Axiom™ Batch SSP Tool

Publication Number 703527 Revision 1

Introduction

The Axiom Batch SSP Tool (BatchSSP) is a standalone software tool used for generating SNP Specific Priors (SSPs) for Axiom AgBio and Human arrays. The tool generates SSPs for biallelic probesets for analysis in Axiom Analysis Suite (AxAS) software.

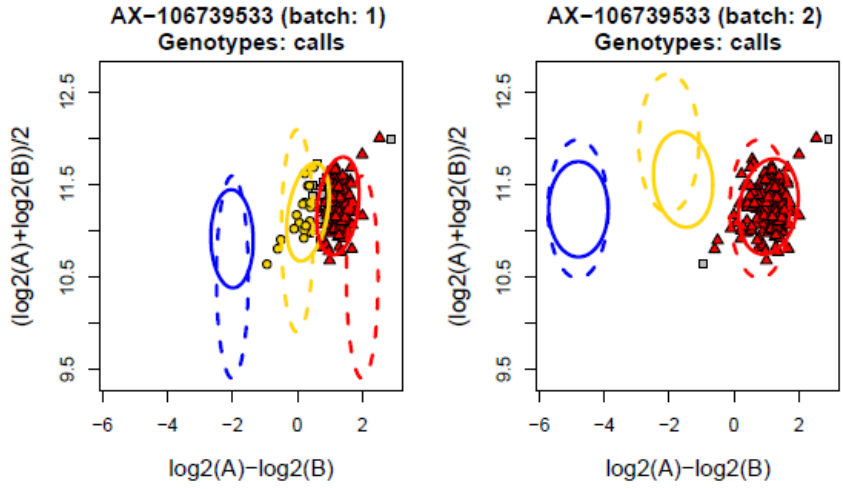
Use and purpose

SNP-specific priors can help improve genotyping results with both accuracy and consistency. During genotyping, prior models for a probeset help inform the genotyping algorithm as to the expected position and size of clusters for that probeset. These models can be generic, or they can be specific for a given probeset (SNP-specific). These prior models in conjunction with the positions and sizes of the clusters from the samples in the dataset create the final models of cluster positions and sizes for the probeset (posteriors).

Priors

The genotyping algorithm uses pre-positioned genotype cluster locations (priors) to calculate the three cluster positions for the sample data, as shown in Figure 1.

Figure 1 Pre-positioned genotype cluster locations: Generic priors (left) SSP (right)

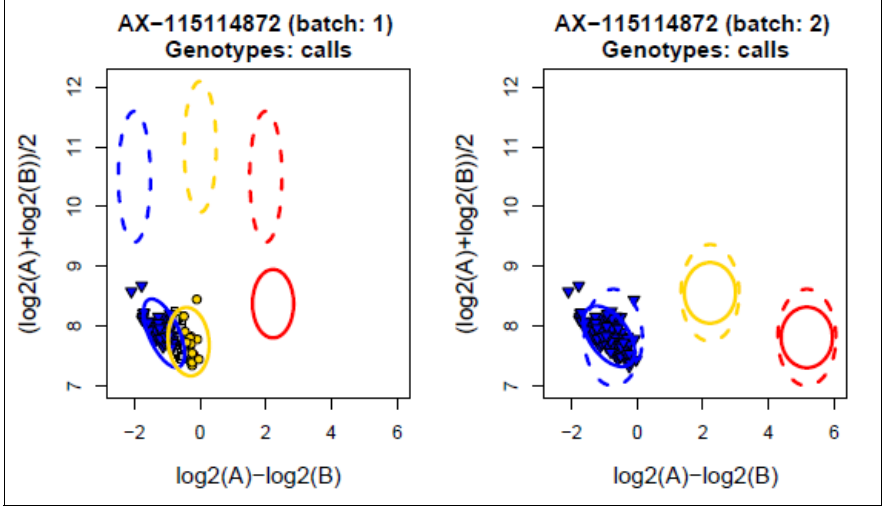


Note: Dashed ellipses represent the priors. Solid ellipses are the generated posteriors.

Generic priors

Generic priors (developed by Thermo Fisher) work with any probeset, yet are not based on previous data. SNP-specific priors are created from genotyping samples across a batch or multiple batches. These samples in the dataset utilize the algorithm as to what the expected cluster positions and size of clusters for a given probeset will be, as shown in Figure 2. For more information see, the **Axiom Genotyping Data Analysis Solutions Guide**.

Figure 2 Cluster plots: Generic priors (left) SSP (right)



System and software requirements

System and software	Requirement
Processor	2.83 GHz (or higher) Pentium Dual Core Processor
Operating System	Windows 7 (64 bit) or 10 (64 bit) Professional with Service Pack 1
Installed software	Axiom Analysis Suite v5.1.1 (or higher)

Sample requirements

The minimum sample size for creating priors is a batch of 96 samples, though it is preferred to use at least 384 samples. The samples should have passed plate QC (average call rate for passing samples ≥ 98.5 and percent of passing samples ≥ 95). There should be a minimum of 40 male and 40 female samples.

Priors can be made for human and for other species. They can also be made using blood, buccal, saliva or other sample types. If sample types are routinely processed separately, then priors should be designed separately for each type, using at least the stated minimum number of samples required.

Installing the tool

IMPORTANT! Axiom Analysis Suite v5.1.1 (or higher) must be installed BEFORE installing the Axiom Batch SSP Tool.

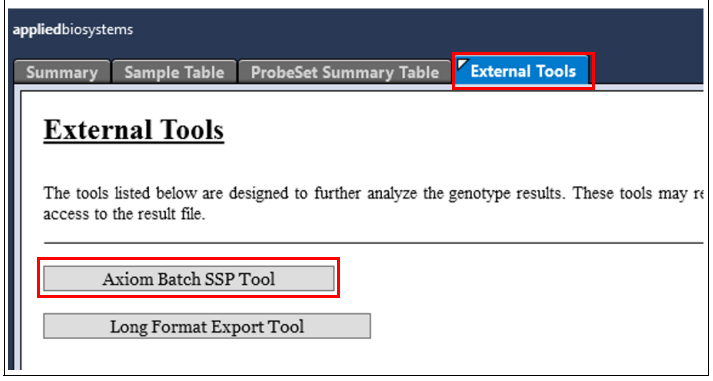
1. Unzip the **Axiom Batch SSP Tool** package file, then double-click on **AxiomBatchSSPSetup**.
2. Follow the prompts to install the tool.

Launching the tool

From AxAS

1. Launch the AxAS software.
2. Open a batch with a Best Practices Workflow.
3. Click on the **External Tools** tab, then click the **Axiom Batch SSP Tool** button. (Figure 3)

Figure 3 External Tools tab



All batch information is displayed in the Tool's main window after launching it from AxAS, as shown in Figure 5 on page 4.

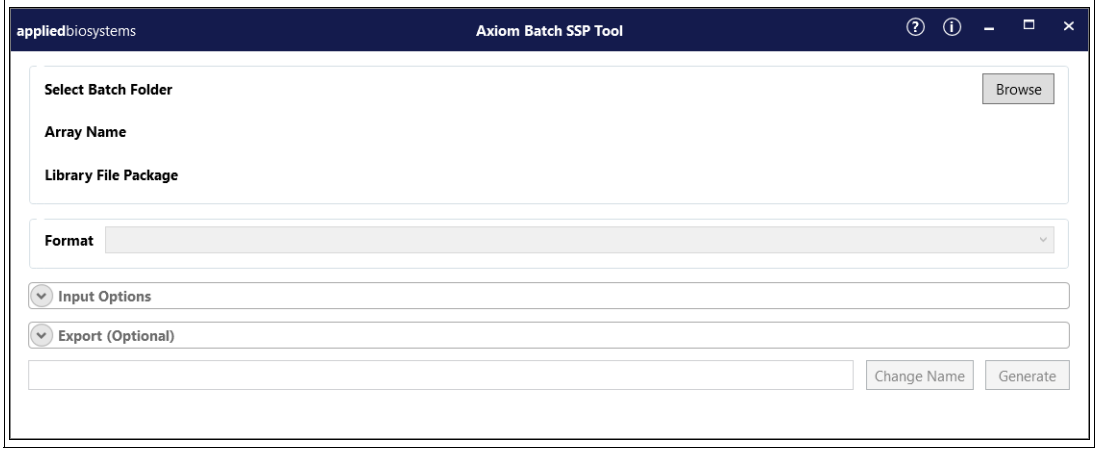
Note: You cannot use the tool if the displayed batch is open in AxAS. If it is, you will be prompted to close it.

From the Start menu

1. After installing the tool, click **Start** → **All Programs** → **Thermo Fisher Scientific** → **Axiom Batch SSP Tool**.

   The tool opens with its fields blank, as shown in Figure 4.

Figure 4 Main window

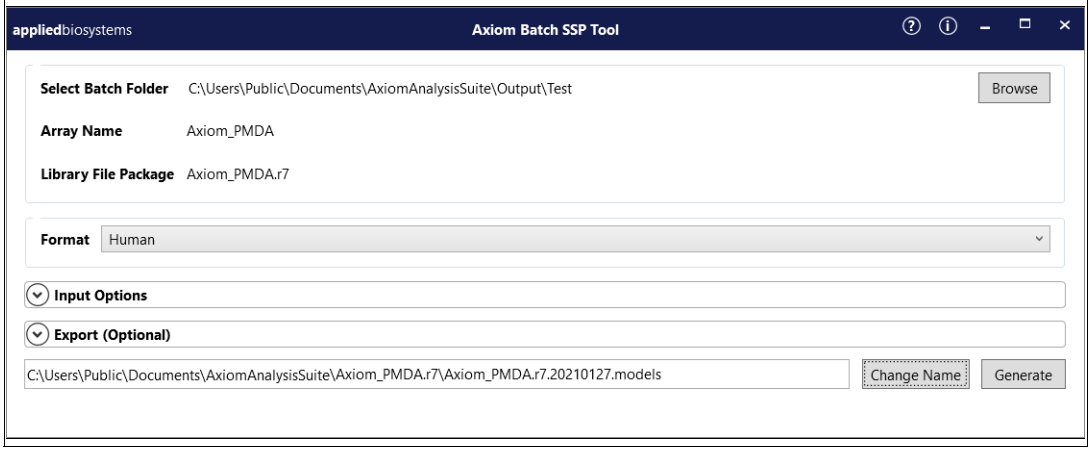


Using the tool

If you launched the tool from the **Start** menu, do the following:

1. Click the Browse button.
   A Select Batch Folder window appears.
2. Click to highlight a batch folder, then click **Select Folder**.
   The main window populates. (Figure 5)

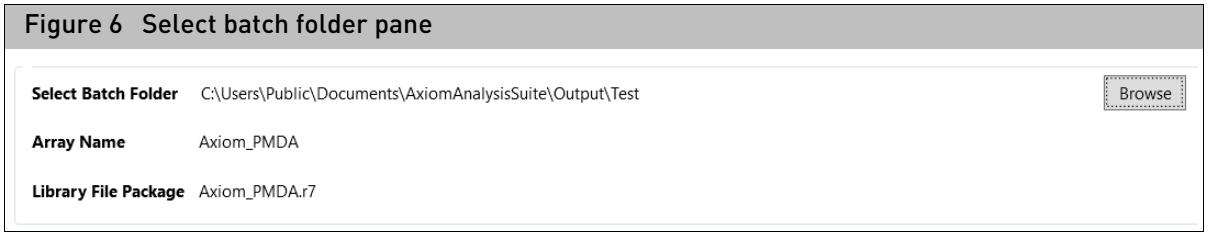
Figure 5 Main window - populated



Select batch folder pane

This pane (Figure 6) displays the following information:

Figure 6 Select batch folder pane

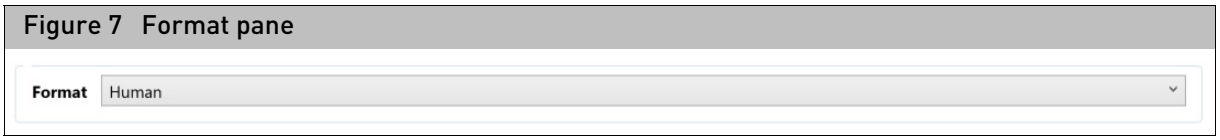


- **Select Batch Folder**: Displays the path of the batch folder you have loaded into the tool. **Note:** The tool requires a Best Practices Workflow batch, because it utilizes this workflow's output files; **Ps.performance.txt** and **AxiomGT1.snp-posteriors.txt**.
- **Array Name**: The Array Name is displayed here. This field auto-populates after selecting the AxAS batch folder.
- **Library File Package**: This field is auto-populated with the library package that was used to create your selected AxAS batch.

Format pane

Format is automatically assigned, as it is specific to the array type.

Figure 7 Format pane



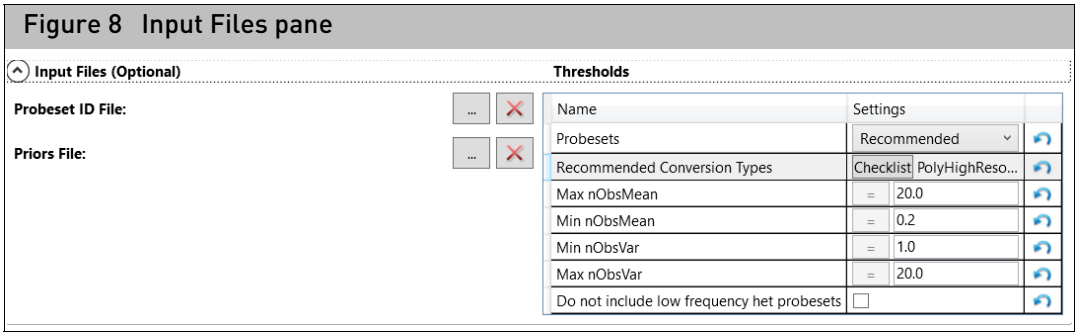
The tool's two default formats are **Human** and **AgBio**. Use the Human format for all human arrays. Use the AgBio format for non-human arrays.

1. Click the **Format** drop-down button to select a different format (if available).

Input files and threshold pane

The Input Files and Thresholds pane (Figure 8) enables you to use a Probeset ID and/or a Priors file. Thresholds can also be edited here. **Note:** The default Input Threshold values are based on the format.

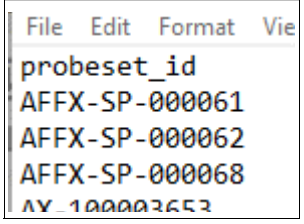
Figure 8 Input Files pane



Probeset ID File

This is a single column text file with a **probeset_id** header followed by a list of probesets. (Figure 9) The tool uses these probesets to create SSPs.

Figure 9 Example: probeset_id file



Note: This option restricts prior file generation to only the probesets in your selected file. It also disables the **Recommended Conversion Type** (in Thresholds).

If Probesets is set to 

, then priors will only be generated for probesets with recommended conversion types in the input batch.

Adding a probeset_id file

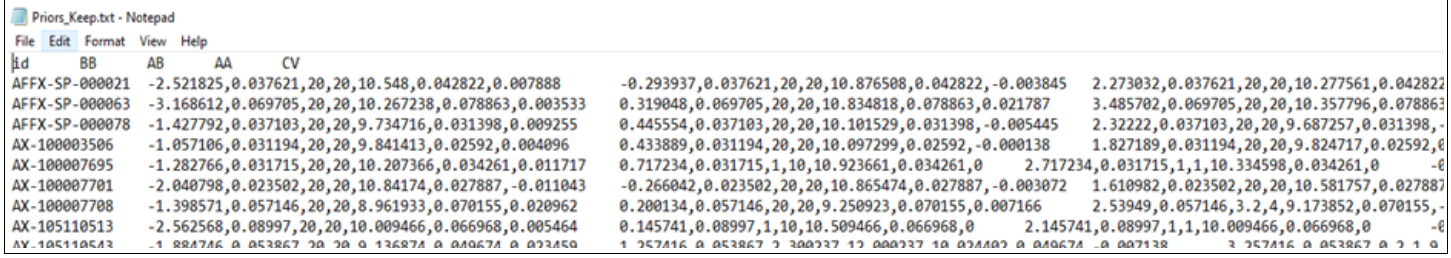
1. Click the  button.
   A Select PID File window appears.
2. Navigate to the file, click to highlight it, then click **Open**.
   The file is added to the tool.

Priors File

When used, the tool will not generate SSPs using the probesets listed in your selected file. Instead, the priors in your selected Priors File will stay intact and be used in the newly generated priors file.

Note: Your Priors File must be in the biallelic models file format, as shown in Figure 10.

Figure 10 Biallelic models file format example



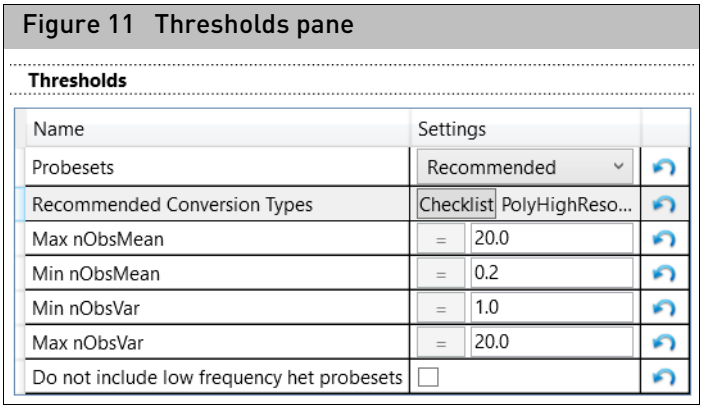
Adding a priors file

1. Click the  button.
   A Select Priors File window appears.
2. Navigate to the file, click to highlight it, then click **Open**.
   The file is added to the tool.

Thresholds

Use the drop-downs, text fields, and check box to change settings and values, as shown in Figure 11.

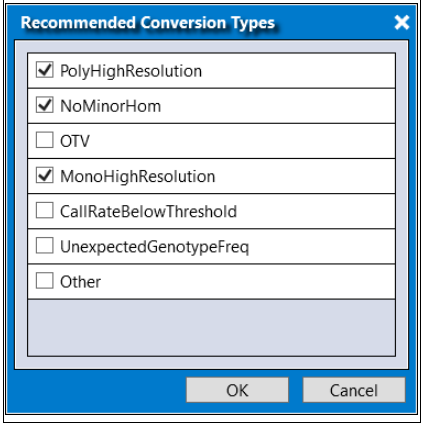
Figure 11 Thresholds pane



1. **[Probesets]** Click the **Recommended** drop-down button to change the setting to "All".
2. **[Recommended Conversion Types]** To change the conversion types, click Checklist.

   A Recommended Conversion Types window appears. (Figure 12) **Note:** This window is not available if a Probeset ID file has been added to the tool.

Figure 12 Recommended Conversion Types window



3. Click to check or uncheck the appropriate check boxes, then click **OK**.
4. **[Max and Min Settings]** Use the text field to enter a different weight value.

IMPORTANT! Maximum and minimum weight values should only be changed under the guidance of your Field Support Specialist.

Click to return a changed value back to its factory default.

– **[Max nObsMean]** The maximum weight allowed for the nObsMean value in the generated priors file.
– **[Min nObsMean]** The minimum weight allowed for the nObsMean value in the generated priors file.
– **[Min nObsVar]** The minimum weight allowed for the nObsVar value in the generated priors file.
– **[Max nObsVar]** The maximum weight allowed for the nObsVar value in the generated priors file.

Additional information about weights and threshold definitions

The nObsMean value is the number of observations for the position of a cluster. nObsVar is the number of observations for the size of a cluster. These are termed weights. Posterior weights are the addition of prior weights and the number of samples in the data. Generic priors have very low weights, allowing clusters to shift and scale with the data. Since SNP-specific priors are generated from a previous run, cluster information is informed by the samples in that previous dataset. Thus, the recommendation is that the weight that was observed in the dataset for a well performing probeset should be kept intact up to a maximum of 20. This cap prevents the priors from having too much influence on the position and size of the clusters in future genotyping runs. In general, the minimum value of weights is set to be equivalent to the generic weights unless the priors are for an agbio array. In these situations, the recommended minimum nObsMean is set to 5. A higher weight on the position of a cluster in the prior helps stabilize the position of the cluster during future genotyping runs, which helps ensure more consistent genotyping.

Threshold	Definition
Format	Default format is based on the batch imported into the tool. Human for human batches with more than 24 samples, and AgBio for all non-human batches. Each format has default values for weights, as listed in Thresholds.
Recommended probesets	Priors will be generated for probesets that are assigned to Recommended conversion types.
Recommended Conversion Types	Prior generation is limited to probesets in selected categories. The categories selected by default are based on the threshold settings that were used in the Axiom Analysis Suite Best Practices Workflow batch.
nObsMean	The number of observations for the position of a cluster in the data.
Max nObsMean	The maximum weight allowed for the nObsMean value in the generated priors file.
Min nObsMean	The minimum weight allowed for the nObsMean value in the generated priors file.
nObsVar	The number of observations for the variation (or size) of the cluster in the data.
Min NoObsVar	The minimum weight allowed for the nObsVar value in the generated priors file.
Max NoObsVar	The maximum weight allowed for the nObsVar value in the generated priors file.
Do not include low frequency het probesets (check box)	When checked, priors will not be assigned to probesets with low het frequency in the Input batch (detection of one to two hets).

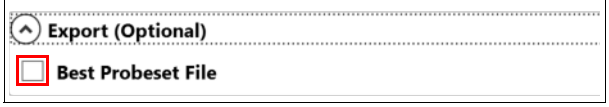
5. **[Do not include low frequency het probesets]** If this check box is checked, priors will not be generated for any low frequency probesets you may have uploaded into the tool.

Export options

The Best Probeset file resides in your batch folder. Use the **Export** pane (Figure 13) to add it to your export.

1. Click the **Export** button.
2. Click to check the **Best Probeset File** check box.

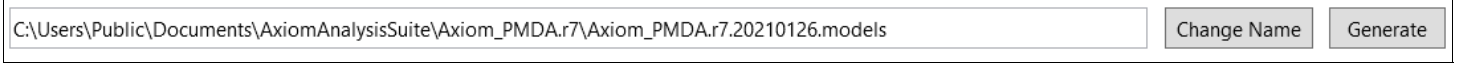
Figure 13 Export pane



Priors filename

By default, the priors filename is auto-generated using the array name, date, and models located in the Array package, as shown in Figure 14.

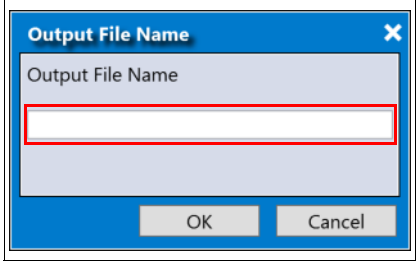
Figure 14 Priors filename pane



Changing the filename

1. If you want to change the auto-generated filename, click the Change Name button.
   A dialog box appears. (Figure 15)

Figure 15 Dialog box



2. Enter a name, then click **OK**.
   Your new filename is displayed.

Generating your output file

1. Click the Generate button.

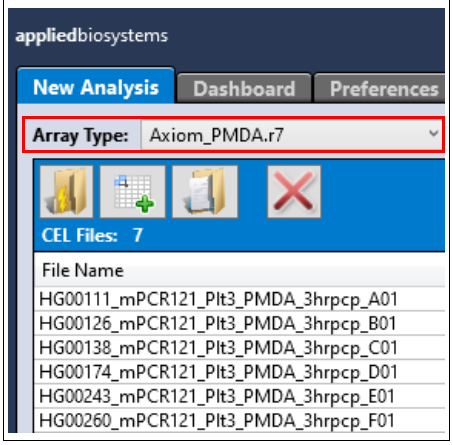
   A Please Wait window appears. After the priors are successfully generated, the word **Complete** appears in the lower left corner.

Loading a new priors file into AxAS

1. Launch the AxAS software.
2. Click on the **New Analysis** tab. (Figure 16)

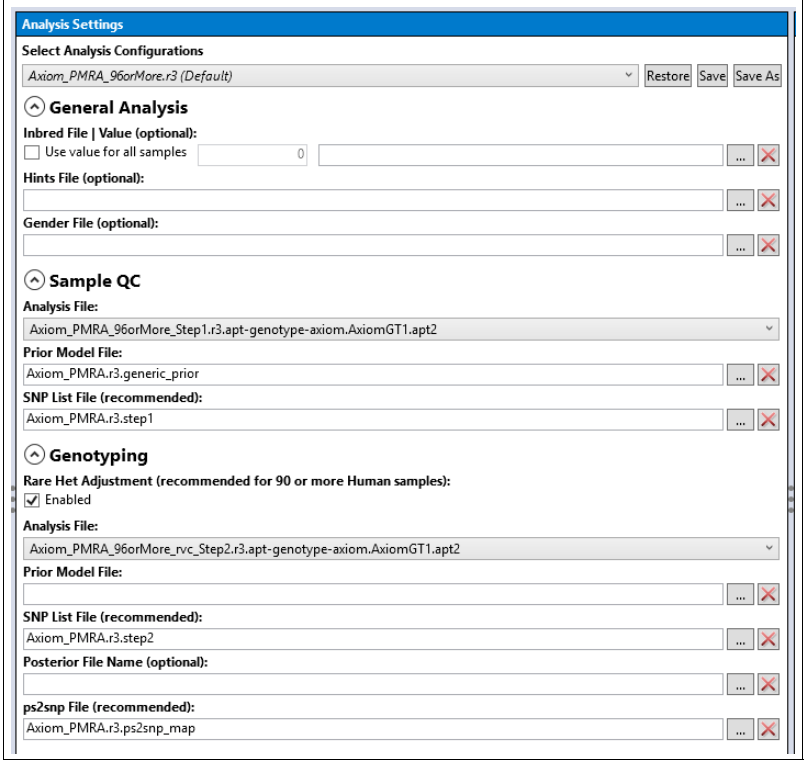
   Note: The array name is displayed in the **Array Type** field.

Figure 16 AxAS New Analysis tab



3. Click the **Workflow** drop-down to select the workflow you want to use.
4. From the Analysis Settings pane (Figure 17), click the **Sample QC** button to reveal the Sample QC file options.

Figure 17 AxAS Analysis Settings pane



5. Confirm the Generic Priors file is displayed in the **Prior Model File** field.
6. Click the **Genotyping** button to reveal the Genotyping file options.
7. Click the **Prior Model File** ... button.

   The Prior Model File window appears.
8. Click to highlight the newly generated priors file, then click **Open**.

   The new priors model file is displayed.
9. Click the Analysis Setting pane's Save As button.

   An Explorer window appears.
10. Enter a name, then click **OK**.

    The Analysis Configuration drop-down menu now contains your saved name.
11. Enter a name for your analysis, then click **Run**.

    After your analysis has successfully completed, it will reside in the Dashboard tab window where it can be opened for viewing.

IMPORTANT! For more feature and workflow information, see the **Axiom Analysis Suite User Guide** and the **Axiom Data Analysis Solution Guide**.

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Revision history: Pub No. 703455

Revision	Date	Description
1	February 2021	Initial release

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