalculating average DAR using selected check boxes. Open results and drug load are zero for non-checked rows. Workaround: Uncheck all rows and then hit recalculate. The drug load values appear for all rows with drug load.	Medium	41362
Medium	Single scan raw files exported from Qual Browser can cause the source spectrum to be blank when switching from sliding window to average over RT. Workaround: create a method with sliding window that is within the RT range of the file.	Medium	40422
Medium	Use restricted time 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 BioPharma 1.0sp1 is upgraded to BF3.0, for custom methods RT range is set to 0 to 0 instead of the value set in time limit parameter. RT range parameter had different meaning in past releases. Workaround: change the RT range manually.	Medium	39721
Medium	When MS2 window is changed to floating by dragging the window and changed back to "Dockable", MS2 data is not displayed any more. Workaround: once this error encountered, select another experiment then load back this experiment. Data will be displayed.	Medium	40794

Table 2. Known defects (Sheet 5 of 7)

Severity	Abstract	Risk	Item ID
Medium	Resolution displayed on the experimental HCD spectra maybe incorrect.	Medium	11778
Medium	An apex RT should be within its RT range	Medium	11958
Medium	When upgrade from earlier version of Protein Deconvolution to BioPharma, with Permanent license key, experiment type and load result is disabled until restarted.	Medium	13612
Medium	(UXLib 14705) When remote desktop to a machine with Trial license for biopharma, intact protein is disabled.	Medium	14462
Medium	For a mixed data of FTMS Full MS and ITMS full MS, the resolution in not correct.	Medium	1918
Medium	The user can set different time limits for sliding window and chromatogram. During processing, chromatogram window is shown.	Medium	4565
Medium	The RT Range for sliding window can be zero for start and finish and, when in auto mode, you do not get the sub-optimal warning in the run queue message	Medium	4258
Medium	Top Down - if you delete the sequence that you have added from Home page - protoeform not present after processing. Workaround: if the sequence is used in an experiment which is being processed or in submitted state, do not delete it from the global reference table.	Medium	63260
Medium	Peptide Mapping: Best Fragmentation MS2 now selected but Predicted MS2 spectrum is not correct fragmentation type. Workaround: Manually select the correct fragmentation method in "Predicted Peptide MS/MS" dialog box.	Medium	62682
Medium	Top Down Xtract parameters Intact deconvolution: M/Z range doesn't correspond with the range on the source spectrum's scan filter header when Intact Deconvolution is unchecked after selecting RT range. Workaround: Manually Change the M/Z range in parameters | Intact deconvolution tab and save the method.	Medium	63022
Medium	Intact: When queue is paused and BF is upgraded to 3.0, it prompts user whether user would like to start the queue> select yes > app crashes. Workaround: Process all data experiment in the queue before upgrading to higher version.	Medium	61937
Medium	Top Down: ProSightBP table is not sorted by relative Abundance on initially clicking on proteoform. Workaround: User will have to sort manually on Relative Abundance	Medium	62214
Medium	MSQC->paste peptide sequences into sequence box with "> name" and this information is not being shown in the table.	Medium	60347
Medium	Intact->Process & Review->XIC disappear in Auto Peak detection experiment when reviewing data. Workaround: Reload the result to view the XIC	Medium	60726
Medium	Non targeted/Targeted->Multiple (and Single) File Experiment->Predicted MS2 not working for some peptides with MS2 spectrum are searched.	Medium	77170
Medium	Targeted Peptide Mapping-> Modification Summary->% abundance values for modifications that use unique peptides in calculation could be incorrect	Medium	79541

Table 2. Known defects (Sheet 6 of 7)

Severity	Abstract	Risk	Item ID
Medium	Installer: During installation, the mongodb access dialog should be visible. **Note** An error—error "1920"—might be displayed if a previous version of BioPharma Finder is updated to BioPharma Finder 3.1. Try this workaround: 1. With the installer is running (displaying the 1920 error), go to C:\Program Files\Thermo\BioPharma Finder 2. Select **ThermoFisher.BioPharma.DBUpgradeUtility.exe**, and then run as Administrator. The "mongodb access dialog" is displayed. 3. Enable access. 4. From the BioPharma Finder installer, 1920 error dialog box, select **retry**. The Biopharma finder installation is complete.	Medium	81387
Medium	Peptide Mapping targeted analysis: Modification summary relative abundance calculations will not use defined peptides when more than one modification is on same peptide, it is excluded from numerator.	Medium	80050
Medium	Installer: IQ report link is not working on a few PC/VM-> Adobe is installed. Workaround: Locate the IQ report in IQ Reports directory C:\Program Files\Thermo\IQ Reports	Medium	119656
Medium	Oligonucleotide Sequence Editor: Gives an error when the formula contains any of the elements with an quantity greater than 100,000 (for example C101,000H20,000)	Medium	119790
Medium	Peptide mapping parameters, beginning and ending peak width, may be 0.00 when processing an upgraded result from previous versions of BPF.	Medium	122165
Medium	During the installation, if the previous version of BPF is installed but has not be launched, during the BPF 4.0 upgrade the installation will fail. Workaround: Before installing BPF 4.0 ensure that the previous version has been opened.	Medium	123001
Medium	Oligonucleotide Analysis: For 'Predicted Oligo MS/MS (kinetic model), when a sequence is added in all lower case, no message is displayed that it should be capital letters or triplet code format.	Medium	123294
Medium	Oligonucleotide Analysis: Process and review page, the 3'termins will not be highlighted completely in the oligonucleotide sequence page.	Medium	117056
Medium	Peptide Mapping: The chain mass is not updated when linking disulfide bond in the protein sequence editor.	Medium	14419
Low	The protein description might not be parsed correctly for some host cell proteins resulting in an incomplete description in the software.	Low	166116
Low	MS Dimer Predicted Spectrum does not show up correctly in dialog box for sequence (Assume MS/MS predicted spectrum is incorrect as well).	Low	12896
Low	Top Down Analysis: On selecting a method or typing experiment name triggers "clear settings" dialog box when home tab is clicked.	Low	61013
Low	Top Down: UI items not Properly aligned on Identification tab; PPM label is truncated. Workaround: This issue is specific to certain VGA card only.	Low	51752

Table 2. Known defects (Sheet 7 of 7)

Severity	Abstract	Risk	Item ID
Low	File order is reversed in Result table.	Low	53190
Low	Peptide Mapping: Performance- Trend MS Area is missing raw file labels on x-axis for a 100-file experiment.	Low	73403
Low	Peptide Mapping Workbook: RT (Min) - 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: Clear filter for a column - does not set back to original filter type.	Low	38384
Low	Peptide mapping: After placing an experiment on run queue - Home page still has method checked.	Low	38709
Low	MSQC: Selecting peptide or protein shows a table of amino acids - N-term is indexed as 1	Low	38710
Low	Top Down Analysis: Selecting a method or typing experiment name activates the Clear Settings dialog box when home tab is clicked.	Low	38712
Low	Top Down: UI items not Properly aligned on Identification tab; PPM label is truncated	Low	38738
Low	Peptide Mapping: Refresh issue- on Mod summary page upon Manual integration.	Low	53410
Low	In the summary table found in the parameters save method page, the report parameters are listed an enabled for multi-consensus experiments. Note that 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	In this release the deconvolution will be processed 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	Multi-consensus merging parameters are not disabled for single file experiments.	Low	34626
Low	Modification summary export with contents, when viewed using Open office is empty	Low	117636

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