

LE DEFI DE LA FORMULATION DES BIOLOGICS

APPROCHES FORMULATOIRES SPECIFIQUES POUR MAINTENIR LA STABILITE ET
LA PERFORMANCE

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L'ORÉAL
RESEARCH
& INNOVATION



AGENDA

Oct 16th, 2024

01

INTRODUCTION BIOLOGICS

02

BIOLOGICS COMPLEXITY

03

TECHNICAL PATHWAY TO BYPASS COMPLEXITY

- STANDARD/AQUEOUS FORMULATION
- POWDER FORMULATION
- ENCAPSULATION FORMULATION



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INTRODUCTION BIOLOGICS

WHY ARE THEY INTERESTING?



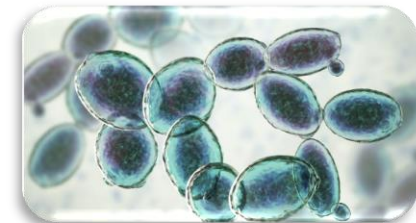
INTRODUCTION BIOLOGICS

WHAT IS A BIOLOGIC ?

WHAT DISTINGUISHES BIOLOGICS FROM OTHER ACTIVES IS THAT **THESE ARE COMPLEX MACROMOLECULE** GENERALLY PROTEINS OR NUCLEIC ACIDS **OBTAINED FROM LIVING CULTURE SYSTEMS** OR ARE **LIVING MICROORGANISM** WHEREAS OTHER ACTIVES ARE CONSIDERED AS “SMALL MOLECULES” AND ARE EITHER MADE SYNTHETICALLY OR OBTAINED FROM PLANTS.

BIOLOGICS ARE THOSE CLASS OF BIOLOGICALLY ACTIVE RM WHICH ARE **GROWN FROM LARGE SCALE CELL CULTURES OF :**

- **BACTERIA;**
- **YEAST;**
- **PLANT OR ANIMAL CELLS;**



INTRODUCTION BIOLOGICS

HOW DO THEY WORK?

POTENTIAL MULTI ACTION ACTIVE



ANTIMICROBIAL WITH **SELECTED SPECIFICITY** (*S. Aureus* /
C. Acnes / *Malassezia*...)

BENEFICIAL IMMUNO MODULATION





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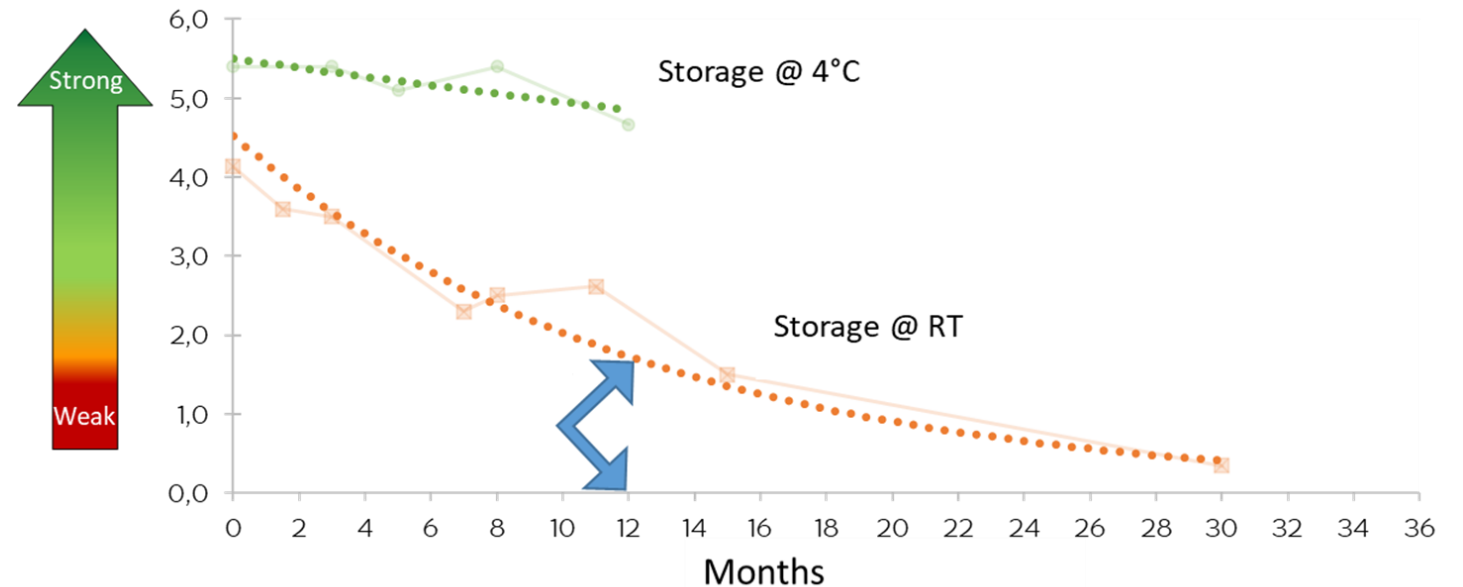
COMPLEXITY BIOLOGICS

CANNOT BE CONSIDERED AS A CLASSICAL ACTIVE/FORMULA

**Sensitive &
Specific**

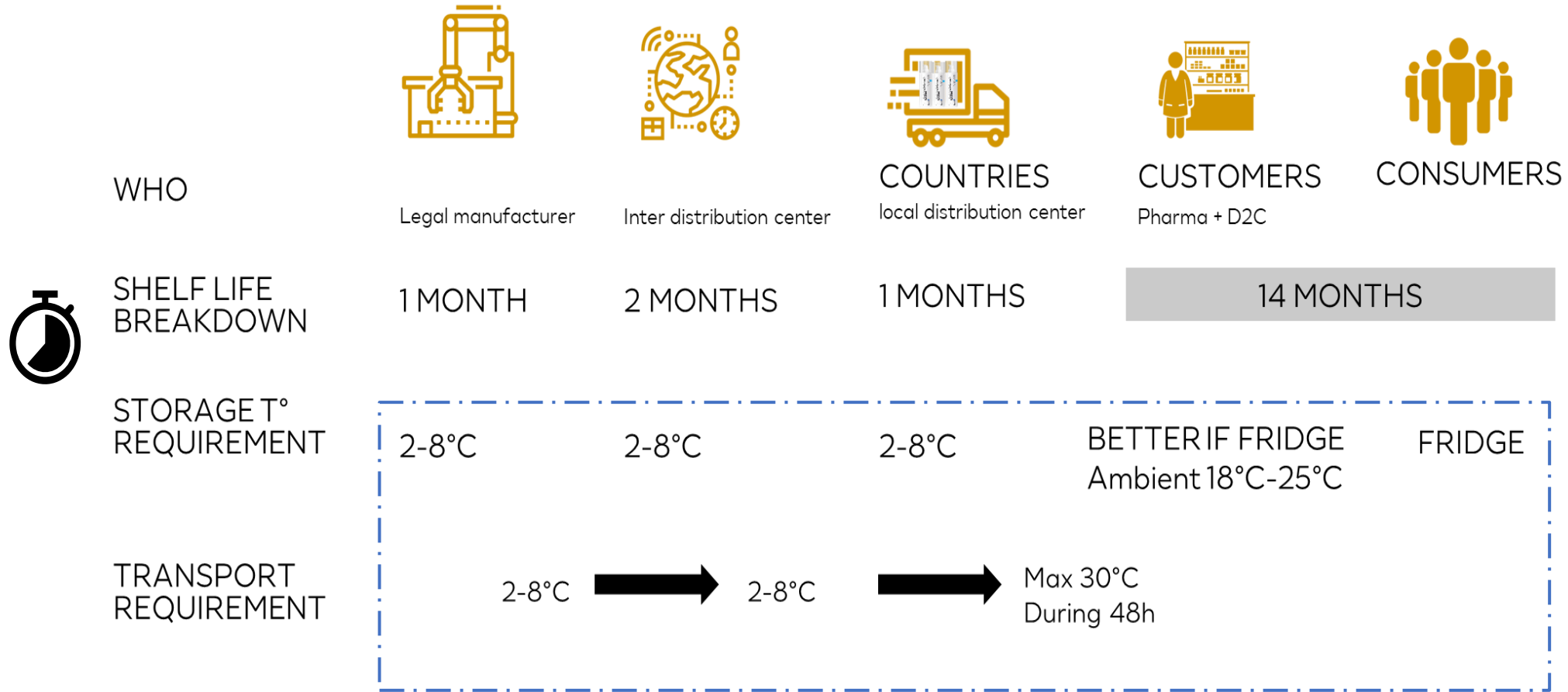
- ❖ TEMPERATURE SENSITIVITY;
- ❖ LOW STABILITY OVER TIME;
- ❖ MIXING/PROCESS SENSITIVITY;
- ❖ INCOMPATIBLE WITH SOME RMs;
- ❖ IMPORTANCE OF THE FORMULA ENVIRONMENT;
- ❖ GAZ-LIQUID INTERFACE;

BIOLOGIC ACTIVITY AMONG TIME



COMPLEXITY BIOLOGICS

COMPLEXITY EXAMPLE : IMPACT DISTRIBUTION/SHELF LIFE





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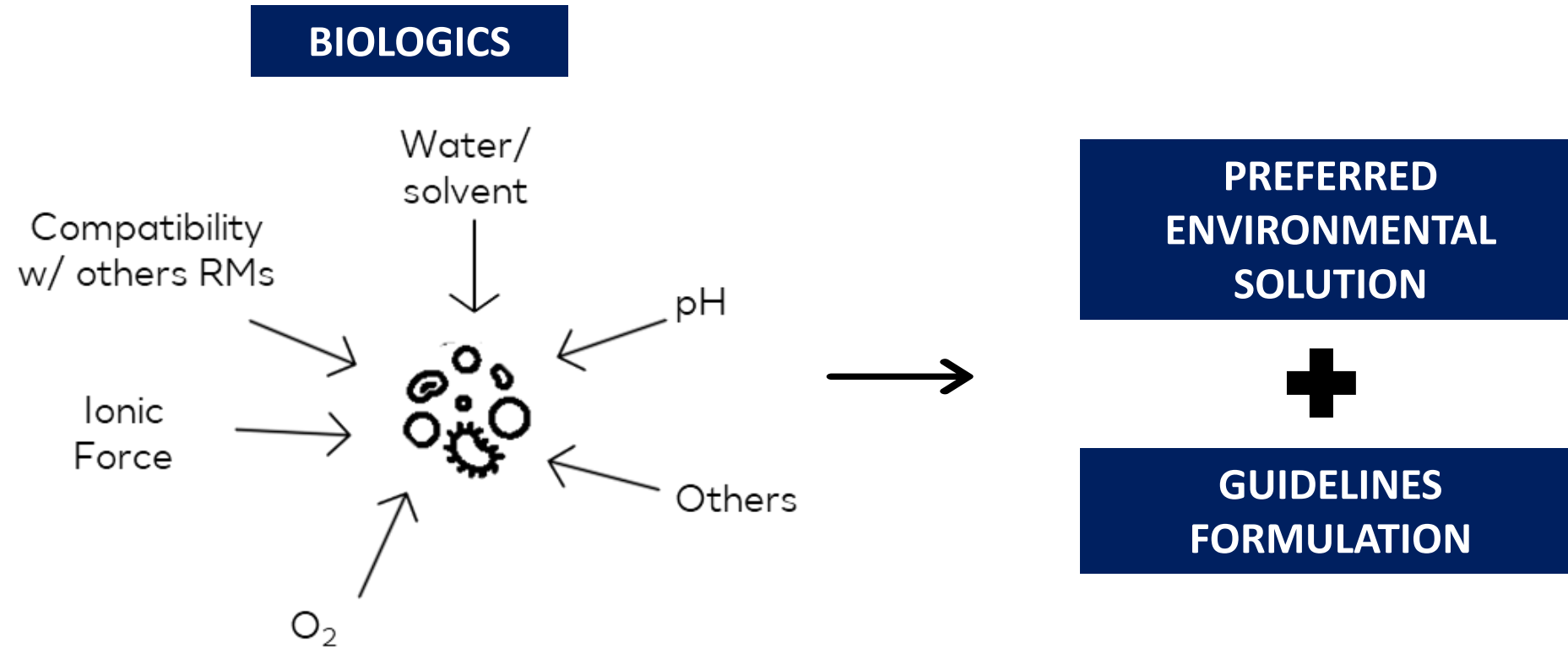
COMPLEXITY BIOLOGICS

03

TECHNICAL PATHWAY TO BYPASS COMPLEXITY

- STANDARD/AQUEOUS FORMULATION
- POWDER FORMULATION
- ENCAPSULATION FORMULATION

SOLUTIONS BIOLOGICS - STANDARD/AQUEOUS FORMULATION



SOLUTIONS BIOLOGICS - STANDARD/AQUEOUS FORMULATION

GUIDELINES FORMULATION

Oily compounds

| | | |
|--------------|---------|---|
| OIL COMPOUND | 570 | CETYL ALCOHOL |
| OIL COMPOUND | 783 | STEARYL ALCOHOL |
| OIL COMPOUND | 1082 | ISOPROPYL MYRISTATE |
| OIL COMPOUND | 1092 | OCTYLDODECANOL |
| OIL COMPOUND | 1300 | STEARIC ACID |
| OIL COMPOUND | 1300 | STEARIC ACID |
| OIL COMPOUND | 52022 | CAPRYLIC/CAPRIC TRIGLYCERIDE |
| OIL COMPOUND | 52080 | GLYCINE SOJA (SOYBEAN) OIL |
| OIL COMPOUND | 52147 | HYDROGENATED POLYISOBUTENE |
| OIL COMPOUND | 52556 | SIMMONDSIA CHINENSIS (JOJOBA) SEED OIL |
| OIL COMPOUND | 52818 | BUTYROSPERMUM PARKII (SHEA) BUTTER |
| OIL COMPOUND | 52818 | BUTYROSPERMUM PARKII (SHEA) BUTTER |
| OIL COMPOUND | 53034 | DIMETHICONE |
| OIL COMPOUND | 53890 | ISONONYL ISONONANOATE |
| OIL COMPOUND | 71615 | DICAPRYLYL ETHER |
| OIL COMPOUND | 75331 | HYDROGENATED CASTOR OIL DIMER DILINOLEATE |
| OIL COMPOUND | 76281 | DICAPRYLYL CARBONATE |
| OIL COMPOUND | 80391 | SQUALANE |
| OIL COMPOUND | 145 B | MINERAL OIL |
| OIL COMPOUND | E511470 | C9-12 ALKANE |

Surfactants

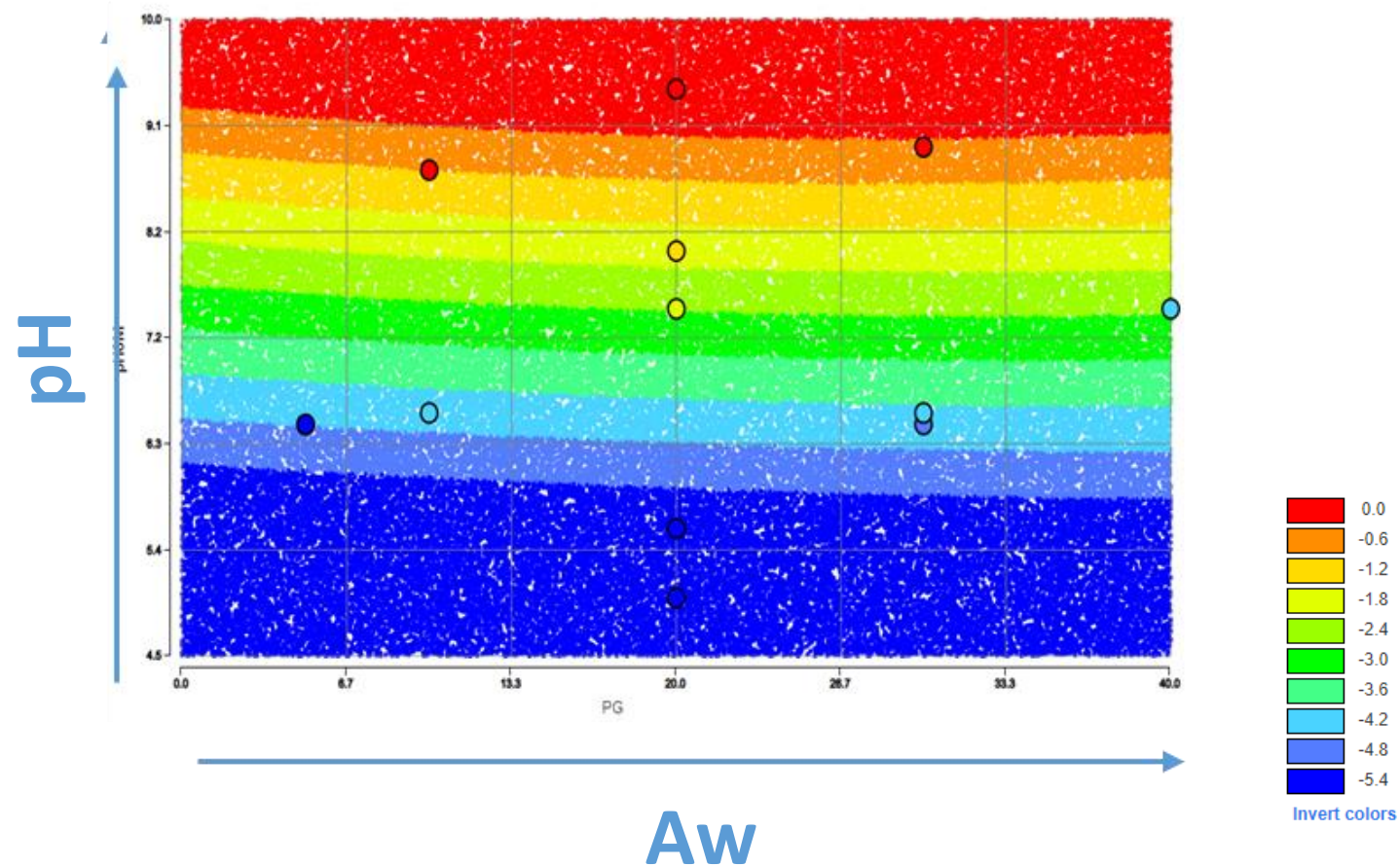
| | | |
|------------|---------|---|
| SURFACTANT | 570 | CETYL ALCOHOL |
| SURFACTANT | 783 | STEARYL ALCOHOL |
| SURFACTANT | 1097 | POLYSORBATE 80 |
| SURFACTANT | 1410 | DISODIUM COCOAMPHODIACETATE |
| SURFACTANT | 2174 | PEG-60 HYDROGENATED CASTOR OIL |
| SURFACTANT | 2730 | COCO-BEATAINE |
| SURFACTANT | 2730 | COCO-BEATAINE |
| SURFACTANT | 52824 | CAPRYLYL/CAPRYL GLUCOSIDE |
| SURFACTANT | 52824 | CAPRYLYL/CAPRYL GLUCOSIDE |
| SURFACTANT | 71454 | POLYGLYCERYL-4 ISOSTEARATE |
| SURFACTANT | 71606 | POLYGLYCERYL-3 METHYLGLUCOSE DISTEARATE |
| SURFACTANT | 71606 | POLYGLYCERYL-3 METHYLGLUCOSE DISTEARATE |
| SURFACTANT | 71673 | SODIUM LAURETH SULFATE |
| SURFACTANT | 71816 | DECYL GLUCOSIDE |
| SURFACTANT | 72043 | CETEARYL ALCOHOL (and) BEHENTRIMONIUM METHOSULFATE |
| SURFACTANT | 73327 | ARACHIDYL ALCOHOL (and) BEHENYL ALCOHOL (and) ARACHIDYL GLUCOSIDE |
| SURFACTANT | 73356 | DISODIUM COCOYL GLUTAMATE (and) SODIUM COCOYL GLUTAMATE |
| SURFACTANT | 79236 | POLYGLYCERYL-4 DIISOSTEARATE/POLYHYDROXYSTEARATE/SEBACATE |
| SURFACTANT | 87017 | GLYCERYL STEARATE CITRATE |
| SURFACTANT | 87017 | GLYCERYL STEARATE CITRATE |
| SURFACTANT | 1350 B | GLYCERYL STEARATE |
| SURFACTANT | 1350 B | GLYCERYL STEARATE |
| SURFACTANT | E508044 | GLYCOLIPIDS |
| SURFACTANT | G22818 | SPICULISPORIC ACID |



SOLUTIONS BIOLOGICS - STANDARD/AQUEOUS FORMULATION

IDENTIFICATION PREFERRED ENVIRONMENT FORMULATION

DOE : BIOLOGIC ACTIVITY
function pH & Aw



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DISRUPTION ON FORMAT WITH PURPOSE

FORMATS THAT SUIT BIOLOGICS – STABILIZATION & DELIVERY



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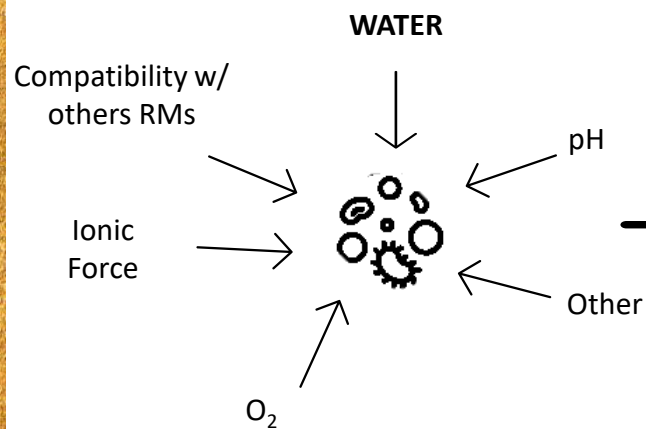
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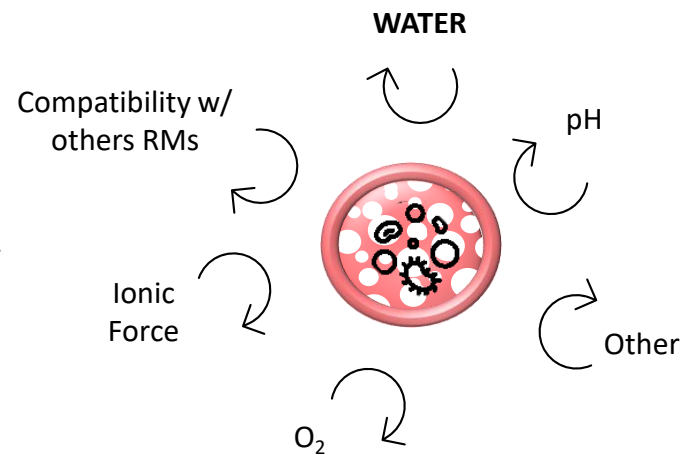
❑ TO PROTECT THE BIOLOGICS - FOR EFFICIENT & SENSORIAL PRODUCTS

SOLUTIONS BIOLOGICS – POWDER FORMULATION

BIOLOGICS



PROTECTED BIOLOGICS



ANHYDROUS FORMULA

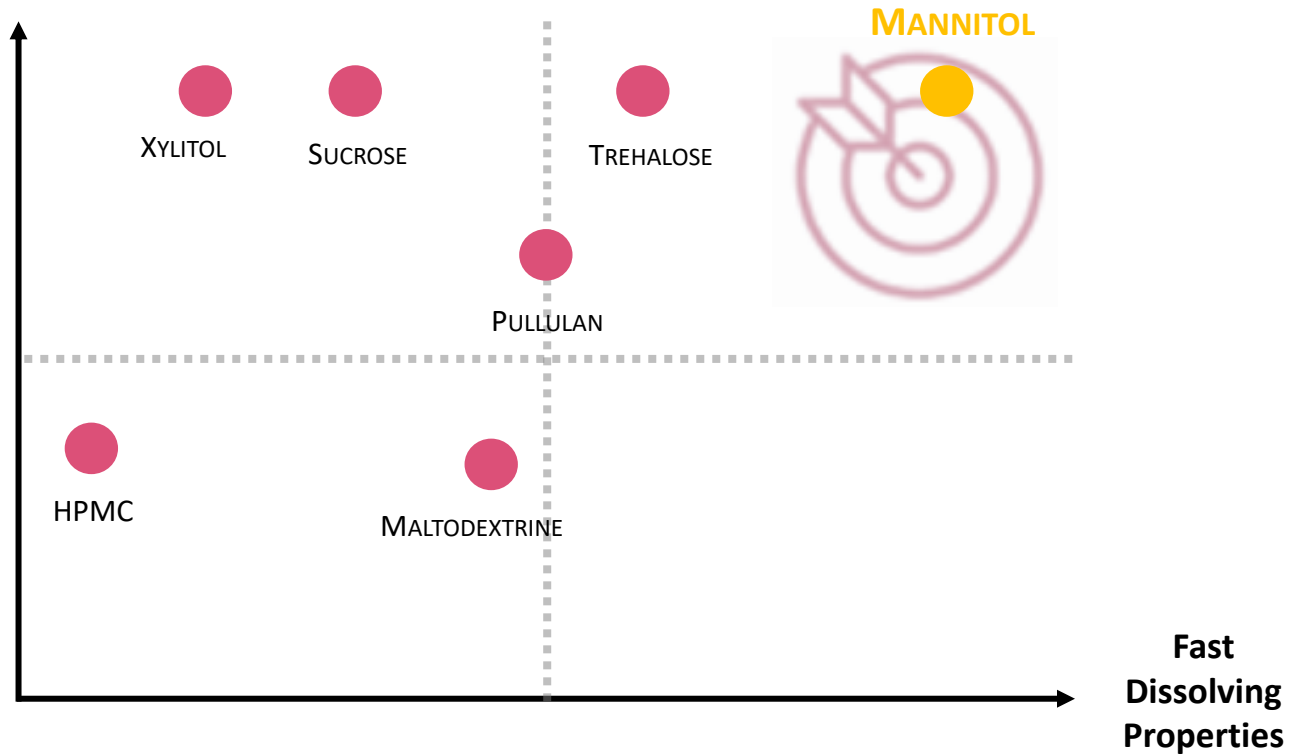


STABLE BUT GALENIC LIMITATION

SOLUTIONS BIOLOGICS – POWDER FORMULATION

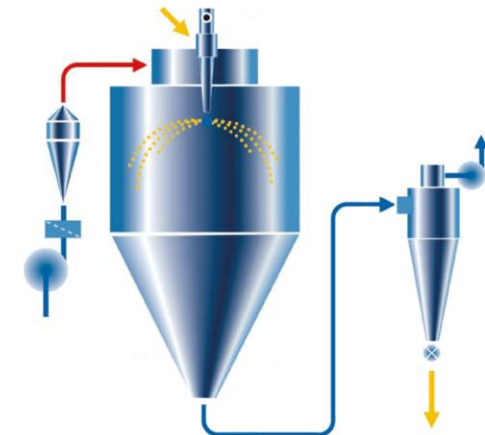
SELECTION RIGHT EXCIPIENT FOR DRYING & FORMULATION

Biologics activity



**BEST EXCIPIENT
TO OBTAIN**

- **Fast dissolving** Dry Form;
- **Effective Dry Form** (even after stability T°C);
- **Stable Dry Form** (ACO & Hygroscopy);



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SOLUTIONS BIOLOGICS – POWDER FORMULATION

STABILITY PHARMA METHOD

USE OF PHARMA INDUSTRY GUIDELINES

ICH Q1A (R2)

The stability studies should be conducted [...] in a container closure system [...] proposed for storage and distribution.

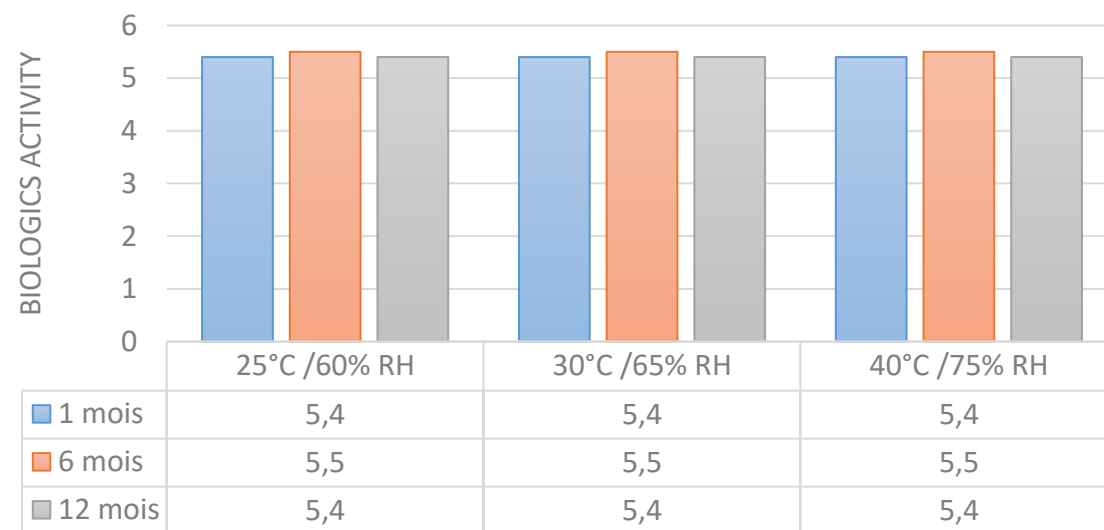
2.2.7.1. General case

| Study | Storage condition | Minimum time period covered by data at submission |
|----------------|--|---|
| Long term* | 25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH | 12 months |
| Intermediate** | 30°C ± 2°C/65% RH ± 5% RH | 6 months |
| Accelerated | 40°C ± 2°C/75% RH ± 5% RH | 6 months |

*It is up to the applicant to decide whether long term stability studies are performed at 25 ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH.

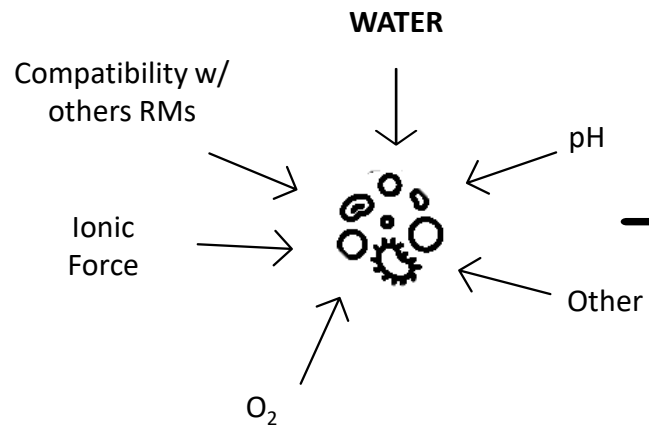
**If 30°C ± 2°C/65% RH ± 5% RH is the long-term condition, there is no intermediate condition.

Stability/Activity in pack function time/T°C/RH

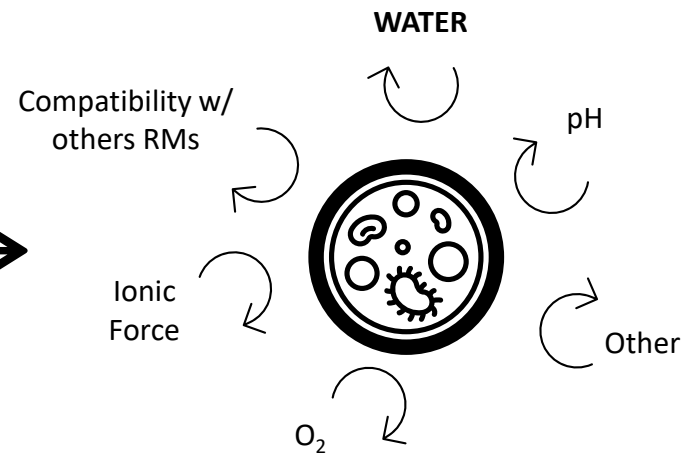


SOLUTIONS BIOLOGICS – ENCAPSULATION FORMULATION

BIOLOGICS



PROTECTED BIOLOGICS



AQUEOUS-BASED FORMULA



STABLE UNTIL THE LAST DROP

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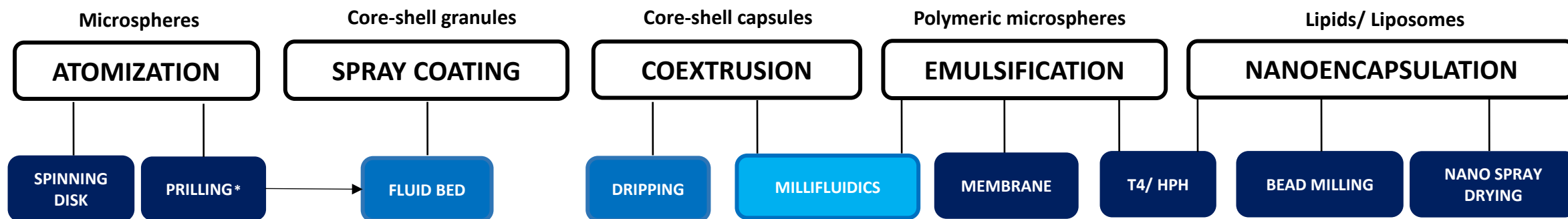
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SOLUTIONS BIOLOGICS – ENCAPSULATION FORMULATION

OVERVIEW BIO-ENCAPSULATION TECHNIQUES

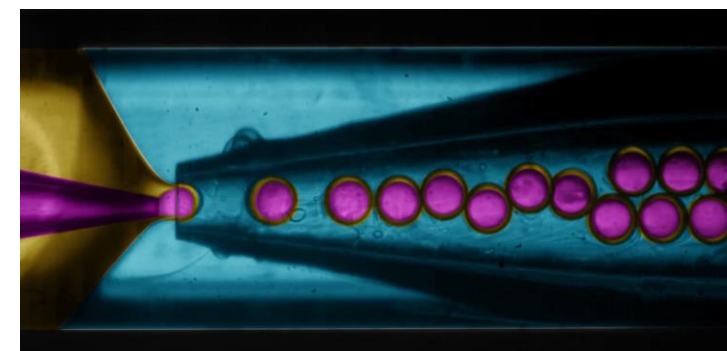
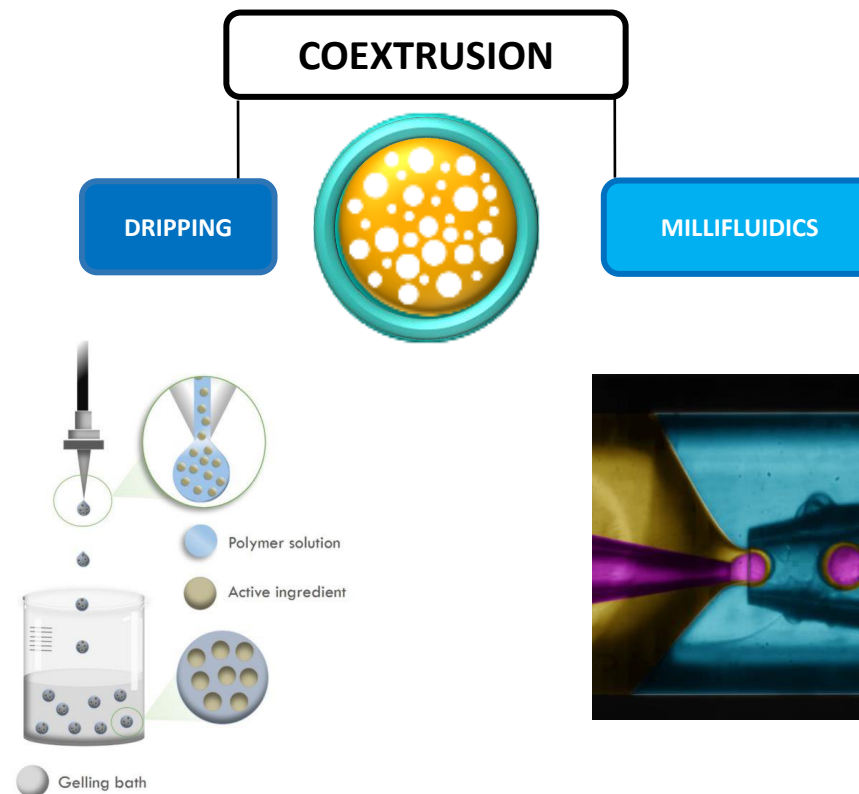
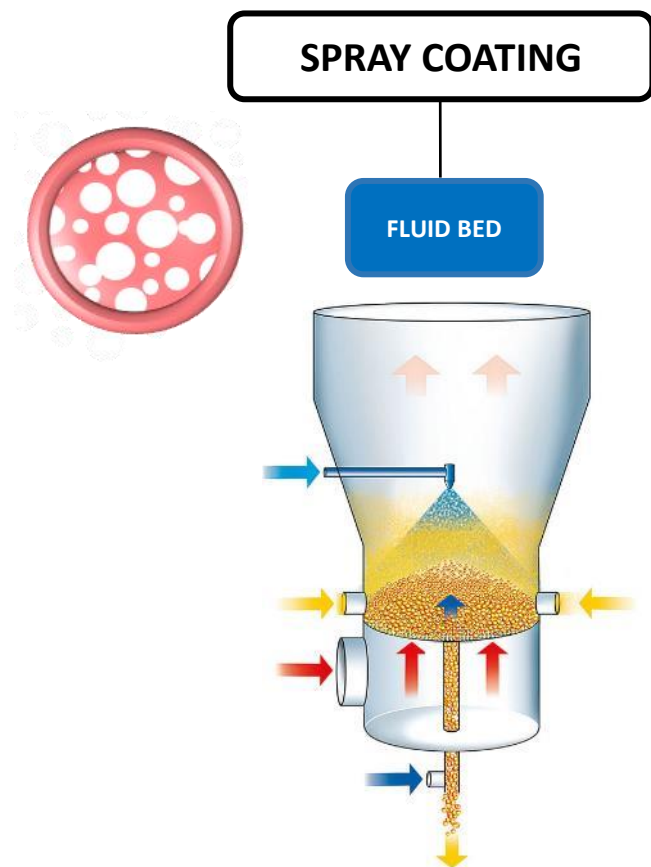


- Prior art
- Selected techniques
- To go beyond



SOLUTIONS BIOLOGICS – ENCAPSULATION FORMULATION

SELECTIONNED BIO-ENCAPSULATION TECHNIQUES

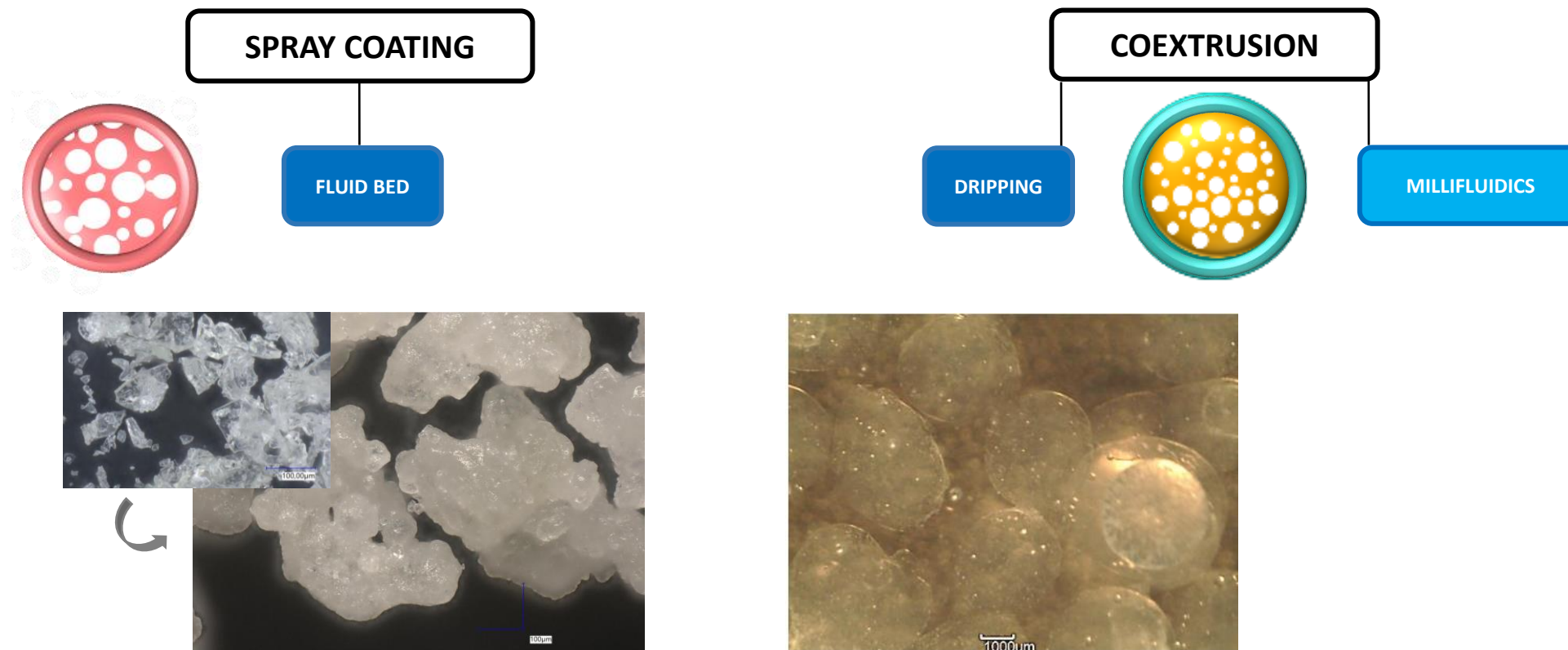


Selected techniques

To go beyond

SOLUTIONS BIOLOGICS – ENCAPSULATION FORMULATION

PROTOTYPES BIO-ENCAPSULATION TECHNIQUES



- Selected techniques
- To go beyond

THANK YOU

Questions ?

