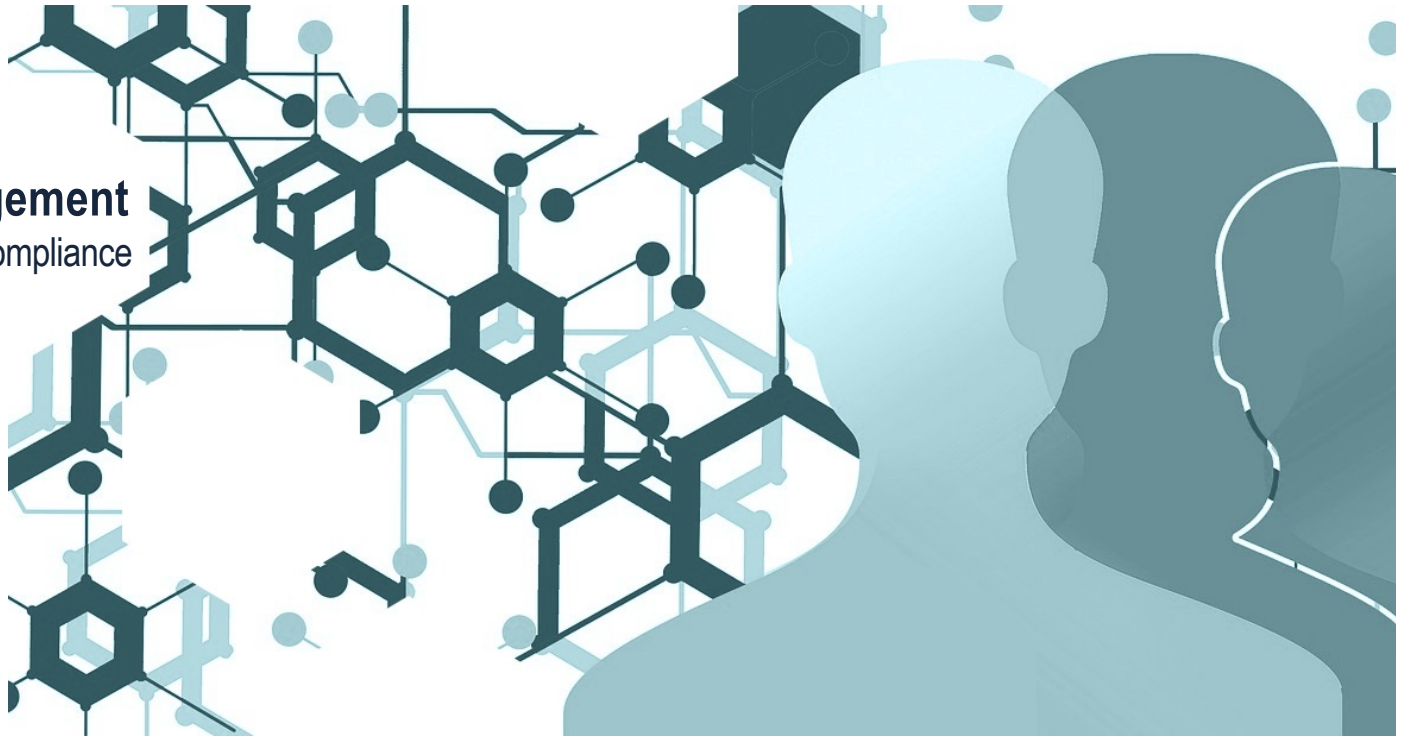
BLYMUM
smart well-being modulations

Clinical Evidence Management

Medical Devices EU Regulatory Compliance



Service Presentation

2023

BLYMUM Srl

BLYMUM
smart well-being modulations

We are an Italian company based in Milan

providing **services**, products, and **knowledge**

for those Companies specialized in developing, producing, and marketing

food supplements, functional foods, novel foods, nutraceuticals, cosmetics

and **medical devices,**

and for those Companies strategically focused on social and workplace sustainability

Our mission

is to contribute to people's health, physical and psychological well-being, longevity, and beauty

Smart Scientific Sustainable Solutions

Our Services and Products

SERVICES

SERVICES

BLYMUM offers professional support

to Pharmaceutical, Food, Healthcare, and other Clients in the following areas:

Clinical Trials Management; **Regulatory Compliance;** Wellbeing Management ; Sustainable Impact Modeling; Change Management & Mentoring

PRODUCTS

PRODUCTS

In parallel, we are directly involved in product innovation processes

The BLYMUM distinctive feature lies in the development of Physiological Modulators, which are scientifically proven solutions for specific human psycho-physical problems, pathological phenomena, and adverse living and working conditions:

BLYMUM Food Supplements; On-demand Formulation Development

BLYMUM

Focus on MD Industry

Medical Device (MD) is any **instrument, apparatus, appliance, software, implant, reagent, material, or other article** intended by the manufacturer to be used, alone or in combination, for human beings for one or more of the following specific medical purposes:

- **Alleviation of Disease -** diagnosis, prevention, monitoring, prediction, prognosis, treatment or;
- **Injury or Disability** - diagnosis, monitoring, treatment, alleviation of, or compensation for;
- **Anatomy/Physiological/Pathological Processes -** state investigation, replacement, or modification of;
- **In Vitro examination of Specimens derived from the Human Body** - providing information by means of (not achieving its principal intended action by pharmacological, immunological, or metabolic means, in or on the human body, but eventually assisted in its function by such means)

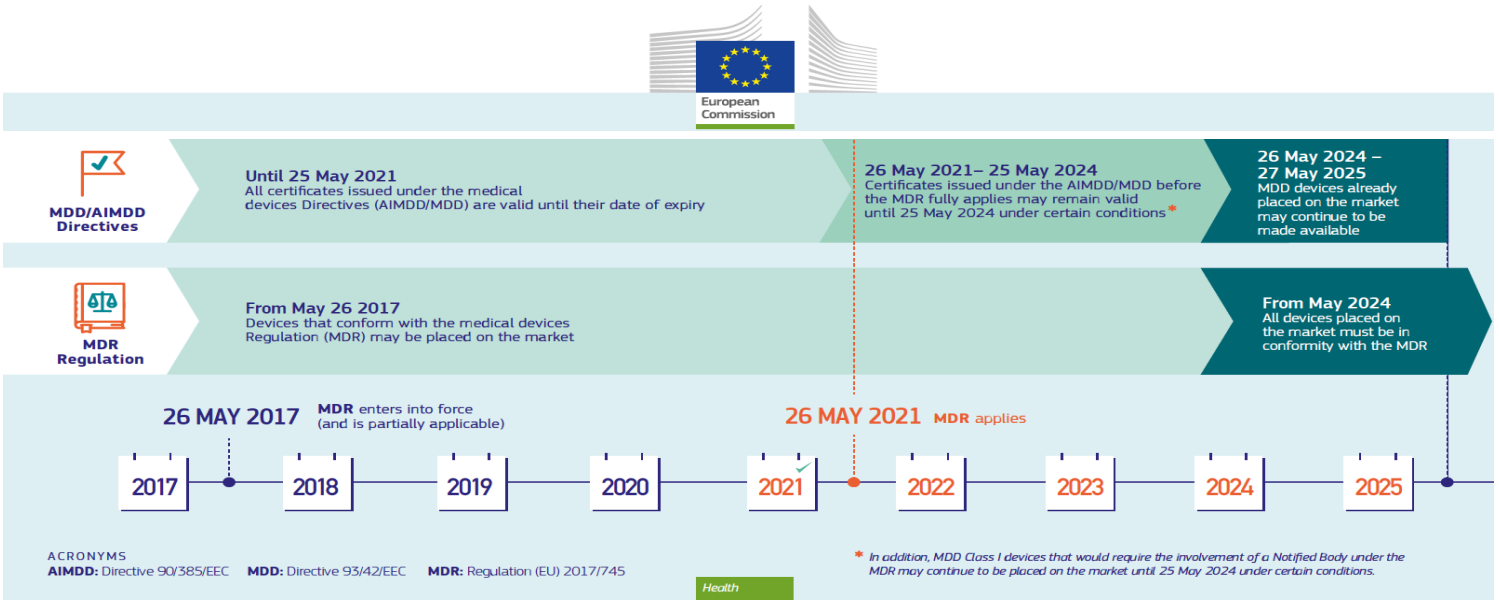
The following products are also be deemed to be MD:

- Devices for the control or **support of conception**;
- Products specifically intended for the **cleaning**, **disinfection, or sterilization of devices**

EU Regulation 2017/745 (MDR) and Transition Timelines

A significant change in legislation has been affecting European MD manufacturers starting from May 2021. It is the new **Regulation 2017/745** of the European Parliament and of the Council of 5 April 2017 on MD.

In contrast to previous Directives, the MDR does not need to be transposed into national law. The MDR will therefore reduce the risks of discrepancies in interpretation across the EU market.



Our Proposal for MD Developers, Manufacturers and Distributors

In general, the medical device industry is **a very heterogeneous area** in terms of production and markets, spilling over into different fields of manufacturing and healthcare services

MD manufacturers are under **increasing market pressure** with rapidly changing expectations on medical device usability, applications, and software development; product quality is always one of the main issues

Although medical technology is the leading technological field in terms of patent applications and patents granted in the EU, **the sector is dominated by globally operating companies**

MD manufacturers of all sizes, need to apply **faster product development cycles**, **enhance quality**, **innovate** and **remain compliant with the MD Industry regulations**

Our Value Proposition is

Clinical Evidence Management

Clinical Evidence Management

Our Services pertaining to Medical Devices EU Regulatory Compliance

and offered to local and global developers, manufactures and distributors of all sizes,

are proposed as

BLYMUM Clinical Evidence Management (B-CEM).

They are aimed at :

Casting professional partners for clinical investigations, inside, and if necessary, outside our business and knowledge network, in order to ensure the collaboration with the most appropriate, specialized and internationally recognized scientists and experts from primary academic and research Institutions

Ground-working, supporting You throughout the scientific documentation assessment, regulatory compliance, investigational site assessment, and risk management (ISO 14971)

Planning clinical investigations, monitoring activities, and post market clinical follow-up; composing, according to the MDR instructions, the clinical investigation plan (CIP) monitoring plan (MP) and clinical follow-up plan CFP)

Monitoring, according to the MP: the rights, safety, and well-being of the human subjects are protected during the clinical investigation; the reported data are accurate, complete, and verifiable from source documents, and the conduct of the clinical investigation complies with the approved CIP

Clinical Evidence Management

CASTING

Clinical Investigational Team Design

We identify professional partners for clinical investigations with the aim of ensuring **the most appropriate team**, managed by specialized and internationally recognized scientists and experts; all personnel involved in conducting a clinical investigation shall be suitably qualified, by education, training, or experience in the relevant medical field and in clinical research methodology, to perform their tasks

We collaborate with primary Italian and international academic institutions
The clinical investigations are conducted in collaboration with the most important universities in Italy, and throughout academic collaborations in USA, UK, and Switzerland, **in accordance with the worldwide requirements**, in primis with Regulation 2017/745 of the European Parliament and of the Council of 5 April 2017 on MD and its amendments, the provisions of the Declaration of Helsinki (current version), the Good Clinical Practice Standards from the ICH, the Federal Data Protection Act and the Italian Personal Data Protection Code

Particular attention is given to the proposal of the **principal investigator**, which should be recognized as qualifying for the role on account of having the necessary knowledge and experience in scientific fields concerning a given MD clinical investigation

The CASTING Service gives You the **advantage of enhancing and accelerating the CI procedure, the investigational site selection, and the investigated subjects' enrollment**, as well as of having a positive impact on **costs and the efficiency** of the CI project in general

Clinical Evidence Management

GROUNDWORK

Scientific Documentation Assessment

Accepted clinical data may be sourced, except clinical investigation(s), from other **studies reported in scientific literature**, from reports published in the scientific literature on other **relevant clinical experiences**, and from clinically relevant information coming from post-market surveillance, in particular, the **post-market clinical follow-up**

We propose **GROUNDWORK Research and Assessment Service** for the collecting and critical evaluation of the relevant scientific and clinical experience literature currently available relating to the safety, performance, design characteristics, and intended purpose of the studied Medical Devices

Research documents, reports, and information are **accurate and up to date, consistent with the requirements of the MDR** concerning the clinical data management

In case the clinical investigation is carried out, the principal investigator and investigation site team are regularly informed and knowledgeable of all relevant **scientific documentation updates**

Clinical Evidence Management

GROUNDWORK

Regulatory Compliance Services

Regulatory compliance deals with the set of guidelines you must follow in accordance with the Law. It is indeed an increasingly complex and critical effort to ensure that Your Medical Device meets all applicable regulatory requirements for commerce and advertising activities

We have an excellent knowledge of Italian, EU and international legislation to be respected for safe and legal dealing concerning MDs, and we deliver a specific **GROUNDWORK Regulatory Compliance Service for clinical investigations**

The maintenance and **continuing regulatory support services**, such as due diligence and licensing support, are available as well

Furthermore, a distinct service is fulfilled for **intellectual property** management:
we assist You (dossier filing, technical assistance, regulatory compliance) in studying, drafting, and deposit of applications for Italian, European, or PCT international patents at the Italian Office for Patents and Trademarks, the European Patent Office, and the World Intellectual Property Organization

Clinical Evidence Management

GROUNDWORK

Clinical Investigation Risk Management

The decision to embark upon or continue a clinical investigation of an investigational medical device requires that the residual risk(s), as identified in the risk analysis, as well as risk(s) to the subject associated with the clinical procedure including follow-up procedures required by the CIP be balanced against the anticipated benefits to the subjects

Risk management principles shall be applied to both the planning and the conduct of clinical investigations, in order to ensure the reliability of the clinical data generated and the safety of subjects

We provide a **Clinical Investigation Risk Management** Service to guarantee the application of ISO 14971 (Medical Devices - Application of risk management to medical devices) to clinical investigations

Our Service includes:

- risk management reporting/review of the sponsor's risk management report and its adequacy for the clinical investigation
- summary of the benefit-risk assessment to be disclosed in the relevant clinical investigation documents
- investigator's brochure drafting
- training support related to the clinical investigation risk management
- risk control during the clinical investigation
- risk management review and follow-up indications

Clinical Evidence Management

GROUNDWORK

Investigation Site Assessment

The facilities where the clinical investigation is to be conducted shall be **suitable for the clinical investigation** and, in collaboration with the sponsor, the criteria necessary for the successful conduct of the clinical investigation are defined prior to the start of the site qualification process

The investigation site's facilities should be similar to the facilities required for the intended use of the investigational device(s), although additional equipment and capabilities may be needed at investigation sites during the clinical investigation to ensure that the necessary safety precautions are available

We identify, select, and evaluate the adequacy of the potential investigation site(s) - **GROUNDWORK Investigation Site Assessment** with the aim of **verifying facilities, laboratories, equipment, investigation site team,** and, eventually**, other requested resources;** the rationale for selecting an investigation site shall be documented in an **investigation site-selection report**.

The investigation site assessment is closely related to our CASTING Service and in their integration, You obtain an important business **advantage of enhancing and accelerating the CI procedure, its efficiency, and efficacy**

Clinical Evidence Management

PLANNING

Clinical Investigation Planning

Clinical evaluation is desired to be a **systematic and planned process**, involving one or more human subjects, to continuously generate, collect, analyze and assess the clinical data pertaining to a MD in order to verify the safety, performance, and clinical benefits of the device

Clinical investigations shall be performed on the basis of an appropriate plan of investigation reflecting the latest scientific and technical knowledge. **The clinical investigation plan (CIP)** shall set out the rationale, objectives, design methodology, monitoring, conduct, record-keeping, and method of analysis for the clinical investigation

In reference to this Service, our activities and delivery are:

- coordination of the clinical investigation planning process
- verification of the accuracy, completeness, alignment, and up to date concerning the information and data provided by the involved investigational team's members
- writing and editing of the CIP, in accordance with the last version of the ISO 14155 international standard and of the MDR Regulation 2017/745
- final CIP document delivery

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PLANNING

Monitoring Planning

The sponsor determines the extent and **nature of monitoring appropriate for the clinical investigation based** on the risk assessment, the objective, design, complexity, size, critical data points and endpoints of the clinical investigation, and on the degree of deviation from normal clinical practice

Monitoring methods can differ between countries and arrangements for source data verification are subject to national or regional regulations regarding personal data protection.

Monitoring activities shall be performed on the basis of an appropriate **monitoring plan (MP)**

The MP shall describe: the risks associated with the clinical investigation and adequate information on relevant risk control measures, the processes that need to be monitored, monitoring methods, responsibilities, the procedures and requirements for the investigation's oversight, the methods for documenting and communicating monitoring results; the methods for managing compliance, and other complementary aspects of the clinical investigation which need special attention

In reference to this Service, our activities and delivery are:

- writing, editing, and feasibility study of the MP, in accordance with the last version of the ISO 14155 international standard and of the MDR Regulation 2017/745
- final MP document delivery

Clinical Evidence Management

PLANNING

Post-Market Clinical Follow-up Planning

Post-market clinical follow-up checks the adequacy of available clinical evidence and risk management, identifies any gaps, and ensures post-market surveillance (PMS) arrangements are adequate

Post Market clinical follow-up activities shall be performed on the basis of an appropriate **post-market clinical follow-up plan.**

In reference to this Service, our activities and delivery are:

- coordination of the post-market clinical follow-up planning process
- verification of the accuracy, completeness, and data concerning the post-market information and data gathering
- writing and editing of the post-market clinical follow-up plan, in accordance with the last version of the ISO 14155 international standard and of the MDR Regulation 2017/745
- final post-market clinical follow-up plan document delivery

Clinical Evidence Management

MONITORING

On-site Monitoring

Usually, there is a **need for on-site monitoring** throughout the clinical investigation; centralized monitoring can be performed in addition to complement on-site monitoring

Monitoring is conducted **according to the monitoring plan** and includes:

- Initiation of the investigation site to ensure that the principal investigator and investigation site team have received and understood all requirements and contents concerning the clinical investigation
- Routine monitoring visits to verify that compliance with the CIP is maintained and that only authorized members of the investigation site team are participating in the clinical investigation
- Follow-up on action items until resolved and/or with protocol violations/data corrections
- Review of declarations of consent and current data privacy and protection
- Coordination among the sponsor, the principal investigator, and the investigation site team
- Monitoring of patient safety including reporting incidents and secondary illnesses/therapies

Clinical Evidence Management

MONITORING

Close-out Activities and Reporting

The monitor conducts clinical investigation-related close-out activities as described in the Regulation 2017/745

Monitoring reports

We draw up **the results of monitoring activities** that are documented in sufficient detail to allow verification of compliance with the monitoring plan

Depending on sponsor procedures or national regulations, we produce **other clinical investigation-related communication(s) and summaries**

The monitor coordinates the production of the **clinical investigation report** and submits it the sponsor; he/she verifies the accuracy, completeness, and alignment of data provided by the involved investigational team's members

Selected Reference | Casting, Groundwork, Planning and Monitoring Activities

A Prospective, Randomized, Double-blind Placebo-controlled Clinical Investigation to Evaluate Weight Reduction (52 Weeks) with Polyglucosamine in Overweight and Obese Subjects

A Randomized Double-blind Placebo-controlled Clinical Study to Evaluate the Effect on Weight of a Medical Device with Polyglucosamine L112 in a Group of Overweight and Obese Subjects

Artificial Saliva in Diabetic Xerostomia (ASDIX): Double Blind Placebo Controlled Clinical Investigation of Aldiamed Versus Placebo

Patent application pertaining to a Class III Medical Device to treat Obstructive Sleep Apnea (OSA)

OCCAM Project - Cerebral Oxidation as a Cause of Metabolic Ageing: Evaluation of the MCI (mild cognitive impairment) Evolution Following Treatment with Support Antioxidants for Cerebral Oxidation

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