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REVIEW ON REGULATORY SCIENCE TRANSLATIONAL MEDICINE: FDA'S COMMITMENT OF ADVANCING PUBLIC HEALTH

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ABSTRACT

US FDA's commitment to advancing public health through regulatory science and translational medicine is paramount in ensuring the safety, efficacy, and timely availability of medical products. Regulatory science encompasses the application of scientific principles to inform regulatory decision-making, while translational medicine focuses on translating research discoveries into tangible medical interventions. USFDA plays a pivotal role in this field by actively collaborating with stakeholders, researchers, and industry experts to develop and implement rigorous regulatory standards. By fostering innovation and streamlining the approval process, the FDA expedites access to novel therapies without compromising patient safety. Through its dedication to translational medicine, the FDA facilitates the translation of groundbreaking research into practical applications, addressing unmet medical needs and improving patient outcomes. Expedited pathways and breakthrough designations further accelerate the development and review of promising treatments, providing hope for patients facing serious or life-threatening conditions. This study explores the critical role of the FDA in regulatory science and translational medicine and its significant impact on public health advancement by striking a balance between innovation and risk assessment, the FDA remains at the forefront of regulatory agencies worldwide, safeguarding public health while fostering the progress of transformative medical solutions.

Keywords: OTS, CDER, Scientific, Data, Research

INTRODUCTION

The term "translation" is widely used to describe the process through which a biological observation gets transformed into an intervention that improves health. "Translational science" is the study of the translational process in order to define its guiding scientific principles, thereby shifting translation from empiricism to predictivity, as it has in other sciences before it **[1]**. Translational science, like all sciences, begins with findings that cannot be explained by present theory; in this case, the observation that the avalanche of successful fundamental discoveries has not resulted in the anticipated therapeutic windfall. Understanding and correcting the causes of this apparent discrepancy is critical to science's promise of reaching all people in need, and it will have a significant impact on how the public perceives science the success of the medical science enterprise and their investment in it **[2]**.

Origin of OTS:

- The Office of Translational Sciences **(OTS)** in collaboration with **the Office of Communications (OCOMM)** in the **Centre for Drug Evaluation and Research (CDER) [3]**.
- It features new developments, opportunities, and initiatives in regulatory science, with the goal of advancing medical product development **[4]**.
- The OTS Immediate Office supports translational medicine efforts for CDER and leads the areas of technology transfer, data mining, health information technology, science and research oversight and knowledge management **[5]**.

Need of Translational science:

The term "translational science" has been used to describe the practise of a variety of scientific disciplines (chemistry, biostatistics, regulatory, clinical trials, etc.) to do translation for a specific target or disease; however, NCATS uses the term to describe the study of translation itself, as a means to accelerate progress in translation performance **[6]**. NCATS defines science as an "intellectual and practical activity encompassing the systematic study of the structure and behaviour of the physical and natural world through observation and experimentation." **[7]**

Core function of USFDA on Office of Translational science:

- The Office of Translational Sciences (OTS) supports the mission of the U.S. Food and Drug Administration (FDA) through a variety of efforts, including by contributing directly to drug evaluation and supporting the

advancement of science by facilitating the conduct of research throughout the medical product life cycle **[8]**.

- Perform core regulatory review efforts and applied regulatory research, facilitate scientific collaborations, and manage intramural and extramural research programs **[9]**.
- In addition to engaging directly with government and nongovernment entities to develop methods, approaches, tools, and standards to streamline drug development, OTS helps other offices in CDER develop collaborations with non-FDA researchers to stimulate innovation in the development, manufacture, and safe use of drugs **[10]**.

OTS Organization Chart:

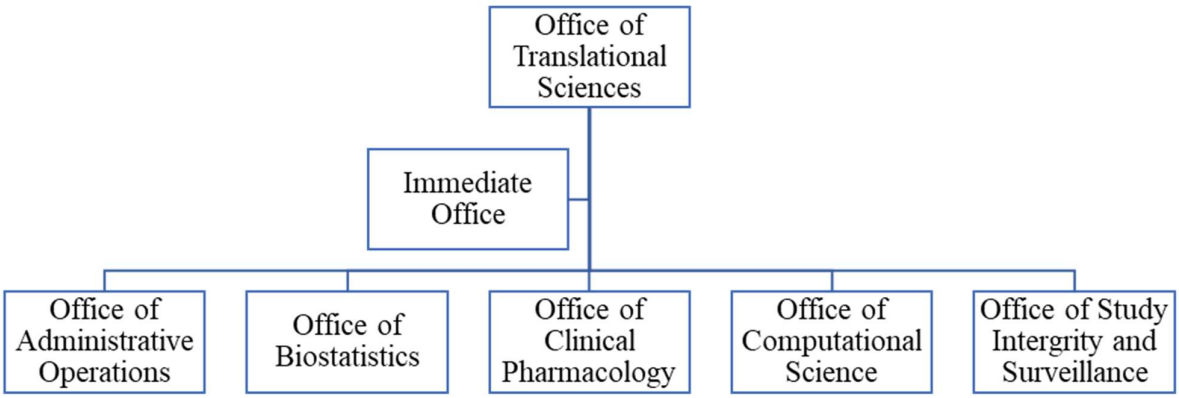

Figure 1: Office Of Translational Science Organization Chart

Office of Administrative Operations (OAO)

OAO provides internal customer service support to enable the OTS scientific, medical, and technical staff to focus on our mission with fewer administrative burdens **[11]**.

Office of Biostatistics (OB)

OB plays a central role in promoting innovative, science-based, quantitative decision-making throughout the drug development life cycle. To support CDER's mission, OB provides statistical leadership, expertise, and advice to ensure that safe and effective drugs are available to the American people **[12]**.

Office of Clinical Pharmacology (OCP)

OCP advances development of innovative new medicines by applying state-of-the-art regulatory science and clinical pharmacology principles. We promote therapeutic optimization and individualization through best practices in research, policy development, and drug

evaluation throughout the product life cycle **[13]**.

Office of Computational Science (OCS)

OCS provides CDER reviewers with innovative, reliable solutions to improve and strengthen the scientific review process by integrating data, tools, and training **[14]**.

Office of Study Integrity and Surveillance (OSIS)

OSIS ensures that data supporting regulatory decisions are reliable by conducting and directing inspections of bioavailability/bioequivalence and nonclinical good laboratory practice studies submitted to FDA **[15]**.

Immediate Office (IO)

The IO supports five suboffices in OTS and engages in activities that focus on business transformation strategy; data analytics and technology assistance; data mining; guidance, policy, and communications; health information technology; knowledge management; strategic partnerships and technology transfer; science and research oversight; scientific collaborations; and training and career development **[16]**.

OTS Efforts to Support Drug Development:

- Regulatory Review Capacity and Expertise
- Inspectional Capacity and Expertise
- Regulatory Science Research
- Guidance and Policy
- Stakeholder Engagement
- Pilot Programs/ Innovative Approaches and Tools Knowledge Management and Communication **[17]**

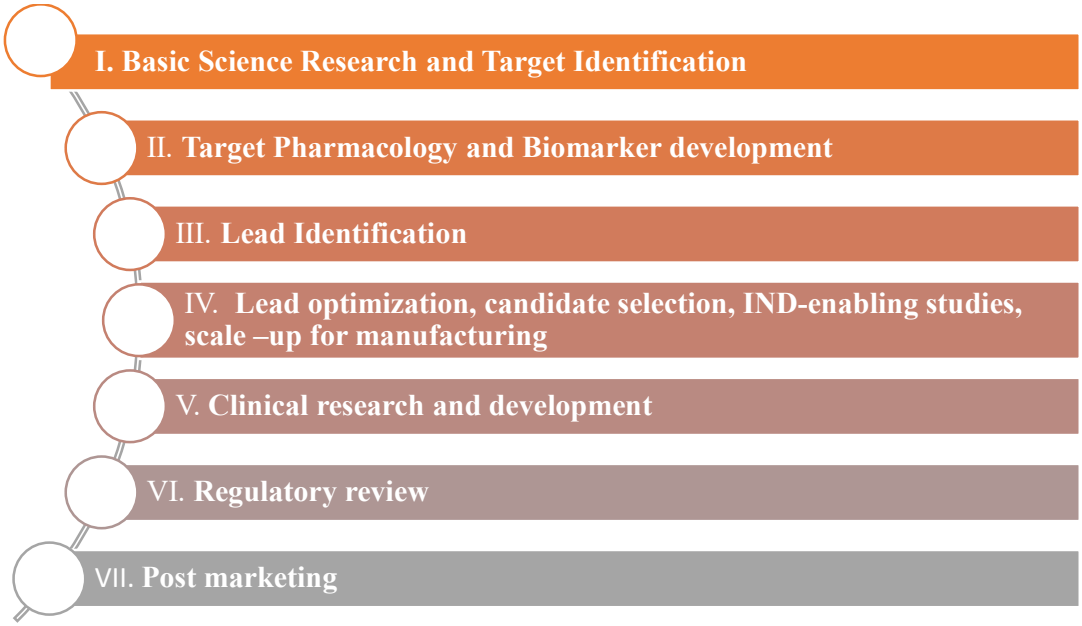

Figure 2: Map For Translational

Functions of OTS:

- Promoting scientific collaboration and innovation in drug regulatory review across the Centre for Drug Evaluation and Research (CDER)
- Assuring the validity of clinical trial design and analysis in regulatory decision-making
- Developing and applying quantitative and statistical approaches to decision making in the regulatory review process
- Ensuring alignment of CDER research with CDER goals
- Serving the CDER scientific community in establishing technology transfer agreements that are vital to collaboration with the broader scientific community
- Maintaining knowledge management databases that can be the basis of improvements in the regulatory review process
- Overseeing bioavailability/bioequivalence and nonclinical inspections to help ensure the availability of safe and effective new and generic drugs **[18]**

Addressing Public Health Emergencies:

- OTS continued its efforts to help curb the COVID-19 pandemic. Staff expedited the review of monoclonal antibodies and antivirals by providing drug development guidance, supporting dose optimization, extrapolating data to paediatric populations, developing models, and helping to determine drug product efficacy in the presence of emerging variants.
- OTS creates and makes available sources of knowledge that enhance operational efficiency and regulatory decision-making. The office also cultivates a variety of dynamic collaborations with internal and external stakeholders to advance solutions to our most pressing challenges **[19]**.

Translate Knowledge into Sound Dosing Recommendations:

- Evaluated drug candidacy by comparing in vitro antiviral activity in relation to clinically achievable concentrations for repurposed drugs
- Explored relationships between drug exposure and disease severity to better understand effects of COVID-19 on pharmacokinetics to inform treatment regimens
- Integrated known pharmacokinetic and pharmacodynamic information, mechanism of action, in vitro activity, neutralization assays, viral dynamics, preclinical animal efficacy models, and prior clinical

experience to predict safe and efficacious dosing regimens

- Used predictive modelling incorporating antiviral/neutralization activity against variants, duration of protection, and exposure targets to inform alternative routes of administration and dosing strategies for prevention **[20]**.

Expand Treatment Options for Diverse Populations:

- Applied knowledge of pharmacodynamic response (interleukin levels and receptor saturation) in COVID-19 pneumonia to evaluate proposed dosing regimens in paediatric patients
- Evaluated weight-based dosing strategies in adult patients to ensure adequate exposure to COVID-19 treatments
- Recommended pharmacokinetic sampling strategies and integrated mechanism of action, pharmacokinetic, and exposure/response information to inform dosing in patients with renal impairment
- Used pharmacokinetic/pharmacodynamic knowledge and supportive modelling to understand the effect of patient factors, such as acute lung injury and conditions of high-risk disease, on treatment selection and dosing
- Utilized data from clinical studies, extrapolation, and model-informed methods to derive dosing recommendations for paediatric patients for treatment and prevention of COVID-19 **[21]**.

Formulate Strategies to Mitigate Risk:

- Encouraged comprehensive drug-drug interaction (DDI) evaluation strategies, model-informed methods, and protocol modifications to lessen drug interaction liability
- Evaluated alternative routes of administration using pharmacokinetic data, viral load reductions in patients, safety findings, and simulated dosing scenarios to ensure adequate exposure and reduce treatment delays
- Identified cardiac toxicity signals related to active metabolite concentrations and accumulation
- Optimized sampling approaches to assess the relationship between maximum concentration and unintended immunosuppressive effects

- Provided advice on ex vivo cardiac studies and clinical protocol design to characterize proarrhythmic potential and cardiac risk **[22]**

CONCLUSION

Regulatory Science Translational Medicine stands as a testament to the FDA's resolute commitment to advancing public health. Through this dynamic approach, the FDA has demonstrated its adaptability and foresight in navigating the rapidly evolving landscape of medical science and technology. By embracing innovative methodologies and collaborative partnerships, the FDA has expedited the translation of cutting-edge research into tangible solutions that benefit patients and consumers alike. This commitment to efficiency does not come at the expense of safety; rather, it reinforces the agency's dedication to upholding rigorous scientific standards and safeguarding the well-being of the public. The FDA's emphasis on transparency and communication has fostered trust among stakeholders, ensuring that decisions are rooted in evidence and publicly accountable. By engaging with the industry, academia, and global regulatory bodies, the FDA strengthens its ability to address emerging health challenges with a comprehensive and internationally harmonized approach. As the world faces unprecedented health threats and opportunities, the FDA's dedication to Regulatory Science Translational Medicine paves the way for transformative advancements in medicine. From gene therapies and personalized medicine to digital health innovations, the FDA remains at the forefront of regulatory science, enabling the responsible and timely integration of breakthroughs into healthcare practice. Looking forward, the FDA's commitment to advancing public health through Regulatory Science Translational Medicine will continue to shape a healthier, more resilient society. As research and technology continue to evolve, the agency's proactive and patient-centric approach will play a pivotal role in promoting innovation while ensuring the utmost safety and efficacy of medical products for the benefit of the nation and the global community.

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CONFLICT OF INTEREST

The authors declared that there is no conflict of interest.

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