

# NRobe: A New, Simple, Flexible Technology for Oral Controlled Release

## Introduction

NRobe is a solid oral dosage form wherein the drug-loaded fill is lightly compressed between two dry, preformed, non-gelatin films and then sealed to provide a non-friable coated dose form.

The NRobe process overview is shown in Figure 1.

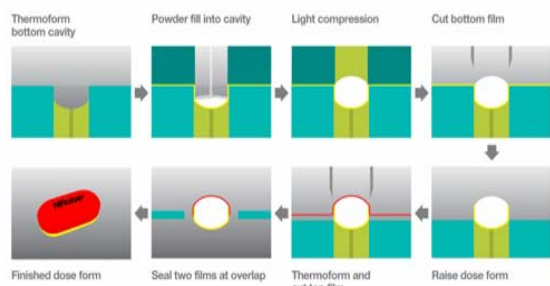


Figure 1 - NRobe process steps

NRobe offers benefits for a variety of applications; the following information relates to oral controlled release applications.

NRobe enables flexibility in formulating oral controlled release products:

1. Dose form robustness is ensured by film rather than tensile strength of compact, enabling lower excipient burden, optimized drug release performance, and a simplified formulation approach.
2. NRobe allows compression-sensitive materials such as coated pellets to be enrobed thereby retaining their integrity.
3. Matrix drug release can be modulated by a combination of formulation and light compaction.

Figure 2 depicts (A) the release of theophylline from free sustained release (SR) pellets coated with Eudragit® (NE30D + Talc 1:2 ratio) compared to two formulated dosage forms containing the same SR pellets: (B) a tablet made from a 1.5:1 ratio of Avicel® PH200 microcrystalline cellulose: pellets blend compressed at 20 kN force, and (C) an NRobe dose form containing three layers in which the coated pellets were sandwiched between an upper and lower layer of Avicel PH200 (1-1.5:1 ratio) compacted at 0.5kN, and then enrobed with a fast-dissolving HPMC-based film.

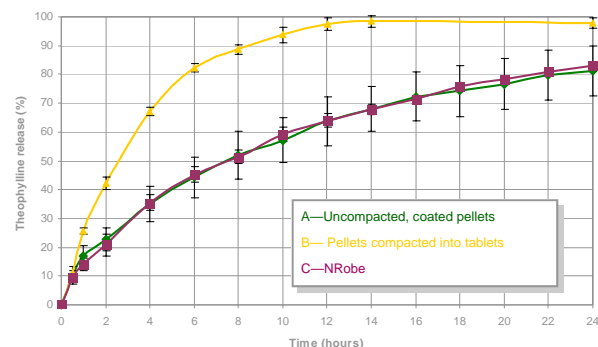


Figure 2—Enrobing compression-sensitive control release materials

As Figure 2 indicates, coated pellets within the NRobe dose form have a drug release profile that is statistically (t-test) identical to the uncompacted coated pellets, while the SR pellets compacted into tablets showed a significantly faster release profile than that of the uncompacted pellets.

Image analysis showed significant damage to the coated pellets compacted into tablets, whereas a minimal number of pellets were damaged in the NRobe dose forms.

Figure 3 shows drug release profiles of two NRobe matrix formulations: (A) NRobes manufactured with a blend of theophylline (95%) and HPMC K100M (5%) in which the powder fill was lightly compacted, resulting in a low density (0.78 g/ml); and (B) two-layer NRobes, with the first layer

comprised of a blend of theophylline (98%) and Ac-Di-Sol® (2%), and the second layer comprised of a blend of theophylline (60%) and HPMC K4M (40%); the powder fill was lightly compacted resulting in a total fill density of 0.97 g/ml.

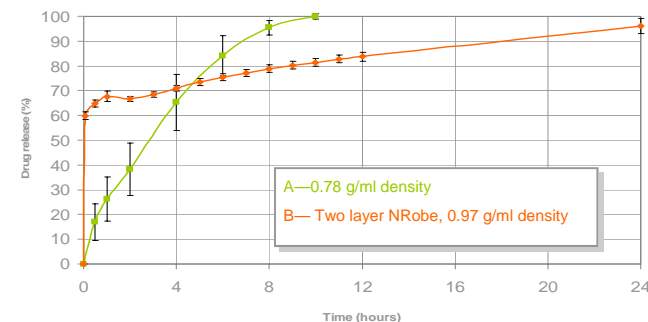


Figure 3 – Enrobing SR matrix materials

Figure 3 illustrates the potential formulation versatility of NRobe and process simplicity of high dose activities for controlled release. Even at only 5% matrix former content, sustained drug release was achieved over a 10-hour period. Drug release from two-layer NRobe showed an immediate release of 65% of the drug in 30 minutes, followed by a prolonged release of the remaining drug over 24 hours. This formulation approach eliminates the need for pore formers or additional excipients (e.g., dry binders). Thus NRobe enabled a tailored release of theophylline from a dose form of minimum size.

## Conclusion

- NRobe technology offers a flexible, simple solution to formulation of oral controlled release dose forms.
- Inclusion of conventional matrix formers such as HPMC or compression-sensitive components such as coated pellets are both possible using the same process technology.
- Other NRobe applications include large dose, fixed combination and fast release products.

FMC Corporation conducts NRobe  
Technical development at :  
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Laboratory and pilot-scale production  
capabilities are available

Full-scale production equipment  
is in progress

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## NRobe™ Technology:



A New, Simple, Flexible  
Technology for Oral  
Controlled Release

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