Pfizer CentreOne

# Regulatory Overview Guide

**Innovation**, **compliance** and **agility** are guiding regulatory approaches across the globe. They might have important implications for your drug program.

Innovation

Compliance

Agility

# Innovation

**The new frontiers in the regulatory landscape are innovation in medical devices and dosing regimens that facilitate patients' self-medication, greater biopharmaceutical diversity and cannabinoids.**

# Medical Device Innovation

**The rapid pace of innovation in devices has erased the traditional boundaries with medicines, leading to increased complexity and new regulations.**

**CFR 21 Parts 862 to 892;**
**FDA Product Classification Database.**

**Regulation (EU) 2020/561;** Product Classification per Annex IX in the Medical Device Directive (93/42/EEC as modified by 2007/47/EC – New Medical Device Regulation (MDR) will become effective in May 2021.

**International Medical Device Regulators Forum (IMDRF):** a group of medical device regulators from around the world that have voluntarily come together to harmonize the regulatory requirements.

# Biopharmaceutical Diversity

**A greater range of biologics (vaccines, cell therapy, viral vectors, gene therapy) has led to greater diversity of biopharmaceuticals. The identification of specific molecules and a pathway to grow them has enabled therapies to be more targeted. Regulators are now more involved in the development process, which can lead to more efficient approvals for new medicines.**

**US FDA Title 21 CFR Parts 600 (Biological Products:** General), 601 (Licensing Biologics), and 610 (General Biological Products Standards).

EMA **Scientific Guidelines on biologicals, vaccines, gene therapy, cell therapy and tissue engineering** help applicants develop and prepare marketing authorization applications for advanced therapies.

**The EU Innovation Network** and the **EMA's Innovation Task Force (ITF)** support emerging therapies and technologies in the early phase of development.

**The Innovative Medicines Initiative (IMI):** a public private partnership between the European Commission and pharmaceutical companies is accelerating the development of innovative medicines, particularly in areas of unmet medical need.

**The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) – Q5A** – Q5E Quality of Biotechnological Products.

# Cannabinoids/ Controlled Substances

**Now that manufacturers of cannabinoid products have to proceed through a standard drug approval process, regulation in this area is evolving rapidly. It's vital to stay on top of these changes to ensure success.**

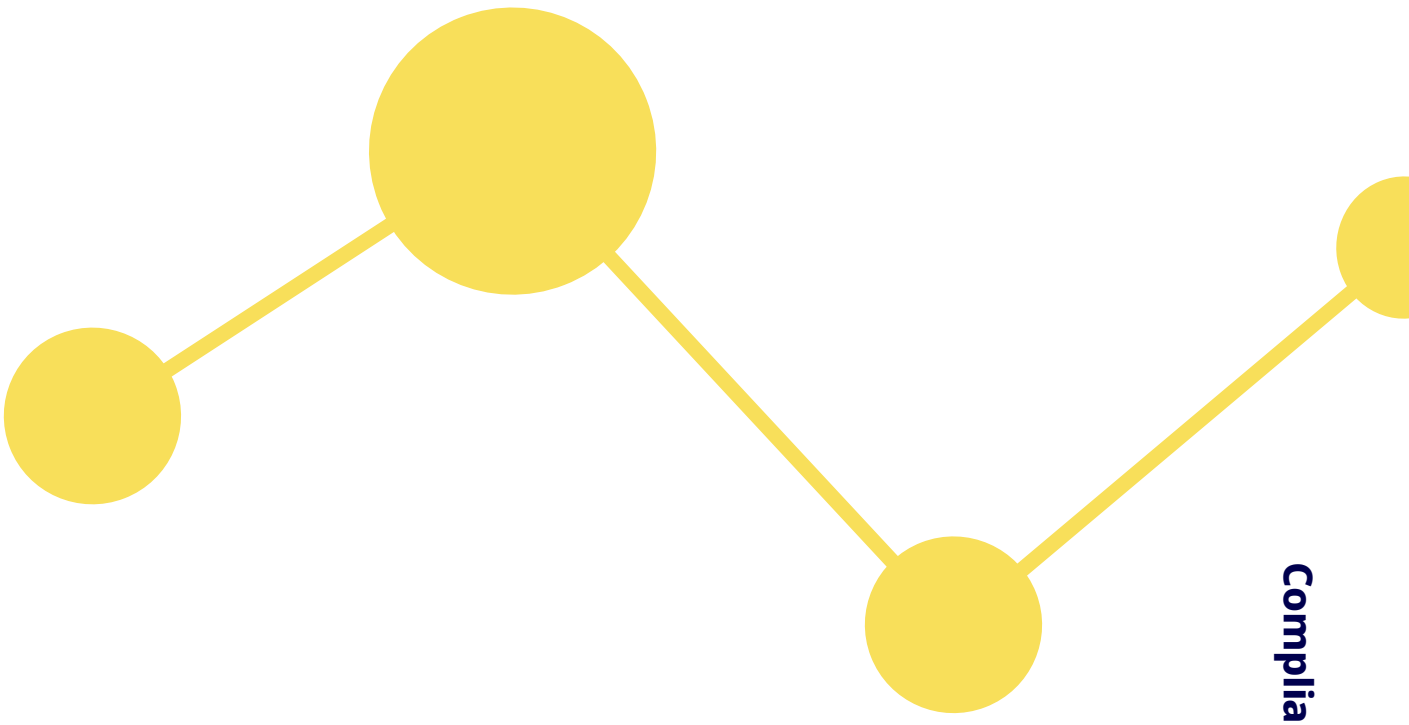
**FDA Regulation of Cannabis and Cannabis-Derived Products, Including Cannabidiol (CBD), March 2020.**

# Compliance

**Ensuring an uninterrupted supply of therapies is vital. Keeping manufacturing facilities fully compliant with regulations through strict quality regiments, regular inspections and open communication with regulators is the best way to achieve this goal.**

# Engaging With Regulators

**A lack of clear regulatory guidance can lead to program choices that appear to be the best approach but may not be right. Regulators are there to assist applicants with the approval process, especially if an unmet medical need is being filled, and consulting directly with them can greatly facilitate the process.**



# Engaging With Regulators (continued)

The FDA has numerous mechanisms to request scientific meetings:

- Guidance for Industry: **IND Meetings for Human Drugs and Biologics;** Chemistry, Manufacturing, and Controls Information, May 2001.
- **Formal Meetings Between the FDA and Sponsors or Applicants of PDUFA Products Guidance for Industry, December 2017.**
- **Critical Path Innovation Meetings, March 2015.**

The EMA offers a range of advice and consultations and provides Scientific Advice on methods and study designs at any stage of a medicine's development.

- The EMA conducts parallel scientific advice with the US FDA for certain important medicinal products.
- The EMA also offers consultations in parallel with the **European Network for Health Technology Assessment (EUnetHTA)** to help applicants generate evidence that satisfies the needs of both regulators and HTA bodies.
- The EU Innovation Network is piloting **Simultaneous National Scientific Advice (SNSA)** from national regulators to strengthen early regulatory support for innovation.

## Tips for engaging with regulators

Be proactive in establishing a collaborative working relationship with the Ministry of Health (MoH) project manager that has been assigned to your program.

Be specific on the questions that you wish to ask so that your program can move forward.

Be transparent and partner with the MoH. Both the product sponsor and the MoH have the shared goals of getting safe and effective medicines to the patients that need them.

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Pfizer CentreOne Regulatory Affairs engages directly with regulatory bodies on your behalf for requests pertaining confidential information from the site or inquiries pertaining to Drug Master Files (DMFs) that we manage.

With a strong reputation for success, our Regulatory Affairs team helps you prepare briefing documents for your important regulatory meetings, but we do not participate in said meetings.

# Mutual Recognition Agreements (MRAs)

**The use of MRAs means certain regulatory bodies are now accepting compliance judgment from other MoHs. The US has an MRA with the European Medical Association (EMA) but has started a pilot to perform joint inspections for certain sterile injectable plants. The intention is to form common approaches to reconcile differences in regulatory viewpoints and ultimately support more efficient industry compliance.**

## Currently, the EMA has MRAs with the following countries:

- Australia
- Canada
- Israel
- Japan
- New Zealand
- Switzerland
- United States

# ICH Guidelines

**The ICH recently proposed ICH Q12 to support quality and safety goals. According to ICH, the guidance is intended to fix issues with implementation of ICH Quality Guidelines Q8, Q9, Q10 and Q11.**

**ICH Q12 was promulgated because pharma's experience implementing and following the previous ICH guidelines had not been as successful as regulators had hoped. A review of compliance practices revealed:**

Technical and regulatory gaps that limited the full realization of more flexible regulatory approaches to post-approval **Chemistry, Manufacturing and Controls (CMC) changes described in ICH Q8.**

More defined guidance to address the commercial phase of the product lifecycle described in **ICH Q10.**

# Agility

**The industry needs to be sufficiently agile to accommodate new kinds of treatment and to address unmet medical needs. This has led to fast-track pathways, increased regulatory harmonization and a greater drive for efficiencies across the development and manufacturing process.**

# Expedited Approval Pathways

**These pathways seek to fast-track medicines that make a significant impact or fill an unmet need.**

**Accelerated Assessment (AA)** – is awarded for medicinal products of major public health interest and from the viewpoint of therapeutic innovation. The time for assessment by the regulators is reduced from the 210-day maximum to a 150-day maximum.

**Conditional Marketing Authorization (CMA)** – is granted to a medicinal product fulfilling an unmet medical need when the benefits to public health of immediate availability outweighs the risk inherent when additional data are still required. It's a "temporary authorization" based on less than complete clinical data, which is normally expected for a given therapy. The MAH provides more data post-licensing in a pre-agreed timeframe and then converts to a full marketing authorization.

**Authorization under Exceptional Circumstances (AEC)** – is awarded with even less data than CMA in very rare diseases and is not expected to ever convert to a full marketing authorization.

# Expedited Approval Pathways (continued)

**PRIME** – a voluntary scheme launched by EMA to enhance support for the development of medicines that target an unmet medical need. This is awarded in early clinical development stages for medicinal products that are of major interest from the point of view of public health and therapeutic innovation. PRIME is built upon the existing regulatory framework, and it was introduced to help drug developers with innovative products engage earlier with regulators to help ensure the final data package is suitable for accelerated assessment.

**Fast-Track** – a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier.

**Breakthrough Therapy Designation (BTD)** – a therapy intended to treat a life-threatening disease when clinical evidence indicates the drug may demonstrate substantial improvement over existing therapies.

**Accelerated Approval** – These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint. Using a surrogate endpoint enabled the FDA to approve these drugs faster.

**Priority Review** – This designation directs overall attention and resources to the evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications. It means the FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review).

**Priority Review** – a fast-track regulatory pathway that accelerates the development of drugs with 'significant clinical value.'

**Conditional Approvals of New Drugs** – Includes technical guidelines for the conditional approval of urgently needed drugs.

**Urgent Drugs Fast Approvals** – Identifies a list of 48 drugs that are already approved overseas, which are 'urgently needed in the clinical setting.' Drug companies are able to provide evidence of a therapy working equally well across races can immediately apply for marketing approval and be eligible for Priority Review.

**Priority Review** – available for treatments where the drug is expected to help improve the quality of healthcare and in targeting serious disease.

**Conditional Early Approval Systems** – have been introduced to put drugs proven to be effective for treating serious diseases into practical use as soon as possible.

**Sakigake Designation** – for innovative medical products aimed at treating serious diseases where prominent effectiveness is expected based on non-clinical and early phase clinical studies. This designation results in prioritized consultation and review.

# Combination Product Regulations

**Combination product regulations continue to evolve globally towards more harmonized definitions that can be used in multiple markets to facilitate the go-to-market process. There are still some key differences in regulatory approach to be aware of:**

The US FDA has been developing and defining the regulatory pathways for combination products for the past 20 years. From these efforts, clearly delineated regulations that govern the development and commercialization of a combination product have been created, such as:

**21 CFR** Parts 3.2 (e), 4 (Subpart A) and 820, Part 11, Parts 210 & 211, 600 & 610 in the United States,

Principles of Premarket Pathways for Combination Products, Guidance for Industry and FDA Staff, Draft, February 2019

There is no legal definition for “combination products” in the EU. Drug-device combination products (DDCs) are regulated either as medicinal products or medical devices, depending on their principal intended action.

However, DDC product development must integrate aspects of both drug and device regulations.

The new MDR requires that marketing authorization applications for drugs incorporating integral delivery devices include a Notified Body opinion on the conformance of the device constituent with the MDR general safety and performance requirements.

Co-regulation between drug agencies and Notified Bodies may lead to extended regulatory review timelines and unnecessary duplication of assessments. Regulatory guidelines are being developed to address this e.g. the draft EMA guideline on the quality requirements for drug-device combinations.

# Information Modeling

**Using data in a more efficient way to create greater efficiencies in the drug development process is becoming more common across the globe. Using information modelling can have a significant effect on speed-to-market and regulatory success and is a vital way of managing resources more effectively.**

**Model-Informed Drug Development (MIDD)** – The FDA is conducting a MIDD Pilot Program to facilitate the development and application of exposure-based, biological, and statistical models derived from preclinical and clinical data sources.

The EMA's **Modeling and Simulation Working Party (MSWP)** supports the development of guidelines on modeling and simulation relating to medicine development, e.g. Guideline on the reporting of physiologically based pharmacokinetic (PBPK) modelling and simulation, Reflection paper on the use of extrapolation in the development of medicines for paediatrics, etc.

In its **Regulatory Science to 2025** plan, the EMA has proposed strategies to optimize capabilities in modelling, simulation and extrapolation.

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