



Introduction to the Novel Alginate Capsules Technology



Introduction

- > **Background to FMC Magenta and Alginate Capsules**
- > **The Novel Alginate Capsules Technology Overview**
- > **Product attributes**
- > **Development Capability and Scale-Up**

FMC Magenta Oral Dose Design Technology Platforms

NRobe

Powder enrobing
system

Alternative to film-
coated or gel-
dipped tablets and
hard capsules



Biopolymer-based soft capsules

Novel process

Non-reflux
applications

Unique product
and process attributes



Conventional process

Minor adaptation to
existing process

Non-animal system
with enhanced
organoleptics



Novel Alginate Capsules Technology

Overview

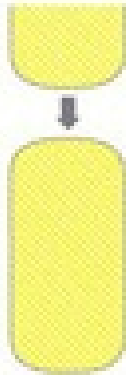


What is the Novel Alginate Capsule Technology?

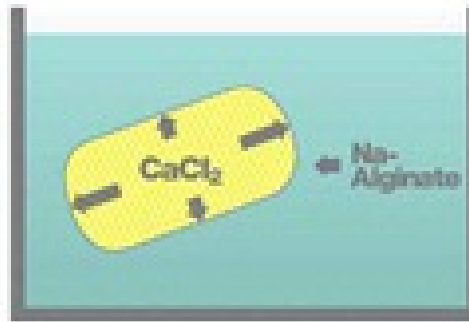
- > **Unique Novel Enteric Non Gelatin Oral Dose Form Technology**
 - ...Presented as a 'softgel'
 - ...Particularly suitable for large dose actives, acid-sensitive actives or actives generating gastric irritation, oxygen sensitive actives
- > **Specific and Unique appearance and attributes which are beneficial in anti counterfeiting and marketing**
- > **Offers potential manufacturing benefits**
 - ...Continuous processing and flexibility of batch size
 - ...Reduced number of process steps compared to conventional alternatives
- > **Being developed around the Principles of P.A.T and I.C.H Q8, Q9 (QbD risk reduction management approach)**

Alginate Capsules Process Overview

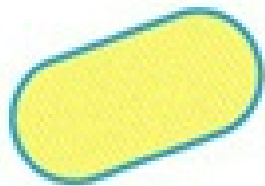
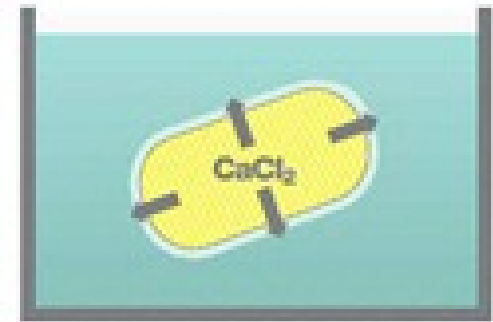
Extrude fragments of emulsion



Introduce emulsion fragment into alginate bath



CaCl₂ diffuses through the emulsion and reacts with sodium alginate at the interface

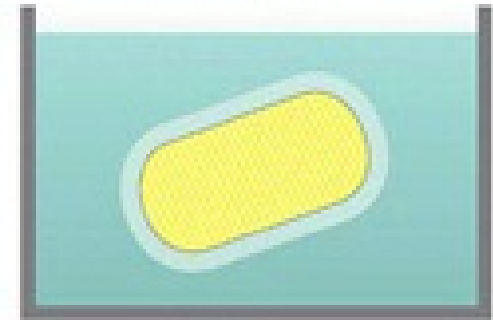


Dry capsule with transparent shell and transparent core

Washing and drying



The capsule wall is formed with the same thickness all around



Alginate Capsules Basic Formulation

> Emulsion

...oil

...CaCl₂•2H₂O

...emulsifier

...water

> Gelling bath

...Alginate

> Washing

...Water

> Plasticizer

> Regulatory evaluation of shell components:

...All of the excipients used in the algicaps shell are established excipients for use in oral dose forms at levels used.

Active

Gelling salt

Gelling agent



Product / technology benefits

- > **Animal free**
- > **Inherently enteric (Alginate), non reflux**
- > **Seamless technology: unique dose form elegance, tamper-evidence, anticounterfeiting**
- > **Thinner Shell and no air space: increased API content**
- > **Non-sticky**
- > **Thermostable**
- > **Good oxygen barrier**
- > **No need for supply of pre-made shells and no change parts for dose form size changes**
- > **Excellent dose uniformity (1-3 % RSD)**
- > **IP protection**



IP Estate

> 2 patent applications filed

- ...“Polysaccharide capsules and method of preparation”

- ...Filed April 4th, 2002

- ...EPO granted

- ...US examination expected within a year

- ...“Method and apparatus for for the preparation of capsules”

- ...Filed March 3rd, 2006

Novel Alginate Capsules Technology

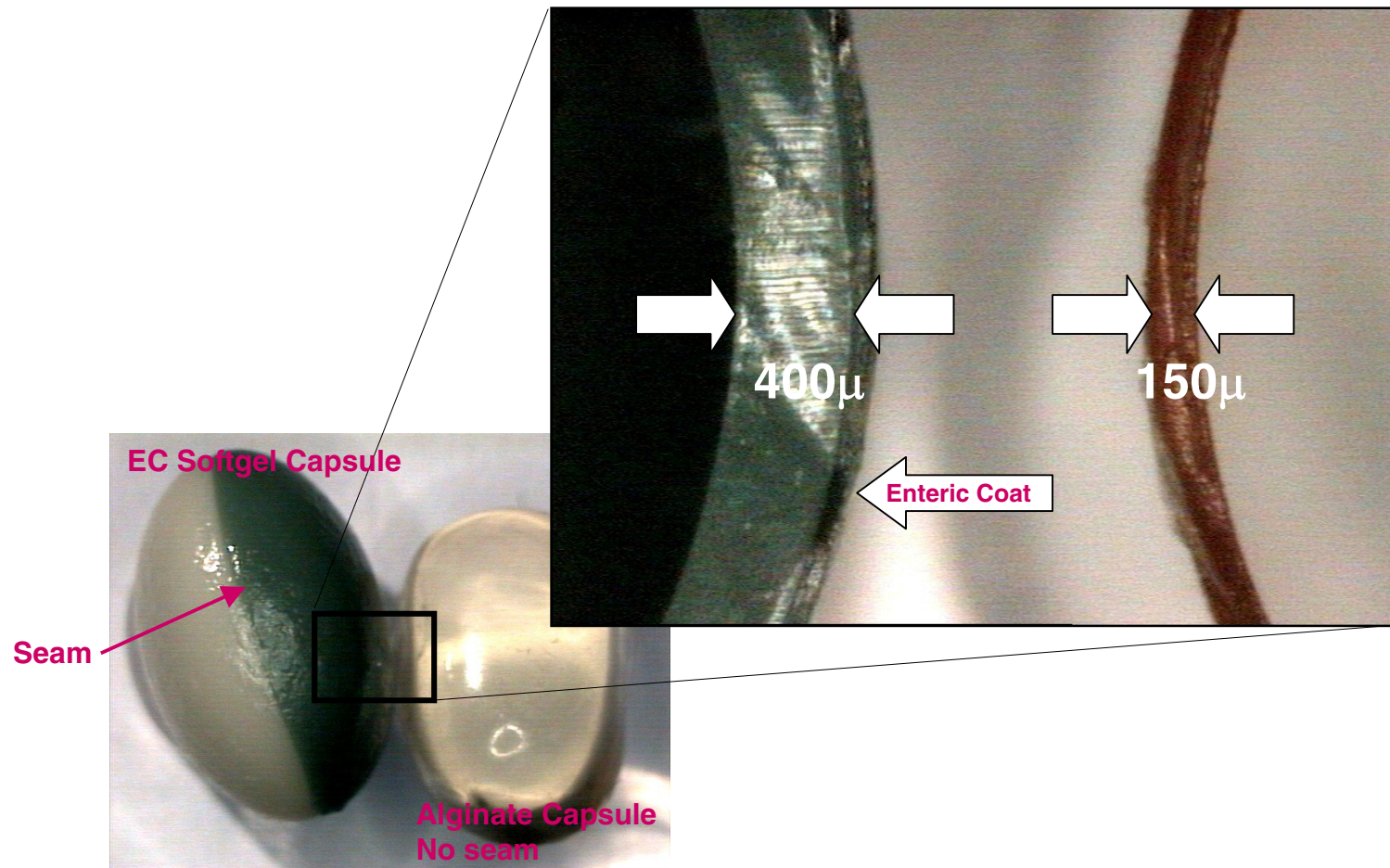
Product attributes



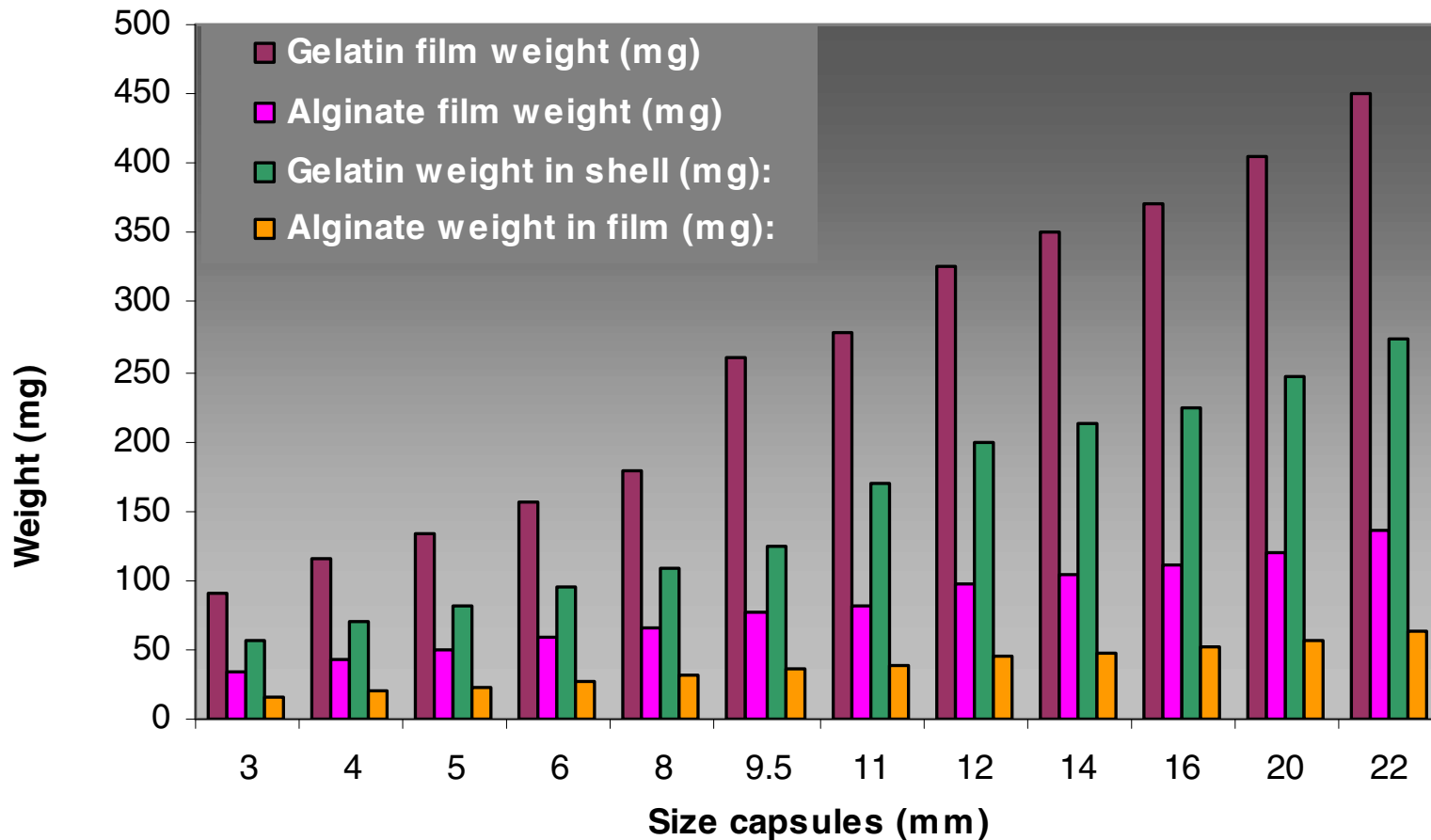
Alginate Capsules - Film thickness

- > **Thinner films than conventional soft capsules, in the range of hard capsules**
 - ...100-150 micron after drying
 - ...Low film thickness variations
 - ...Conventional seam variations avoided
 - ...Smaller capsules
 - ...Easier to swallow
 - ...More product per capsule
 - ...Film thickness determined by formulation and process conditions
 - ...Amount of Ca^{2+} used
 - ...Amount of alginate used
 - ...Gelling temperature
 - ...Gelling time

Alginate Capsules - Film thickness (Cont'd)



Alginate Capsules – Minimal Film Weight compared with conventional softgels



Novel Alginate Capsules Technology Equipment and Scale - up

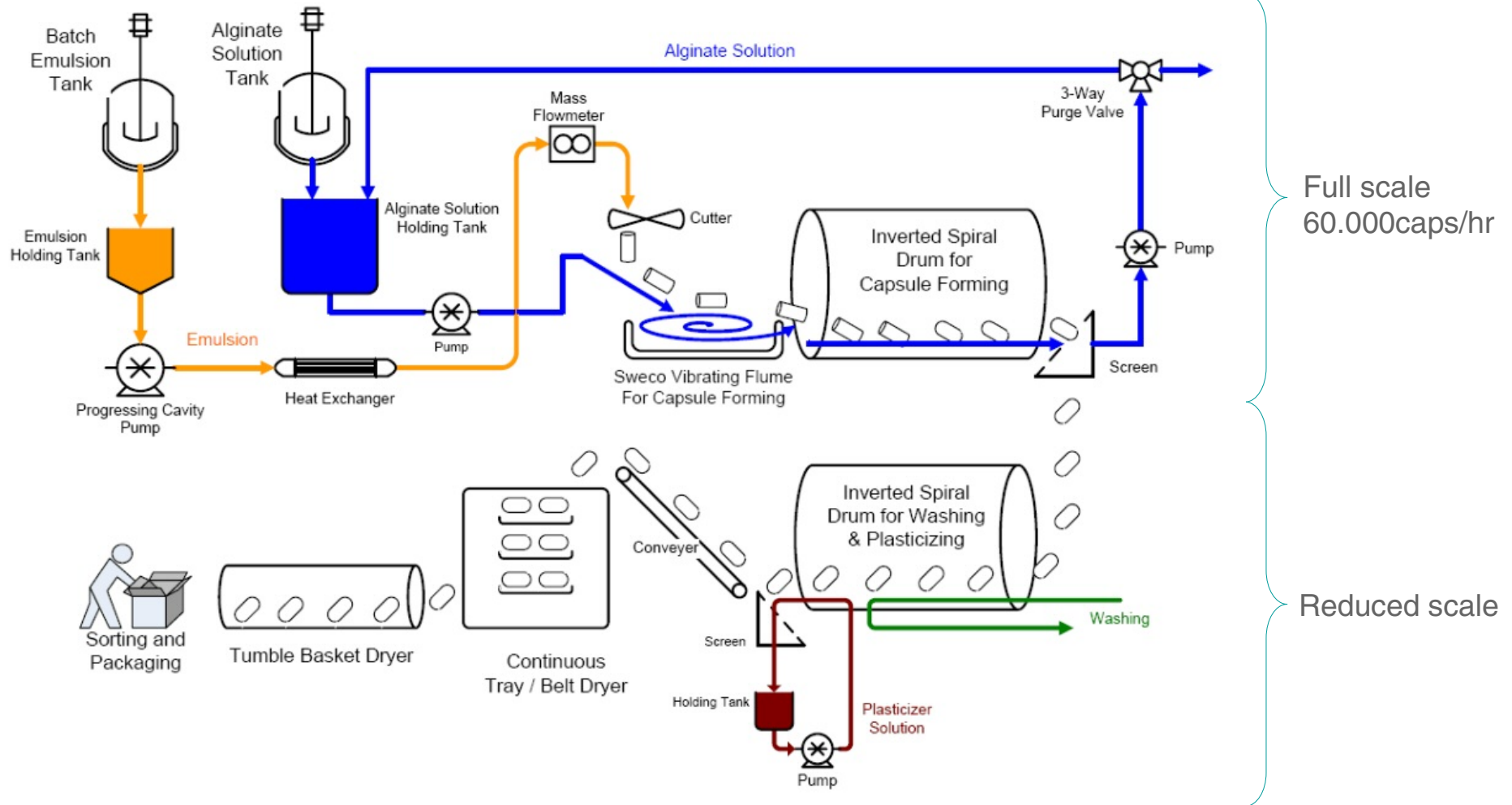


Alginate Capsules - Capability at Lab-Scale

- > **Laboratory equipment based in Sandvika, Norway**
- > **Semi automated equipment**
- > **Good for assessing initial feasibility**
 - ... Allows assessment of process simplicity for specific active formulation
 - ... Final elegance of dose forms produced with target active dose
 - ... Ability to perform Oxygen-controlled runs
 - ... Samples for disintegration, stability, pre-clinical studies, marketing assessment
- > **Batch size: 2000-3000 capsules**
- > **Usual starting point for customer collaboration – charged according to resource/time necessary to produce samples/scope of study**

Alginate Capsules - Scale Up

Current process flow diagram – Rockland, US



Alginate Capsules - Scale Up (Cont'd)

- > **Current scaled-up process: proof of concept, non-GMP (60k/hr for nutraceutical market)**
- > **Commercial production scaled up in the VMS market.**
- > **Engineering house engaged to assess current process for pharmaceutical compliance**
 - ...Conceptual design identified
 - ...Risk-based approach to development (ICH Q9): use of FMEA
 - ...Develop control solutions for O₂-sensitive API's
- > **Ready to start detailed design of clinical scale line**
- > **Pharmaceutical production design concept also being developed**



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