Application Note AN-RS-044

利用 MIRA P 优化原材料识别和验证 (RMID)

Validation model transfer increases productivity

Using a verification model on multiple instruments expands a manufacturer's raw material identification/verification (RMID) capabilities by speeding up incoming inspection, imparting flexibility to an operation, or avoiding downtime.

In a scenario where several operators use multiple MIRA P systems at different locations, the ability of any operator to use any MIRA P to validate a new shipment streamlines operations and allows that shipment to be quickly released to production.

In most cases, a well-designed model with inherent sample variability can be built on one MIRA P and transferred to another. In some cases, variance must be added to a training set with a few additional samples. This Application Note describes how a model transfers from one MIRA P to another in order to scale MIRA P usage across an entire operation.

INTRODUCTION

Model building (including training and validation set samples, operating procedure (OP) settings, and necessary variance) has already been well-established for RMID with a unique MIRA P [1,2].

In summary, MIRA Cal P generates PCA-based (principal component analysis) models using Training Set data and Operating Set parameters to verify target substances. Ideally, a model can be created on one instrument («MIRA P 1»), downloaded onto a second instrument («MIRA P 2»), then validated on the second unit and used directly.

The model must be expanded if the initial transfer does not produce satisfactory p-values or does not pass validation. This involves **introducing variance** in the model and/or **optimizing model parameters** and/or ensuring **consistent usage by each operator** of the instrument.

MODEL TRANSFER

This Application Note details the:

1. transfer of a material verification model from one MIRA P to another MIRA P
2. validation of the success of the model transfer
3. expansion of the model using a transfer matrix, if necessary

Contact your local Metrohm Sales and/or Service Representative for the full MIRA P to MIRA P Transfer Protocol.

Parameter optimization and/or inclusio n of additional data that includes instrument variance and variance based on historical and current samples are both simple ways to expand a model.

Using an established model, new validation data is collected from both MIRA P units and added to the Training Set. Parameter optimization is recommended at this step. After this updated model is uploaded to the new MIRA P unit, it must be validated on the new unit.

VALIDATION

Validation of a model demonstrates that the model adequately assesses a material on a new instrument. In other words, validation data serves as a «diagnosis» of how the model performs on the new unit.

Validation is an assessment of a method using test samples:

- that are expected to PASS (positive samples). These are samples of the target material but are different than the samples used to build the Training Set.
- that are expected to FAIL (negative samples). These can either be dissimilar materials or similar yet different materials. This ensures the specificity of a model.

It is a simple task, requiring just a few minutes, to run a validation set. This will inform successive steps.

HOW MANY OPTIMIZATIONS ARE NEEDED?

A good way to assess the success of a transferred model is to look at p-value distributions of positive and negative Validation Set samples. This is a good measure of a model's **robustness**—its ability to correctly assess new data, not just the data it was trained on. For example, **Figure 1** contains Validation Set results for sodium bicarbonate on the receiving MIRA P device (MIRA P 2).

Initial Validation results for sodium bicarbonate show all the characteristics of good validation results (**Figure 1a**).
Red bars indicate that negative validation samples are failing appropriately, and positive samples are also passing with high p-values.

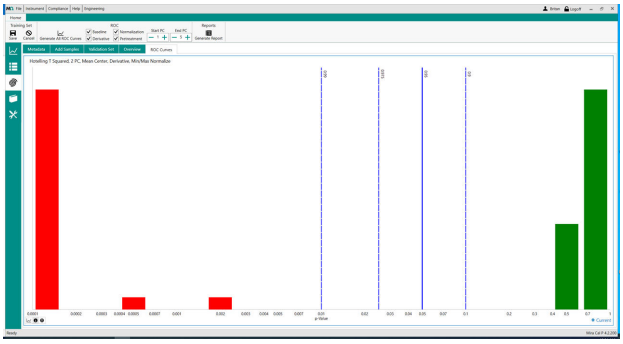


Figure 1a. Validation results for sodium bicarbonate on MIRA P: the original model.

After transfer to MIRA P 2 (**Figure 1b**), p-values for negative and positive samples show greater variance, but all are passing/failing appropriately.
Ultimately, this is a good example of a model that was transferred and used immediately.

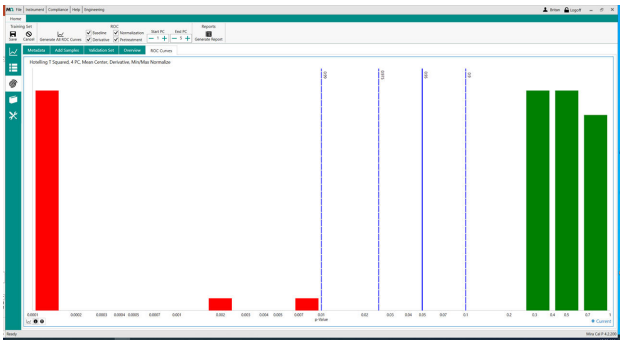


Figure 1b. Validation results for sodium bicarbonate on MIRA P: the model after transfer to another unit.

Lactose fluoresces with 785 nm Raman, but a well-built model can accommodate such fluorescence. This is a good test of the model transfer capability.
The lactose model transfers easily, requiring only parameter optimization in MIRA Cal P and addition of a small number of scans from the new instrument to the training set (**Figure 2**).

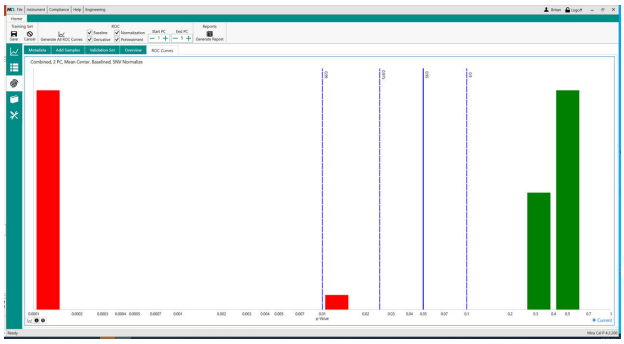


Figure 2a. Validation results for lactose on MIRA P: the original model

P-values exhibited slightly more variance on the new instrument (**Figure 2b**), but the model was robust.

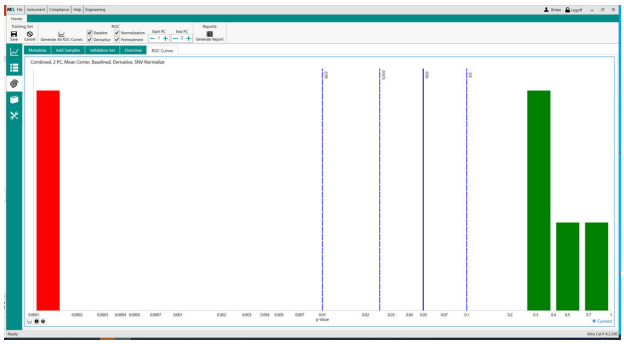


Figure 2b. Validation results for lactose on MIRA P: the model after transfer and parameter optimization.

Microcrystalline cellulose (MCC) is a challenging sample for 785 nm Raman, as it is very fluorescent. This can be seen in the wider distribution of validation set p-values in the original model (**Figure 3a**).
Thus, it was not expected for the original model to transfer without the Transfer Matrix.

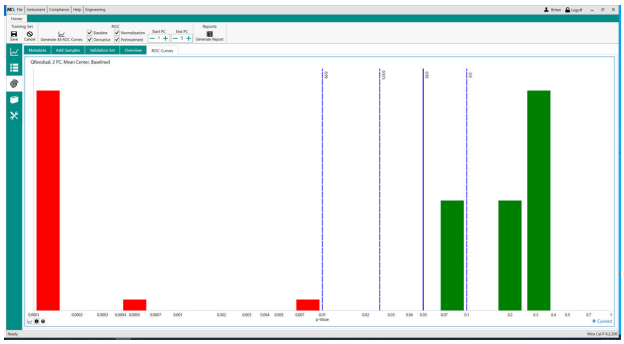


Figure 3a. Validation results for microcrystalline cellulose (MCC) on MIRA P: the original model

Ultimately, the optimization of parameters and utilization of the Transfer Matrix provided a robust model that could be used on a second MIRA P instrument and with a smaller spread of p-values.

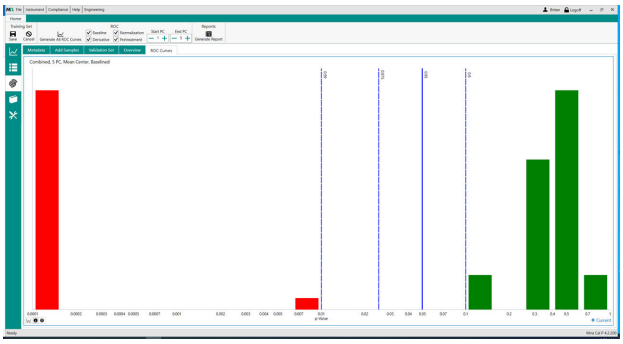


Figure 3b. Validation results for microcrystalline cellulose (MCC) on MIRA P: the model after parameter optimization and Transfer Matrix.

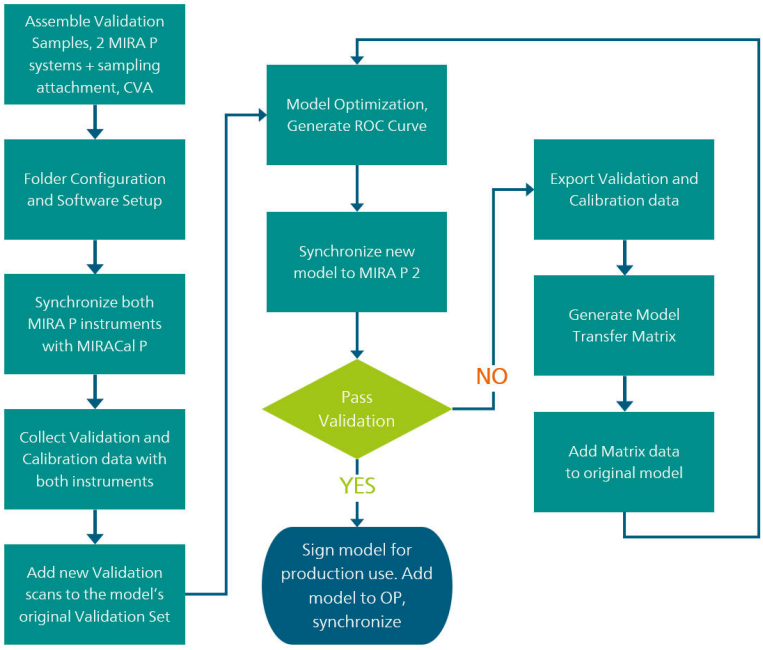
COMPLIANCE

Compliance with 21 CFR Part 11 requires document control at the highest level. Specifically, all model metadata is preserved, ensuring traceability after model transfer. The manufacturer-supported means for this are simple: MIRA P Model Transfer Protocol includes a sign-off sheet to record and track data from MIRA Cal P export, through the transfer matrix, and import back into MIRA Cal P.

CONCLUSION

The benefits of using multiple MIRA P devices for raw material verification include smoother operations and faster turnaround of products. This Application Note is intended to guide users through model transfer and enable the deployment of multiple MIRA P instruments.

From tips for the simplest transfer to tools for more challenging tasks, we want you to be confident in taking your inspection with MIRA P to the next level. This flowchart is a quick reference for the basic flow of operations during MIRA P to MIRA P transfer.



REFERENCES

1. Metrohm AG. Simplified RMID Model Building – Mira Cal P and ModelExpert; AN-RS-031; Metrohm AG: Herisau, Switzerland, 2021.
2. Gelwicks, M. J. Real World Raman: Simplifying Incoming Raw Material Inspection. *Analyze This – The Metrohm Blog*.

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CONFIGURATION

MIRA P Basic

瑞士万通快速拉曼分析仪 (MIRA) P 是一款性能强大的便携式拉曼光谱仪,可用于各种材料类型的快速无损测定和验证,例如药物有效成分和辅助材料。尽管 MIRA P 体积很小,但是其采用了坚固的设计,并且具 ORS特色技术。MIRA P 符合 FDA 21 CFR 第 11 部分的准则要求。

使用 MIRA P Basic-Paket,用户可以根据其需求对 MIRA P 进行调整。MIRA Basic-Paket 是一款入门级套装,其包含了运行 MIRA DS 所需的基本组件。

基本套餐包含了 MIRA 校正/验证配件、USP 功能库和用来在瓶子或袋子里进行分析的 LWD 附件。激光防护等级 3B 的使用。

MIRA P Advanced

瑞士万通快速拉曼分析仪 (MIRA) P 是一款性能强大的手持式拉曼光谱仪,可用于各种材料的快速无损测定和验证,例如药物有效成分和赋形剂。MIRA P 小而坚固,配备了瑞士万通的ORS技术。MIRA P 符合 FDA 联邦法规 21 章第 11 款的规定

。Advanced Package 包含一个附加透镜,可用它直接分析材料或者在材料容器中分析(3b 级激光器),还有一个小管支架套筒用于分析玻璃小管中的样本(1 级激光器)。

MIRA P Flex

使用 MIRA P Flex Package,用户可以根据其需求对 MIRA P 进行调整。Flex Package 包括了用来运行 MIRA P 的所有基本组件,无需采样用附件。运行需要一个采样用附件。MIRA P Flex Package 包括了 USP 功能库,用于校正/验证的附件和一根 USB 电缆。以 3B 级投入使用。