# PrepEngine

## METHOD DEVELOPMENT


DISTEK®
CREATING A STIR™

PREPENGINE

# METHOD DEVELOPMENT

There are two PrepEngine operational parameters that need to be optimized during method development: Rotation Speed (RPM) and Run Time.

## CHOOSING THE ROTATIONAL SPEED

Lower rotation speeds (RPM) produce less friction, heat and noise. They require less motor torque which results in less variation in motor speed and wear on the PrepEngine. Higher speeds are available for products that require them but should be used for the minimal time required for successful extraction.

The ideal rotational speed is chosen to optimize the time the product is in contact with the PrepTube blade. Lower speeds increase the contact time with the blade but may not impart enough force to disintegrate and mix it. Higher speeds increase the contact pressure applied by the blade to product. However, higher speeds may also reduce the overall time the product is in contact with the blade, thus decreasing the overall extraction efficiency and actually increasing the required run time.

Typically the optimum PrepEngine Rotation Speed is around 3000 RPM.

## CHOOSING THE RUN TIME

The PrepEngine run time is chosen to guarantee complete extraction from the product. Extraction time is controlled by one of two parameters: Disintegration times and solubility times.

**DISINTEGRATION LIMITED PRODUCTS:** Often, extraction time is strictly limited by the time it takes to disintegrate the product. Once exposed to the media, the solute of interest effectively immediately goes into solution. In these cases, the run time is selected to match the disintegration time. A typical example of this type of method would be to run at 3000 RPM for 5 minutes.

**SOLUBILITY LIMITED PRODUCTS:** In products where the solute exhibits low solubility in the media, it may be necessary to add a mixing stage after the product has been disintegrated. In this type of method, the product is disintegrated into suitably sized particles during a disintegration stage. Once the product is sufficiently disintegrated, the mixing stage of the method is run where the particles continue to be mixed at a reduced speed until all the solute is extracted into the media solution. Here a typical example would be to again run at 3000 RPM for 5 minutes, fully disintegrating the product, followed by 1500 RPM for 10 minutes, fully extracting the solute.

To get started defining your method and selecting the RPM and Run Times follow the flow chart on the following page:

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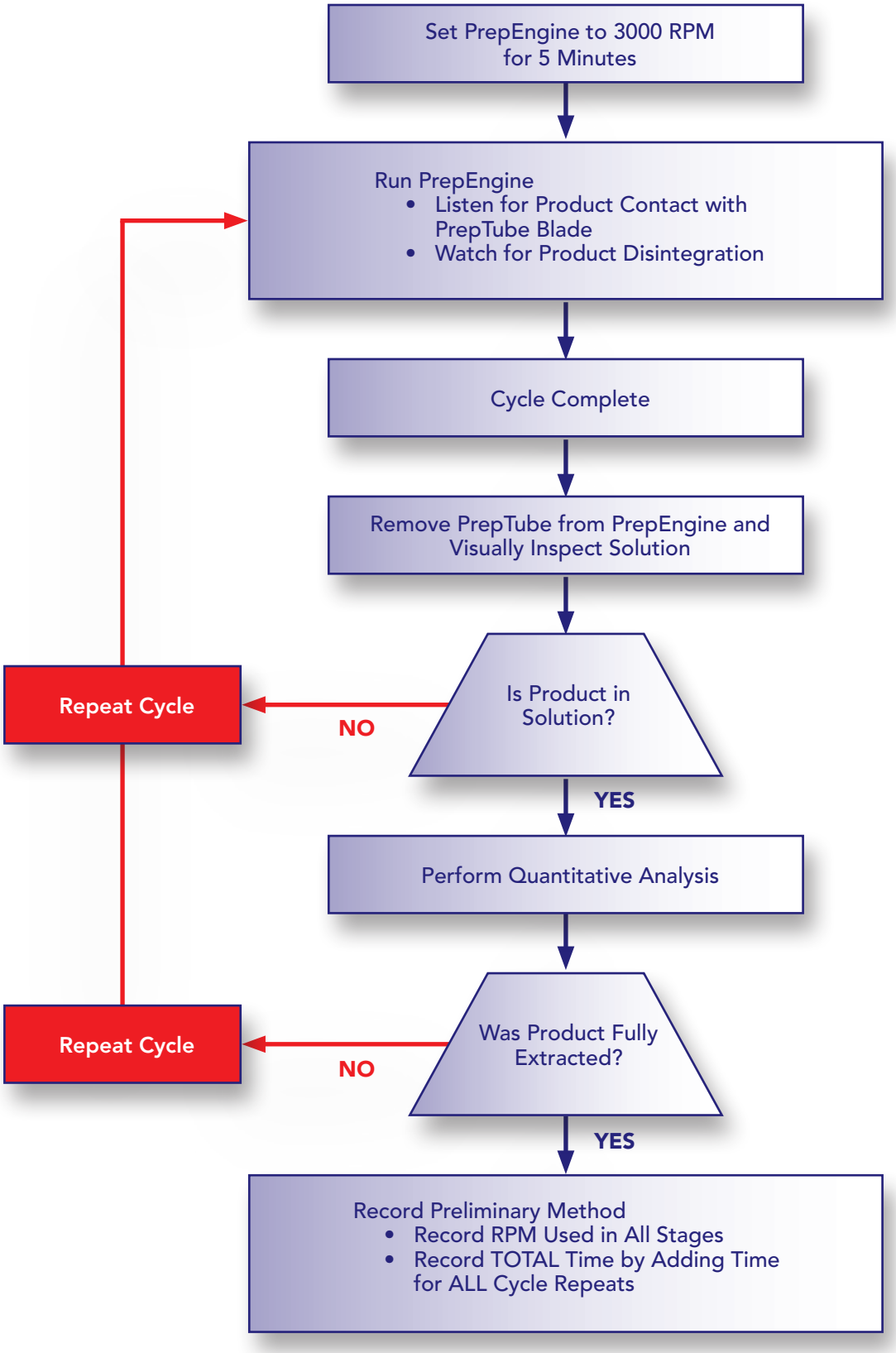
## PRELIMINARY METHOD DEVELOPMENT



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## METHOD OPTIMIZATION AND FINALIZATION

Based on the information gathered above one can start developing an optimized method.

If the product disintegrated and went into solution in 10 minutes or less, the starting method is already suitably optimized. Skip the next section and go to the **METHOD SAFETY FACTOR SETTING** section.

If the product took 15 minutes or longer to disintegrate:

1. Start again. Increase the RPM to 4000 and try it again.
2. If it still takes over 15 minutes, start again. Try 5000 RPM.
3. If it still has not fully disintegrated after 15 minutes at 5000 RPM, start again. Go back to 4000 RPM and keep adding 5 minute cycles until the product disintegrates.
4. If it takes longer than 30 minutes, start again. Go back to 5000 RPM and run it until it disintegrates.

Now that the run time and RPM to disintegrate the product have been determined, perform a quantitative analysis and determine if the product was fully extracted. If it was, skip the next section and go to the **METHOD SAFETY FACTOR SETTING** section.

If the product was not fully extracted, add a mixing stage:

1. Start with 1500 RPM and repeat sampling and analysis every 5 minutes to confirm full extraction. Remember to correct for the loss of volume effects with each sample removed.
2. If after 15 minutes the product is not fully extracted, start again. Run the disintegration stage as before, then run 5 minute mixing stages, but now at 3000 RPM.
3. If after 15 minutes the product is not fully extracted, start again. Run the disintegration stage as before, then run 5 minute mixing stages, but now at 5000 RPM.
4. If it takes longer than 15 minutes, go back to 3000 RPM and run it until it disintegrates.
5. If it takes longer than 30 minutes, go back to 5000 RPM and run it until it disintegrates.

At this point the optimized method parameters are set.

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# METHOD OPTIMIZATION AND FINALIZATION

## METHOD SAFETY FACTOR SETTING

The Method Safety Factor is defined as the ratio of Final Method run time divided by the Minimum Method run time. The Method Safety Factor is intended to allow for natural process variation, providing a Final Method that guarantees consistent extraction.

For most products this turns out to be a factor of 1.5 to 3. For example, if the run time suggest by the method optimization is determined to be 3 minutes, the Final Method may be set for 6 minutes based on a Method Safety Factor of 2.

## PREPTUBE USAGE

Each step in the method development process should be performed with a new, clean PrepTube. The number of times a PrepTube can be reused should then be determined by repeating the flow chart test and verifying reproducible disintegration and extraction after each use until the number of repetitions is reached when a run no longer results in complete extraction. That number should again be divided by a safety margin and set as the limit of the number of times a PrepTube can be reused. In no case should a PrepTube be used for more than a total of (5) runs of a duration of 10 minutes. The use of some solvents may reduce the maximum number of runs to 2 - 3.

With some products, the cost and effort of cleaning PrepTubes after each run or concern about carryover may justify the single use of the PrepTubes. Also note that if required, sterilized PrepTubes are available.

## PREPTUBE FILLING

PrepTube efficiency is increased when the liquid level is low enough to leave some headspace between the liquid surface and the cap. PrepTubes are also not intended to run without liquid and should not be run dry in normal operation.



| REPLACEMENT PREPTUBES | 50 ML | 250 ML | 500 ML |
|---|---|---|---|
| **PrepTube & Cap w/ Hole** | TS-05-000380 | TS-05-000340 | TS-05-000360 |
| **PrepTube & Cap w/o Hole** | TS-05-000381 | TS-05-000341 | TS-05-000361 |
| **PrepTube & Cap w/ Hole (Amber)** | TS-05-000384 | TS-05-000344 | TS-05-000364 |
| **PrepTube & Cap w/o Hole (Amber)** | TS-05-000385 | TS-05-000345 | TS-05-000365 |
| **PrepTube Cap Only w/ Hole** | TS-72-000016 | TS-72-O00002 | TS-72-O00012 |
| **PrepTube Cap Only w/o Hole** | TS-72-000015 | TS-72-O00001 | TS-72-O00011 |

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