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Pharmabiotics: a Regulatory Hurdle in Europe

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PHARMABIOTICS: A REGULATORY HURDLE IN EUROPE

I. Introduction to Pharmabiotics

II. Historical regulatory status for Pharmabiotics

III. Main challenges in Pharmabiotics registration

IV. A light at the end of the tunnel - the PRI

V. Conclusion

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INTRODUCTION

Probiotics => WHO definition

"live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host"

Definition does not refer to any type of population in particular
⇔ “General population”

Definition does refer to “health benefit”
⇔ Health Allegation at the European Level

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INTRODUCTION

However => important aspect to be discussed here:

“Health Claims” ≠ “Medical Claims”

Medical Claim

=> dedicated to a population of patients (WHO list of pathologies)

=> restricted to drug products

In the last 15 years => Science

Has shown the importance of the microbiota for Human Homeostasis

Has shown proof of concept in prevention and treatment of numerous pathologies

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INTRODUCTION

Directive 2001/83/EC: definition of a drug product -

(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings;

or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis

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Strains showing these types of properties
Could be considered as medicinal products
= Pharmabiotics

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HISTORICAL REGULATORY STATUS

Regulatory status in Europe:

Food supplement => health allegation => EFSA

Medical device

Medicinal products (MA granted in the ’70’s)

Medicines Agencies’ Mandates

EMA
or
National Agencies

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HISTORICAL REGULATORY STATUS

Medical Device:

New Regulation of the European Parliament and of the Council on medical devices, and amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009.

"Like for products that contain viable tissues or cells of human or animal origin, that are explicitly excluded from Directives 90/385/EEC and 93/42/EEC and hence from this Regulation, it should be clarified that products that contain living biological substances of other origin that achieve their intended purpose by pharmacological, immunological or metabolic means are also not covered by this Regulation."

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Medical device status => **no longer applicable for Pharmabiotics**

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HISTORICAL REGULATORY STATUS

Medicinal Product:

(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings;

or

(b) Any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis

=> **medicinal product marketing authorization**

Demonstrate:

Quality
Safety
Efficacy

} **Pharmaceutical Standards:**

Common Technical Document
EMA and ICH guidelines

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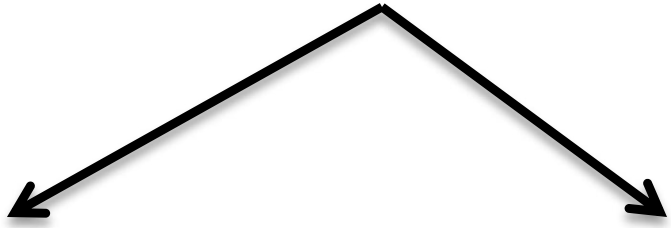
REGISTRATION AS MEDICINAL PRODUCTS

Demonstrate:

- Quality
- Safety
- Efficacy

Pharmaceutical Standards:

Common Technical Document
EMA and ICH guidelines



Biologicals / biotechnologicals

applies to proteins and polypeptides, their derivatives, and products of which they are components (e.g. conjugates). These proteins and polypeptides are produced from recombinant or non-recombinant cell-culture expression systems and can be highly purified and characterized using an appropriate set of analytical procedures.

New Chemical Entities

applies to small molecules

REGISTRATION AS MEDICINAL PRODUCTS

Ultimately => Health authorities see medicinal products as molecules

Often this is not adapted to Pharmabiotics

⇔**Active Substance is a living microorganism**

=> no specific regulation or guidance for living microorganisms
=> exception ⇔ vaccines

Where does the industry stand?

- Uncertain regulatory framework
- Significant risk in developing such products

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REGISTRATION AS MEDICINAL PRODUCTS

How can we reduce such risk?

1) Understand the current pharmaceutical regulatory framework

- Understanding the limits of the current regulation
- Finding the parts of the regulation that can and should be applicable for Pharmabiotics
- Working on the right justifications when guidances are not applicable
- Work with the existing regulation as thoroughly as possible

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REGISTRATION AS MEDICINAL PRODUCTS

How can we reduce such risk?

2) Understand how health agencies might evaluate Pharmabiotics

- Important: national agencies evaluate according to their knowledge of such products

presence of medicinal probiotics in their pharmacopoeia
consumer feeling about this type of product
history of safety of the products on the market nationally

Large variability in the evaluation of such type of products by the various national medicines agencies

REGISTRATION AS MEDICINAL PRODUCTS

How can we reduce such risk?

3) Get answers at the European level

- The EU has harmonized the evaluation of drug products for more than a decade now
- Initially: EMA's mandate = innovative products
- EMA = committees of experts sourced from the national agencies

The European level seems to be more adapted to Pharmabiotics

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REGISTRATION AS MEDICINAL PRODUCTS

Important points to consider when developing pharmabiotics

- Pharmaceutical development
  - Requires several years
  - Costly

- Medicinal product markets are
  - Stable
  - Long-term

EFSA requirements in terms of Clinical Trials (health allegations)
- Corresponds to ICH requirements (Good Clinical Practice)
- Becoming more and more expensive
- Biological markers used => not always accepted by EFSA
- Need for a large population ⇔ healthy subject variability

REGISTRATION AS MEDICINAL PRODUCTS

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PROBIOTICS

HEALTH ALLEGATION

EFSA

- One-shot evaluation
- No possibility to discuss with the authority

High Cost (becoming very high)
Difficulty to obtain health allegation ↗
Restricted to prevention (patient pop. excluded)
Shorter time to market
Larger market

PHARMABIOTICS

DRUG MARKETING AUTHORIZATION

EMA
Or national medicines agencies

- Sponsor may discuss with the authority when needed during development ⇔ **Scientific Opinions**
- Results of the discussion kept in the product's dossier for final evaluation
- Centralized procedure => single dossier but MA in the 28 of the EU

Very High Cost
Significant constraints
Restricted to patient populations
Longer time to market
Stable & Long-term in Europe
Medical sector confidence

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A LIGHT AT THE END OF THE TUNNEL

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How can we reduce such risk ?

1) Understand the current pharmaceutical regulatory framework
2) Understand how health agencies might evaluate Pharmabiotics
3) Get answers at the European level

PRI

A NETWORK

- Good regulatory practices sharing
- Information on national / European medicines agencies' opinions
- Companies with expertise for every step of the development
- Companies developing/producing according to Pharmaceutical Standards

TO SUPPORT THE INDUSTRY

- support in scientific opinion dossier engineering
- support in collaborative R&D project engineering

A LIGHT AT THE END OF THE TUNNEL

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PRI

We already have answers to some major questions -

EMA in 2013:

- There is no guidance in the current regulatory framework which completely addresses Pharmabiotics.

- Living microorganisms which restore, correct or modify physiological functions by exerting a pharmacological, immunological or metabolic action can be considered as drug products.

- Medicinal Product Marketing Authorization may be granted if quality, safety and efficacy are proven according to the current European Pharmaceutical Standards.

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CONCLUSION

When a strain can have a therapeutic potential -

=> medicinal product definition ?

strain = medicinal product

strain = Pharmabiotic

Development of Pharmabiotics

No specific regulatory framework in Europe

Need for clarification

Based on existing guidance that could be applicable => PRI can help you

Registration of Pharmabiotics

Important to request Scientific Opinions along a product's development

- helps for making important decisions during development
- helps for future registration

PRI can help its members for dossier engineering

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CONCLUSION

Important to be part of a network:

Share good regulatory practices

Have a good knowledge of the Pharmaceutical regulatory Framework
=> be able to make strategic decisions

Be aware of any modifications in the regulation

Anticipate such changes in your development

Be part of an organization which can be consulted if new dedicated regulations are discussed at the European level.

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