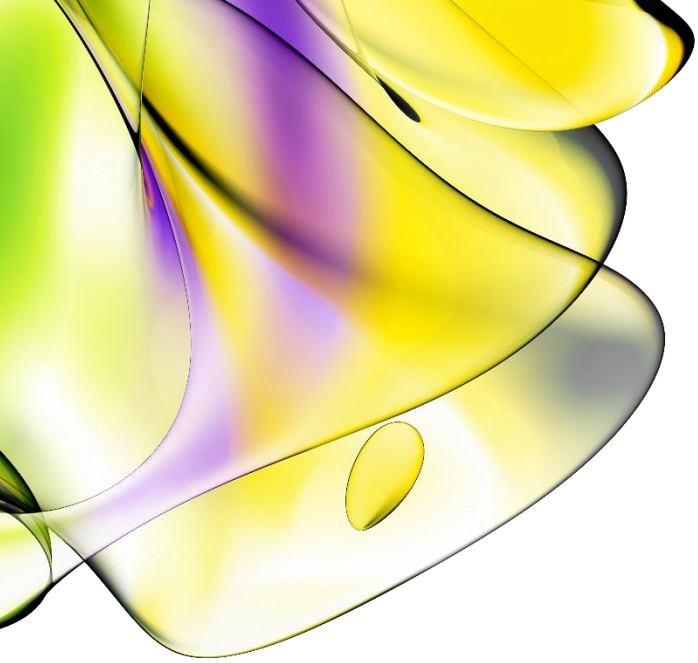

Revvity Signals VitroVivo™ 3.5.0

Release Notes

Powered by Spotfire®

Last Updated: March 20, 2024

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1. General Description

Signals VitroVivo™ is a Spotfire® based solution that allows analysis of multivariate and univariate data extracted from instruments and image analysis software for High Throughput Screening (HTS), High Content Screening (HCS), and from Surface Plasmon Resonance (SPR) instruments. Signals VitroVivo also includes a Pharmacokinetics (PK) parameters app, that allows the user to review PK curves and calculate the PK parameters. The power of Signals VitroVivo is focused on providing users with the ability and freedom to build personalized Workflows and enabling scientists to perform advanced features such as normalization, profiling, curve fitting, kinetic fitting, and data visualization on a user-friendly, yet powerful environment.

Signals VitroVivo includes:

- Signals Screening Domain Apps (HTS and HCS)
- Signals Surface Plasmon Resonance Domain Apps (SPR)
- Signals In Vivo PK Parameters App
- Calculations Explorer (CE)
- High Content Profiler™
- SciStream™
- Image Import for Spotfire®
- Image Discovery and Images Service

2. Distribution Limitations

Signals VitroVivo 3.5.0 is compatible with Spotfire® 12.0 LTS and Spotfire® 14.0 LTS.

3. Release Qualification

3.1 Scope of Testing

To ensure the quality of Signals VitroVivo, in depth functional and regression testing has been performed. The following are the environment(s) where testing has been conducted.

3.2 Testing Environment for Signals VitroVivo

Machine Type	Operating System	Database Version	Browser Analyst	Spotfire version	.NET Framework
Spotfire® Server	Windows Server 2019 Datacenter	MSSQL Server 2019		12.0.8 LTS	4.8.3752
Spotfire® Server	Windows Server 2019 Datacenter	PostgreSQL 14		14.0.1 LTS	4.8.3752

Machine Type	Operating System	Database Version	Browser Analyst	Spotfire version	.NET Framework
Spotfire® Web Player	Windows Server 2019 Datacenter	MSSQL Server 2019		12.0.8 LTS	4.8.3752
Spotfire® Web Player	Windows Server 2022			14.0.1 LTS	4.8.3752
Client 1	Windows 10 (64 bits)		Chrome Embedded Framework (CEF)* Chrome 119.0 Firefox 118.0 Microsoft Edge 119.0	12.0.8 HF-028 14.0.1 HF004	4.8.3752

4. Installation Instructions

4.1 Release Installation

Please refer to the *Revvity Signals VitroVivo™ Installation Guide*.

4.2 Prerequisites and System Requirements

The Installation Guide explains the steps required to deploy and set up Signals VitroVivo based on the assumption that the user has previously installed and configured the system requirements described in the *Revvity Signals VitroVivo System Requirements* document.

4.3 Manifest

The Signals VitroVivo 3.5.0 release bundle includes:

Goods

- TSS installation folder with .sdn files for deployment on Spotfire®
  - Signals-VitroVivo.sdn
- TSSS installation folder with additional modules required for the use of a TSSS when using Signals VitroVivo Apps in the Spotfire® Web Player client or when Data Functions are configured to use a TSSS for Data Functions
  - itghcs.python.resources.zip[1]
  - itghcs.resources.zip[1]
  - TERR_bundle_3.3.0.150_Stable.zip[1]
- Signals VitroVivo Metastore Docker Compose artifacts for Linux OS

[1] This is needed only for the TSSS installation.

    - docker-compose-linux-3.5.0.203.tar.gz
    - docker-compose-linux-ssl-3.5.0.203.tar.gz
    - image-3.5.0.203.tar.gz
- Images Service installer
    - Signals Images Service-1.0.2.759.exe

Modules included in the SDN, available in the TSS after deployment of the Signals VitroVivo.sdn

- Calculations Explorer_2.0.0.4199
- Image Discovery_1.0.2.759
- Image Import_14.10.0.432
- Integromics.Hcs_3.5.0.630
- Integromics.Hcs.Help_3.5.0.630
- Integromics.Hcs.Python_3.5.0.630
- Integromics.Hcs.ThirdParty_3.5.0.630
- Integromics.Hcs.Web_3.5.0.630
- Integromics.Python.Executor_3.5.0.630
- Integromics.Python.Runtime.2.7_1.0.1.20
- SciStream_23.28.2.1275
- Signals Analytics Apps for Screening_3.5.0.10779
- Signals Analytics Historical Data App_3.5.0.10779
- Signals Analytics Signals Data Import App_3.5.0.10779
- Signals Apps_5.5.9156.0
- Signals Apps Groups Panel_5.5.9156.0
- Signals Notebook Spotfire Opener_1.0.0.21
- Signals Screening Common_3.5.0.10779
- Signals SPR Alignment App_3.5.0.10779
- Signals SPR Blank Subtraction App_3.5.0.10779
- Signals SPR Common_3.5.0.10779
- Signals SPR Cropping App_3.5.0.10779
- Signals SPR Data Import App_3.5.0.10779
- Signals SPR Data Readers_3.5.0.10779
- Signals SPR Export Report App_3.5.0.10779
- Signals SPR Hit Selection App_3.5.0.10779
- Signals SPR MultiCycle Kinetic Analysis App_3.5.0.10779
- Signals SPR RAC App_3.5.0.10779
- Signals SPR Reference App_3.5.0.10779
- Signals SPR Relative Potency App_3.5.0.10779
- Signals SPR ReportPoints App_3.5.0.10779
- Signals SPR Single Cycle Kinetics App_3.5.0.10779
- Signals SPR Solvent Correction App_3.5.0.10779
- Signals SPR Steady State Analysis App_3.5.0.10779
- Signals SPR TraceDrawer Export App_3.5.0.10779
- Signals SPR Zeroing App_3.5.0.10779
- Signals VitroVivo Product_3.5.0.10779
- Signals.InVivo.Common_1.8.3002.0
- Signals.InVivo.PKParameters_1.8.3002.0

- Signals.Utils.Metastore_1.0.0.281

Important

- The modules from previous versions that have been deprecated should be removed manually from the Spotfire® server.
- For Analyst Spotfire® server version should be 12.0.8 or greater for Spotfire® 12.0 and 14.0.1 or greater for Spotfire® 14.0 (TERR version 6.1.1).
- For WebPlayer Spotfire® Statistical Services should be version 12.0.4.

Documentation

- Documentation Folder
  - Revvity Signals VitroVivo 3.5.0 System Requirements.pdf
  - Revvity Signals VitroVivo 3.5.0 New User Installation Orientation.pdf
  - Revvity Signals VitroVivo 3.5.0 Installation Guide.pdf
  - Revvity Signals VitroVivo 3.5.0 Release Notes.pdf
  - Revvity Signals VitroVivo 3.5.0 User Guide.pdf
  - Revvity Signals VitroVivo 3.5.0 Quick Start Guide – Screening Workflow.pdf
  - Revvity Signals VitroVivo 3.5.0 Quick Start Guide – SPR Workflow.pdf
  - Revvity Signals VitroVivo 3.5.0 Quick Start Guide – In Vivo Workflow.pdf
  - Revvity Signals VitroVivo 3.5.0 SciStream User Guide.pdf
  - Revvity Signals VitroVivo Curve Fitting Descriptions.pdf
  - DemoDataset.zip
    - DemoDataset.txt
  - SampleData.zip (includes supporting files for OotB Workflows including Quick Start Guides)
    - OotBScreeningWorkflows
      - 1st Demo - 4P Dose-Response IC50 Assay
      - 2nd Demo - Single-point HTS
      - 3rd Demo - ELISA Assay with Standard Curve
      - 4th Demo - FLIPR Kinetic Assay
      - 5th Demo - Signals Pipeline Curve Fitting - QA-QC
    - OotBSPRWorkflows
      - 1st Demo - SPR Kinetic Assay

5. What's New in this Release

5.1 New Features for Signals VitroVivo 3.5.0

General

- To avoid confusion and errors due to the use of unsupported Apps, **all deprecated Apps will generally be removed one version after their deprecation**. This means any .dxp that contains deprecated Apps will need to be updated to the new version of the App(s) or regenerated without the deprecated App(s) if it will be opened in newer versions of Signals VitroVivo.
- Signals VitroVivo has been rebranded to Revvity.

Metastore

- The Metastore no longer supports installation on a Windows server. Only Linux servers are supported.

5.2 Defect Fixes in Signals VitroVivo 3.5.0

Workflows

- Import workflow was not working correctly in some cases when the connection was slow.

Calculations Explorer

- Wrong fit for small values has been corrected.
- In some cases, columns from transformations were not captured.

Image Import

- An error by which the preview image was not displayed has been corrected.

Editable Data Grid

- Previous run configuration is no longer displayed when running the Editable Data Grid in a Workflow.

Documentation

- Some corrections have been added to the *Revvity Signals VitroVivo System Requirements* document.
- Some clarifications have been added to the *Revvity Signals VitroVivo User Guide* document.

5.3 Planned changes in the next versions:

TSSS

- TSSS support will be discontinued in future versions. Use of TERR nodes for datafunction executions will be required.
- Images Services will be deprecated and will no longer be provided as a separate executable.

6. Known Issues, Limitations and Workarounds

6.1 Limitations and Known Issues:

SPR Data Import

- B4000 support is limited to exported curve files where the concentration is provided in molar units (nM, uM, mM or M) and both ligand and target information are present in the curve export file.
- Loading of report points from multiple input files is not supported.
- If a table named ‘Sensorgrams’ is present in the document the SPR Data Import App will not function correctly.
- Data files with their extensions in capital letters are not fully supported.
- Decimal concentrations are not properly loaded in some cases when the decimal separator is different from the expected regional settings configured.

QA-QC

- Decimal points are not supported in the report point size window.
- Exclusion controls will not work with data that does not follow the Screening Data Model (data that is not loaded using the SPR Data Import App).

Zeroing

- When using the Spotfire® 'delete rows' functionality in the *After Zeroing* visualization, all points disappear from the visualization.

Alignment

- B4000 and Octet data alignment are not supported.

Referencing

- When opening a .dxp with the Referencing App where all visual groups are hidden the left configuration panel will occupy the available display area.

Steady State Analysis

- If negative values are provided by mistake an error is raised.

Multi-Cycle Kinetics

- A '0' is added before manually input numbers if the textboxes are emptied.
- Due to some differences in the calculation engine in TERR 6.0.3, in some cases minor differences may be observed in some parameters when re-executing the app after the upgrade to the new TERR engine.

Non-Regenerative Kinetics

- If a .dxp containing the NRK App is saved with the focus on a different tab, when opening the App the analysis in the NRK will be executed with an incorrect configuration, to fix this simply re-apply the NRK analysis.

Hit Selection

- Hit and non-hit entries are not colored correctly in the *Hit Exploration* table.
- When the values for a curve are too close to the threshold, they may be labeled incorrectly due to precision issues.

Relative Active Concentration

- Modifying the Analysis or the 'Molecule' type after loading the pairs causes the RAC App to fail.
- When the pairing file is replaced, a Spotfire® popup asking the user to pair the columns of the files appears.

Image Import

- In some cases, the user might experience a brief interruption in the connection to the server, waiting a few seconds will re-establish the connection.
- URLs containing a trailing slash will not work correctly.

Editable Data Grid

- Editing the 'Ligand' and 'Sample' columns imported by the New SPR Data import App from a saved .dxp in the Editable Data Grid is not supported.
- When a very large file is pasted into the Editable Data Grid this may cause a freeze which can be avoided by using the 'Load from file' option.
- With some Non-English regional settings, the Editable Data Grid cannot correctly interpret the type of column. This may happen with regional formats that normally use a comma as a decimal separator where the Windows decimal symbol is set to dot, and the numerical column has exactly two decimal places. This can be prevented by avoiding the above combination of settings.

- When samples are updated in the Editable Data Grid within an SPR Workflow the changes are not propagated to the Sensorgrams table if the document has been saved previously with the tables embedded.
- Adding a single row of headers to the Editable data grid is not supported in Web Player.

Grid Plate Editor

- Copying and pasting large amounts of data is not currently supported.
- In some cases, when the App is closed the selected annotation table may remain in the document.

HTS QA/QC

- This App cannot be opened unless a Screening table is present in the document. This screening table is generated by the Data import or Image import Apps.

Extensible Normalization

- When running a CE Template, if the dataset used has different names for the control column these settings may need to be reconfigured.

Signals Data Import

- When using WebPlayer it is not possible to log out of the Signals Data import App to use a different user. To do so, the current user must close the session in the browser.
- Using different security configurations for Spotfire® and SDF is not supported. Spotfire® server and SDF servers should both use https or both use http.

Calculations Explorer

- When updating a CE Template, the tree names are not updated if changed in the CE panel. To update these, it must be done from the properties.
- In the CE Template, only trellis using panels with a manual layout is supported.
- When using Y weighting with a K=1, if there are many Y=0 values, a fitting may fail to be returned.
- Using the 'Include transformations' toggle to create several CE Templates in the same .dxp is not supported.
- When using log function in the CE the long R syntax should be used.
- When using the Schild Fitting the data must be in log scale.
- When creating a CE Template, a calculated column can only belong to one CE Template. Because of this if a calculated column needs to be used in two CE Templates they should be created separately, with one CE Template creating the column and the other using it.
- A curve fit cannot be created from a scatterplot based on fit results from another fitting in the same template.
- If the Spotfire® 'Cancel' button is used while applying a CE Template, the CE panel will still be created. To fix this remove the tab and reapply the CE Template.
- Creating a fitting with the same name as an existing one or with the same name (2) is not supported.
- When a user navigates to manage fit settings before marking selection of one per "color" in the Lines & Curves for the curve fit in the template, the column is not visible in the column selection for edit by parameters.
- In some cases, the layout of a hierarchical template may be incorrect in a section after refresh. This can be solved by choosing another section in the hierarchy and then going back to the initial section.

In Vivo Apps (General)

- In Vivo Apps version 3.5 are not backwards compatible with any previous version of the Apps.
- Web Player is not supported.

- Clicking on any button in left panel after marking any curve point makes the contextual marker appear on the top left of the visualization.

Other

- PDF reports are limited to 96 pages.
- Exporting a .pdf report from the workflow where the tables in the document are very large may take a long time. If a document contains a sensorgram table where the size can be quite large exporting the report using the workflow option is not recommended.
- When an App takes too long to open, the Workflow UI appears.
- In some low-resolution cases the UI layout is not correct. This can be fixed by increasing the size of the affected panel and/or increasing the resolution.
- VitroVivo only supports English regional settings, however when working with the Screening domain Apps, if a user imports data containing dots (.) as a decimal separators SciStream will correctly parse them regardless of regional settings.
- Modifying the analysis table using 'Replace table' and/or 'Add columns' to add information used by the Workflow (such as adding ligand or sample names with these functionalities as opposed to using the compound and target controls in the SPR Data Import App) is not fully supported and may cause errors in downstream analysis.
- Executing Kinetics and Steady State Apps on the same document will produce a duplicated CHISquare column.
- In some cases, the numbers displayed in the App panel will be formatted using the "." as a decimal separator regardless of the regional settings configured in the system.
- In some cases when performing an analysis in the Web Player, the browser language settings may cause problems. In this case changing to a language that uses "." as a decimal separator should fix the problem.
- In some cases, mainly when using SPR data when importing data with special characters, it may be incorrectly identified as chemical structures and rendered accordingly. This can be fixed by removing the 'Content' type entry or by modifying the renderer settings for the chemical structures to use 'Text' instead of ChemDraw. The required data types that require changes are:
    - chemical/x-md-molfile Text
    - chemical/x-daylight-smiles Text
    - chemical/x-mdl-chime Text

  This needs to be done from Tools > Options > Application > Renderer Settings menu.
- Web Player Support Note: Although Signals VitroVivo does not fully support Web Player execution, most of the functionality works in the Web Player with some exceptions:
    - VitroVivo Data Import does not allow the creation and edition of data formats in the Web Player.
    - Image Import is not supported in the Web Player.
    - SciStream is not supported in the Web Player.
    - Image Discovery is not supported in the Web Player.
    - Calculations Explorer does not allow the user to download the CE Templates locally from the Web Player.
    - In some cases, App tabs may display a different name when a .dxp is opened from the Web Player.
    - In some cases, cross tables opened in Web Player from a local .dxp do no have the axes configured correctly. This can be avoided by saving the .dxp from the analyst in the Library and opening it in the Web Player from the Library.
    - Web Player is not supported by In Vivo domain Apps.
    - Web Player does not allow the creation of headers-only tables.
- Signals Notebook integration:
    - Opening a .dxp from Signals Notebook is only supported if the .dxp is within an experiment.

    - Opening a .dxp from Signals Notebook only supports the opening of Spotfire® Analyst
    - Integration is not supported from the Web Player, only from the Analyst Client.
    - Integration between Signals Notebook and VitroVivo is not supported if there is more than one instance of Spotfire® Analyst opened in the user's system.
- Automating analyses on the cloud:
    - When automated, the 'Median' calculation in Signals VitroVivo Pipelines is calculated using the lower boundary of the 50th percentile – in smaller datasets this may result in slightly different result than the median generated in Spotfire®.
- Notes on updating from older versions:
    - Although the exploration of a document created with a version of the Apps deprecated in the current release is supported, the addition of new data to an existing document created with an older version of the Apps is not supported, as there has been changes in the way some data is added.
    - **Deprecated Apps will be supported only for one version**. After this they will be removed and documents containing these Apps will not be usable. **Importantly**, those .dxp that should remain usable after future updates should be modified to remove any deprecated Apps.
    - Some of the new features provided by the latest Signals VitroVivo version will not be available in the case of data loaded with an older version of the Apps.
    - When upgrading an App from an older version, existing data functions will be re-placed and re-executed automatically with the settings existing in the document. In the case of Apps that allow for different settings to be applied to different curves in the data function such as the Multi-Cycle Kinetics App, users should reapply the desired settings if these were different between curves.
    - When running the Signals Apps for the first time after updating, an update window will automatically appear to update old existing protocols to the new Workflows.
    - When opening a document containing a table with an Image column rendered with Image Discovery that was created in a previous version that was not Revvity, the image renderer for the column needs to be chosen again by right-clicking on the table and choosing **Properties > Columns Renderer >Signals Image Renderer** for the column that should be rendered as an image.

7. VitroVivo 3.5.0 App Descriptions

7.1 Screening Domain Apps

App Name	Description
Data Import	Provides a Spotfire® connector to instrument formats in the local SciStream installation to facilitate the importing of data from raw instrument files.
Signals Data Import	Imports screening results published in a Signals Data Factory instance into Spotfire® as tables. Note that this App requires Signals Inventa credentials.
Image Import	Provides a Spotfire® connector that supports the performance of advanced search and filter features in Image Artist and remote Columbus servers, retrieving the resulting selections directly into Spotfire®.
Grid Plate Editor	Provides the necessary controls to create, store, edit, and apply plate designs for single or multiple plates in a user friendly and flexible manner.
Editable Data Grid	Provides functionality for inserting and editing grid-like data from the clipboard and files, editing existing data in the document, and loading data from the Spotfire® library and Signals Notebook.

App Name	Description
Extensible Normalization	Provides functionality to perform inter-plate and intra-plate normalization operations by using a set of predefined normalization algorithms or alternatively using custom normalization templates defined by an author using the Calculations Explorer.
New Curve Fitting	Provides a flexible and powerful tool to calculate, review, and report assay curve fitting results using out-of-the-box or custom curve fit equations.
t-SNE	Supports the visualization and analysis of multidimensional data using the t-Distributed Stochastic Neighbor Embedding (t-SNE) technique which reduces the dimensionality of a dataset to a lower dimension map according to the probability density of each point.
Calculations Explorer	Provides the ability to save and apply a Calculations Explorer Template as part of a Workflow to enable the capture and automated replay of transformation, calculations, and visualizations.
HTS QA-QC	Allows for the review of plate statistics and QA-QC results for single-point, high-throughput screening (HTS).
Historical Data	Pull all historical results for equivalent compounds or compound batches into the current Workflow via Spotfire® Information Links, allowing the user to confirm consistency with historical trends before publishing new data.
High Content Profiler	A Spotfire® add-on that allows the analysis of multivariate and univariate data extracted from instruments and image analysis software. An automated guided Workflow coupled to simple wizards and dialogs enables scientists to perform advanced features such as normalization, selection, classification, profiling, and hit selection in a powerful and user-friendly environment.

7.2 SPR Domain Apps

App Name	Description
SPR Data Import	Provides an automated solution for importing SPR data into Spotfire® as well as a set of interactive visualizations allowing manual exploration and analysis of the imported curves. This App can import data in a variety of formats, depending on the instrument source.
Zeroing	A preprocessing tool that aligns the sensorgrams on the Y-axis.
Alignment	A preprocessing tool that performs curve alignment for IBIS MX96 data.
Cropping	A preprocessing tool that crops the sensorgrams to the region of interest and removes extraneous data.
Referencing	A preprocessing tool that subtracts the sensorgram data corresponding to a reference flow cell from the sensorgram data to be analyzed.
Blank Subtraction	A preprocessing tool that allows the user to select and subtract a blank from the analyte sensorgrams.
Solvent Correction	A preprocessing tool that provides functionality to correct any signal distortions caused by the solvent used in small molecule signal measurements. The App permits the selection of solvent correction regions in the solvent cycle, and the position on the reference for the correction.

App Name	Description
QA-QC	Supports the addition of custom report points, displaying a set of visualizations that provide, for each of the sensorgrams in the analysis, information on the response at specific points of the curve marked by the report points.
Relative Active Concentrations	Provides the user with a set of analyses and visualizations to determine relative responses of different curves compared to a reference.
Multi-Cycle Kinetics	Allows the fitting of the sensorgram data to obtain association and dissociation rate constants, ka and kd, as well as Rmax, bulk refractive index (RI) or mass transport coefficient (kt) using the analytical solution derived in Sigmundsson, K. et al.
Steady State Analysis	Calculates the equilibrium dissociation constant, KD, based on concentration vs. response units (RU) when the interaction has reached a steady state (plateau).
Non-Regenerative Kinetics	Provides a solution for analysis of non-regenerative kinetics (single-cycle) in Spotfire®. A set of interactive visualizations are provided to easily explore the results.
Hit Selection	Provides a solution for the selection and classification of SPR analysis results data in Spotfire® and the manual exploration and analysis of the results.
Relative Potency	Allows the user to analyze 4-parameter logistic regression curves created from concentration-response data to identify differences in activity between the analyzed compounds.
Export Report	Allows the selection and exporting of SPR analysis results in Spotfire®. A set of interactive visualizations are provided to easily configure the previewing and exporting of results.
Export to TraceDrawer	Allows the users to export the information in the loaded SPR files to a format accepted by TraceDrawer.

7.3 In Vivo Domain Apps

App Name	Description
PK Parameters	Allows the user to review and QA the PK curves and calculate the final PK parameters.

7.4 Deprecated Apps

To avoid confusion and errors due to the use of unsupported Apps, **all deprecated Apps will be removed one version after their deprecation**. This means any .dxp that contains deprecated Apps will need to be updated to the new version of the App(s) or regenerated without the deprecated App(s) if it will be opened in newer versions of Signals VitroVivo.

Apps that are currently deprecated are:

Screening

- Data Import
- Curve Fitting
- Normalization
- Custom Calculation

SPR

- Data Import
- QA-QC
- Parallel Line Analysis
- Kinetic Analysis
- Referencing

8. Technical Support

This software is supported by Revvity Signals Software Support.

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