Key regulatory elements for accelerating the drugs/cell therapy/diagnosis in PRONAII

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Abstract

The Strategic National Programs (PRONACES) are institutional efforts led by the National Council of Science and Technology (CONACyT) to look for solutions to priority national problems, among them, those related to health. Due to their impact on the public health, pediatric leukemias are a huge challenge not only in Mexico, therefore multidisciplinary teams must develop strategies that contribute to decreasing the mortality rate of this disease in Mexican childhood. One of the National Projects of Research and Outcome (PRONAII), a part of PRONACES, has been focused on pediatric leukemias. To augment the possibilities of a lab bench discovery becoming a product that accomplishes the regulatory requirements to be in the market, it is mandatory to accomplish certain kinds of practices depending on the stage and area of the development (GLP, GCP, and GMP), pediatric leukemia investigation is not an exemption. This work aims to identify the most important regulatory elements to take into consideration to accelerate the process for Mexican authority's approval of the developments achieved by the researchers involved in any of the projects of the PRONAII of pediatric leukemias, accordingly with the stage of their developments and the area. The three main areas of this PRONAII are: 1) Diagnostics (phenotyping and genotyping); 2) Drugs (new developments and off-label use); and 3) Cell Therapy (e.g. T-CAR cells, allogenic T regs cells).

Normative and Legal National framework

DRUGS	CELL THERAPY	DIAGNOSIS
NOM-059-SSA1-2015 Buenas Prácticas de Fabricación de Medicamentos. **NOM-073-SSA1-2015** Estabilidad de fármacos y medicamentos. **NOM-177-SSA1-2013** Que establece las pruebas y procedimientos para demostrar que un medicamento es intercambiable. Requisitos a que deben sujetarse los Terceros Autorizados que realicen las pruebas de intercambiabilidad. Requisitos para realizar los estudios de biocomparabilidad. Requisitos a que deben sujetarse los Terceros Autorizados, Centros de Investigación o Instituciones Hospitalarias que realicen las pruebas de biocomparabilidad. **NOM-249-SSA1-2010** Mezclas estériles: nutricionales y medicamentosas, e instalaciones para su preparación. **NOM-257-SSA1-2014** En materia de medicamentos biotecnológicos.	Reglamento de la Ley General de Salud en materia de control sanitario de la disposición de órganos, tejidos y cadáveres de seres humanos. NOM-253-SSA1-2015 Para la disposición de sangre humana y sus componentes con fines terapéuticos. PROY-NOM-260-SSA1-2017 Para la disposición de células troncales y progenitoras con fines terapéuticos y de investigación.	NOM-241-SSA1-2012 Buenas prácticas de fabricación de dispositivos médicos. NOM-137-SSA1-2008 Etiquetado de dispositivos médicos. NOM-007-SSA3-2011 Para la organización y funcionamiento de los laboratorios clínicos

VALID FOR ALL AREAS

- Constitución Política de los Estados Unidos Mexicanos
- Ley General de Salud
- Reglamento de la Ley General de Salud en materia de control sanitario de actividades, establecimientos, productos y servicios
- Reglamento de la Ley General de Salud en materia de investigación para la salud
- Reglamento de Insumos para la Salud
- Ley Federal y reglamentos de protección de datos personales en posesión de particulares

Technology Readiness Levels (TLR)

From the idea to the market

Researchers must identify the TLR of theirs (I+D+i) activities. Schematization of the organization of related activities with research, technological development, and innovation, with an adaptation of the scheme TRL.

Research Process

Research Protocol

Technical-Scientific relevance of the proposal

Applicable Committees (Ethics in Research, IACUC, Biosafety)

Execution

Standardization and validation of techniques under QMS

Recruitment and treatment of individuals (if applicable) or running the experiments *in vitro* or *in vivo* (animals) under QMS

Final Report

Recopilation and analysis of results under QMS

Final report containing all assays individual reports approved by QA

IACUC: Institutional Animal Care & Use Committee
QA: Quality Assurance
QMS: Quality Management System

Quality Assurance

GLP: Good Laboratory Practices
GMP: Good Manufacturing Practices
GDP: Good Documentation Practices
GCP: Good Clinical Practices

The personnel must have training and qualifications in the study area (Director of study, analists, tech personal, among others).

Periodical calibration of equipment/ instruments and volumetric material

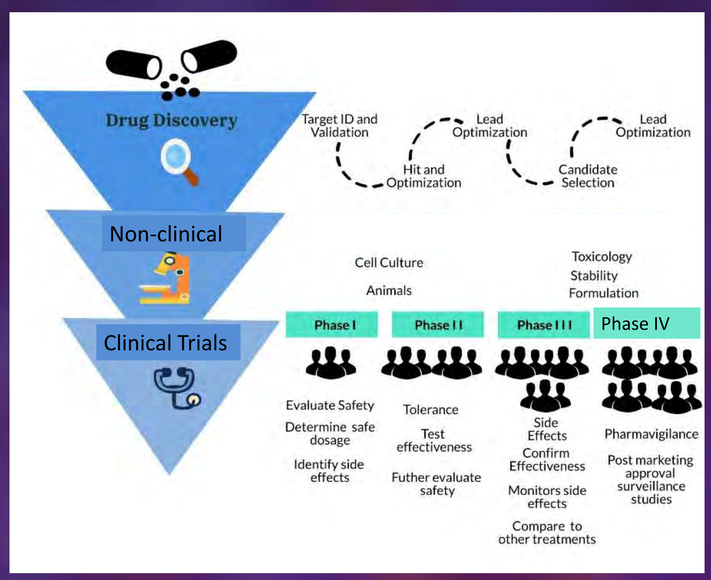
Quality of reference standards, analitycal reagents, and chemicals.
Records and supervision of the preparation of standard solutions and reagent solutions

Proper documentation of analitycal methods, specifications, protocol, results, and reports.
Validation of analitycal methods specially non-pharmacopoeial

Regulatory requirements for the approval of a drug

	GLP	GCP and GMP	GMP
Stage 1	Stage 2	Stage 3	Stage 4
Research and Discovery	Non-clinical	Clinical	Post aproval
Study based		Process based	

Drug discovery and development process



The process to achieve that a drug be authorized for human use can be divided into two parts, the non-clinical phase which involves drug discovery, and the clinical phase which entails drug development along with the clinical trials (from phase I to phase IV).

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Summary

Pediatric leukemia is a major health problem in México, therefore federal government efforts have been deployed through the specific PRONAII. Overall, in order to accelerate the progression of the new developments made by the researchers in this PRONAII to achieve the authorization by the Mexican regulatory authority (COFEPRIS), it is mandatory that these scientific community take into account different essential aspects such as the type of national normative and legal framework applicable for the specific area; the stage of TRL of their developments; the compliance with a QMS; and the accomplishment of GLP, GDP, GCP, and GMP depending on the stage of these and that be applicable for their area. Once all this elements being full-fitted, there will be high likelihood of approval of their developments that will contribute to Mexican children.

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