LEARNINGS FROM MODELING OF CONTINUOUS MANUFACTURING OF EXCIPIENTS

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PQRI Workshop:
Managing Excipient and API Impact on Continuous Manufacturing
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OUTLINE

Modeling Approaches

Examples with METHOCEL™ models

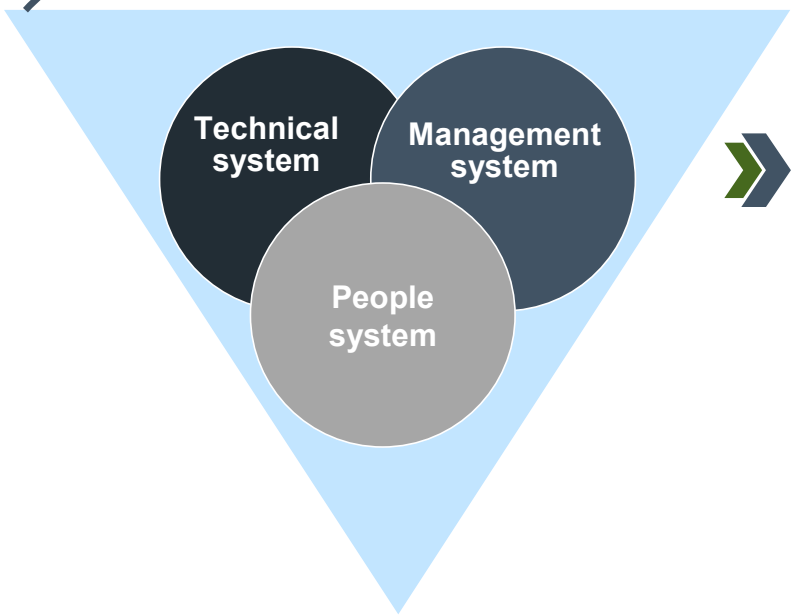
Learnings

IFF SOUGHT MANUFACTURING EXCELLENCE THROUGH NEW DIGITAL TECHNOLOGIES

Productivity improvement

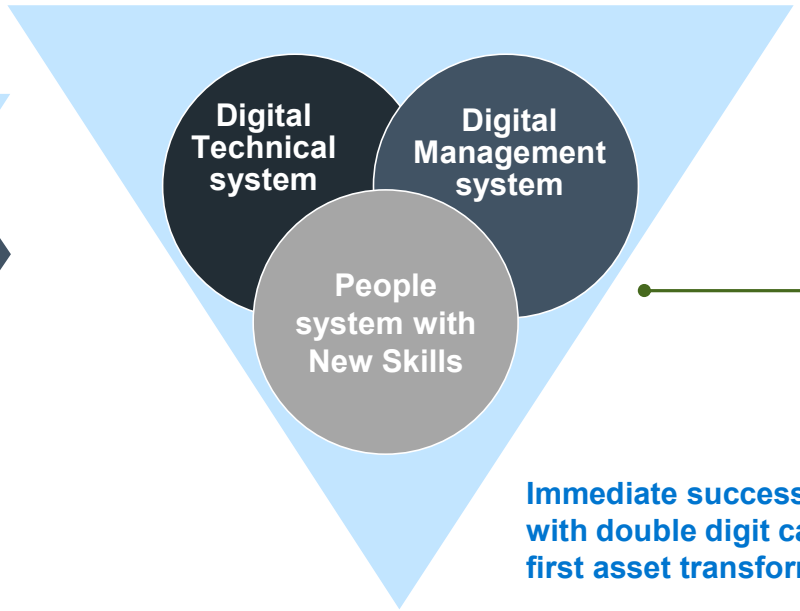
Past **ANALOG functional transformation**

Manufacturing excellence



Future **DIGITALLY ENABLED functional transformation**

Digitally enabled manufacturing excellence



Core technical enablers include:

- New digital and analytics capabilities
- Technology and data infrastructure
- **Process modeling**

Immediate success stories experienced, with double digit capacity increase in first asset transformed

A MODEL is a simplified representation of a system using mathematical terms. Models can enhance scientific understanding and possibly predict the behavior of a system under a set of conditions.

– Points to consider for Q8/Q9/Q10 guidelines

Benefits

Improved throughput

Cost savings

Consistent quality

Process monitoring and control

Univariate/Multivariate Statistical Models

- Often used to detect special cause variability in Batch processing

Feed-Forward/Feedback

- Important for CM processes (like adjusting parameters in downstream process based on upstream results)

TYPES OF MODELS

Mechanistic

- Theory, causation
- Complex equations and not widely used in industrial applications

Empirical

- Observation, correlation
- “Simple” statistical equations and frequently used in process optimization/scale-up

WHO BUILDS THE MODELS?

Pros and Cons Analysis

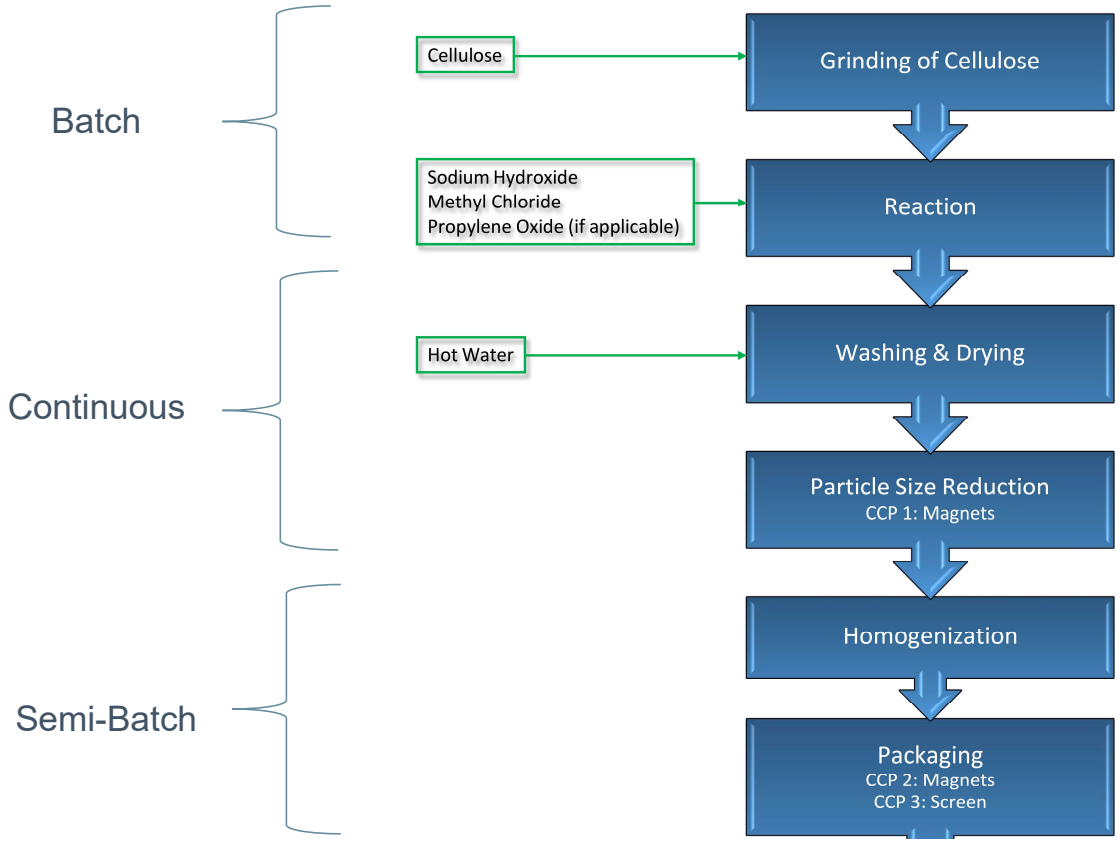
Third Party

- Experienced in model building and validation
- May not fully understand the process
- Expensive
- Likely needed for model updates in the future
- Large personnel available to build models

In House

- May not have extensive modeling experience
- Experienced in process
- May be more cost effective
- Updates to models would be faster with in-house expertise
- Need to carve out personnel time or add resources

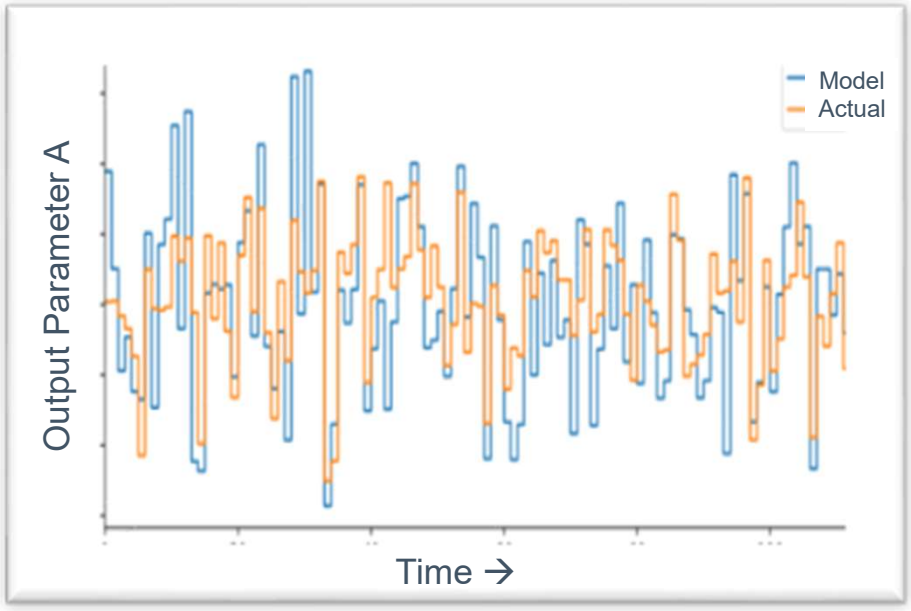
METHOCEL™ EXAMPLE OF MODEL IMPLEMENTATION



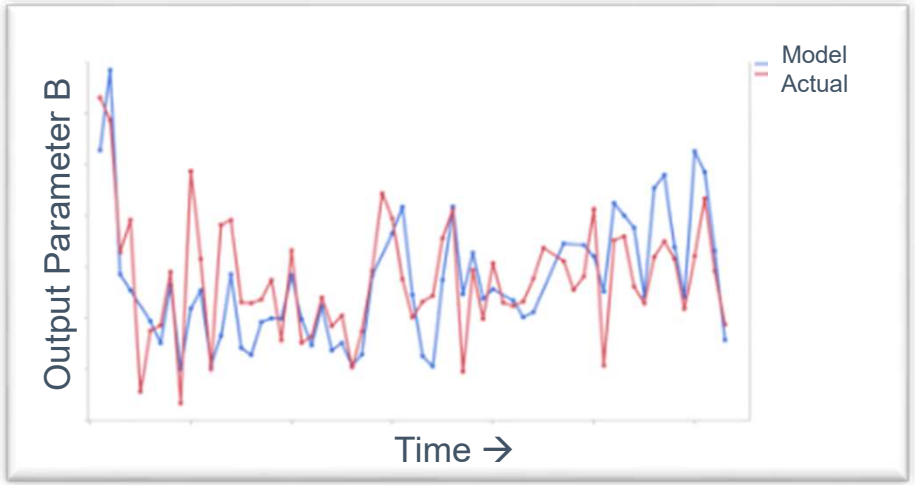
NOT EVERY MODEL IS WORTH IMPLEMENTING

~1 billion data points taken from the process over ~3 years used to develop models
Implementation of one model resulted in over $1.5 million capacity release in the first month

Poor Model – Not used

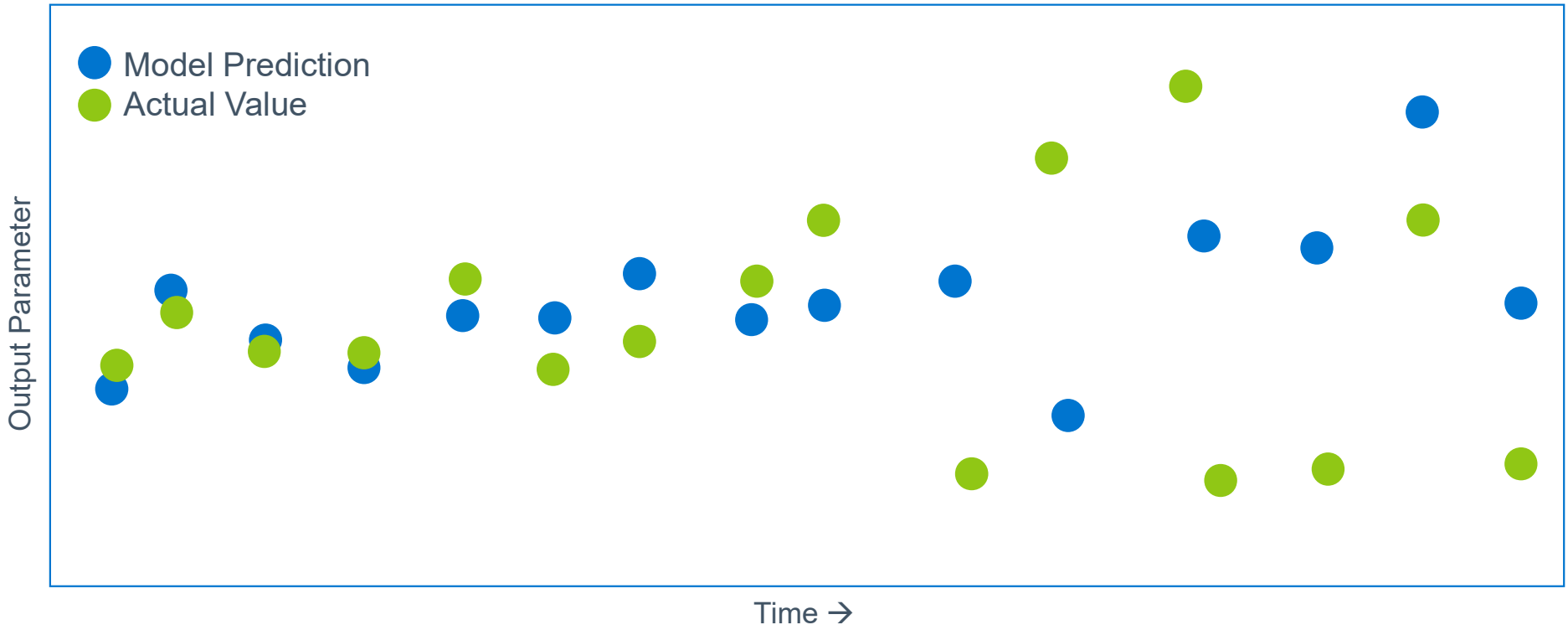


Good Model – implemented

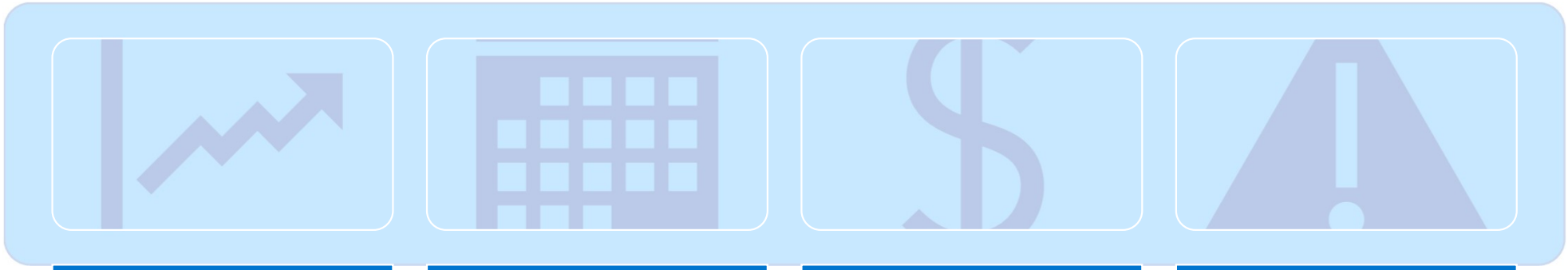


THE MODEL WORKS... UNTIL IT DOESN'T

Processes in place to catch divergence
Models may need retraining



ADVICE BASED ON OUR EXPERIENCES



Working models can improve throughput!

→ Advantageous to use functional models

Conditions under which the data were collected significantly impact the model

→ Attempt to use data that is collected over many campaigns, different times of year, etc. Retraining model periodically is needed.

Don't want to pay third party every time an update is needed to model

→ Consider modeling in house with dedicated digital leaders responsible for updates/retraining of models.

Monitoring critical to quality/success parameters is key to detect when models are starting to fail

→ Engineering is still critical to success of process - know when to override model.

SUMMARY

Modeling can be a powerful tool

- Quality control
- Cost savings
- Improved throughput

Understand model limitations

- Start with good data
- Choose how to best maintain models that fit your needs

RECOGNITION

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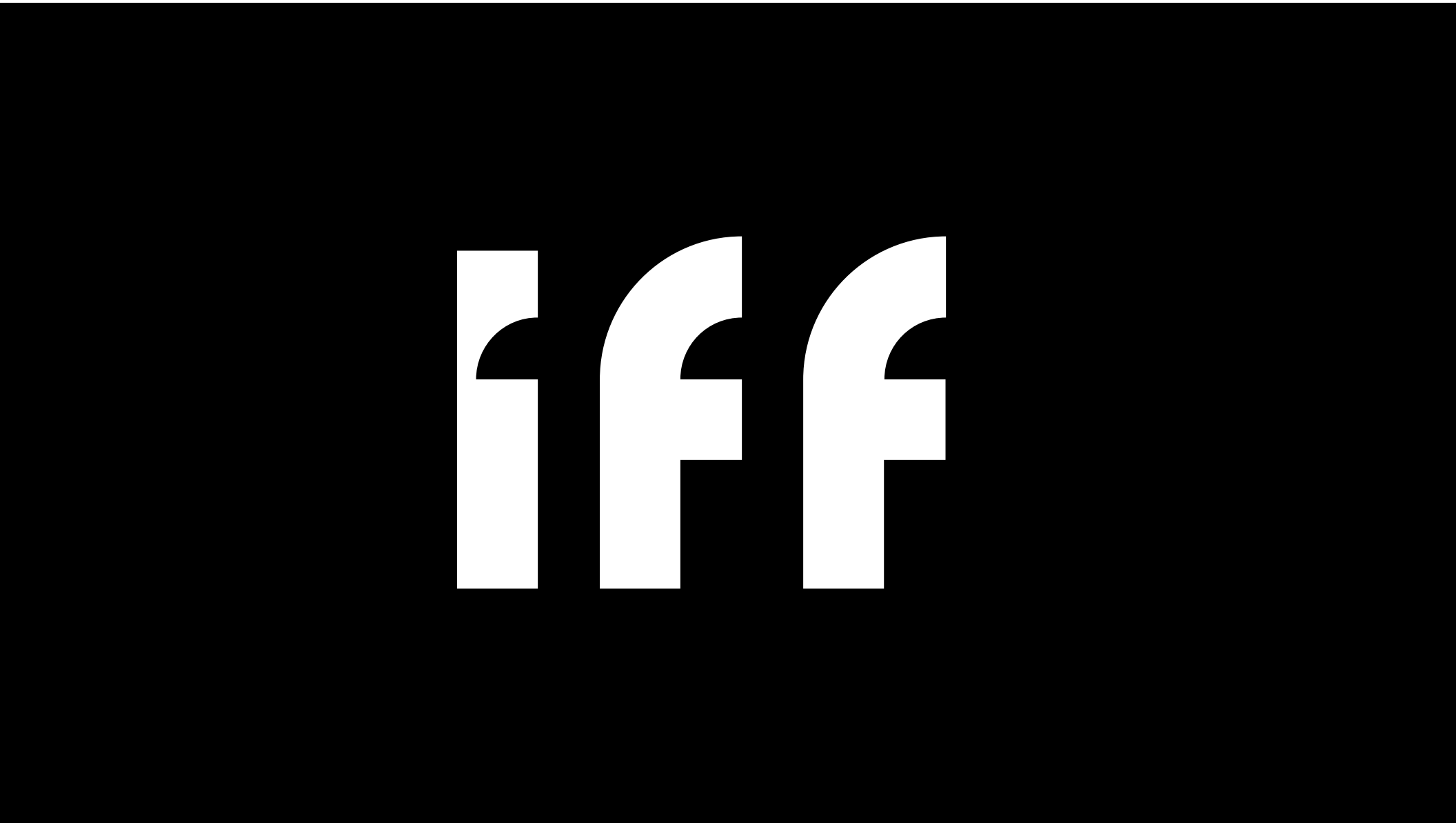
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