Strengthening the innovation ecosystem in India

Subgroup 1: Regulatory

Session Document

July 2020

Subgroup created to draft and finalize policy on Regulatory Issues

Subgroup created to simplify regulatory hurdles to enable rapid drug discovery and development

The sub-group, after detailed deliberations, submitted their report to the core group on the specific issues allotted to them

Consolidated draft report created by subgroup

4 pre-defined objectives of the subgroup

Objective	Scope
Identify issues and challenges	Identify the current issues and challenges in the existing regulatory structure and requirements
Study global best practices	Study global best practices based on USFDA and European regulatory systems
Propose interventions	Use the learnings from global best practices to identify interventions in Indian context to simplify regulatory structure and requirements
Frame policy	Frame policy for accelerated drug approvals under various categories

Constitution of the Regulatory subgroup

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Chairman
Executive Chairman, Biocon Limited

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Contents

Indian Innovation will need enabling and globally benchmarked regulations

Deep dive ahead

Challenges	Detailed description
Processes	**Multi-ministerial rounds of regulatory approvals** leading to inordinately long timelines **Need for defined timelines for regulators** to review and respond
Guidelines	**Need for defined guidelines** across drug classes. *(e.g. Biosimilar Guidelines were well thought out based on risk rationalization and key clinical & quality criteria)*
Predictability	**Improved visibility (real time tracking)** of applications through online submissions at various stages
Regulatory Capacity	**Strengthen capacity in regulatory bodies to augment capabilities** **Improved consistency in expert guidance/ regulatory processing.**
Governance	**Need for dedicated project management capacity** for new drug applications to optimize review and approval timelines.

Access & Affordability

Safe, Efficacious & Quality Medical Products

Guiding Principles

India’s aspiration to innovate will require a regulatory system in line with International guidelines.

Abbreviated Regulatory pathways must be based on a robust regulatory review process that has scientific justification.

Addressing the country’s socio-economic necessities through essential and unmet medical needs must drive pharmaceutical innovation. Affordable access must be the driving principle.

Digital platforms must aim to deliver efficiency, predictability, transparency and confidentiality.

Fast track regulatory pathways must address national emergencies, new technologies, orphan and rare diseases and life saving therapeutics

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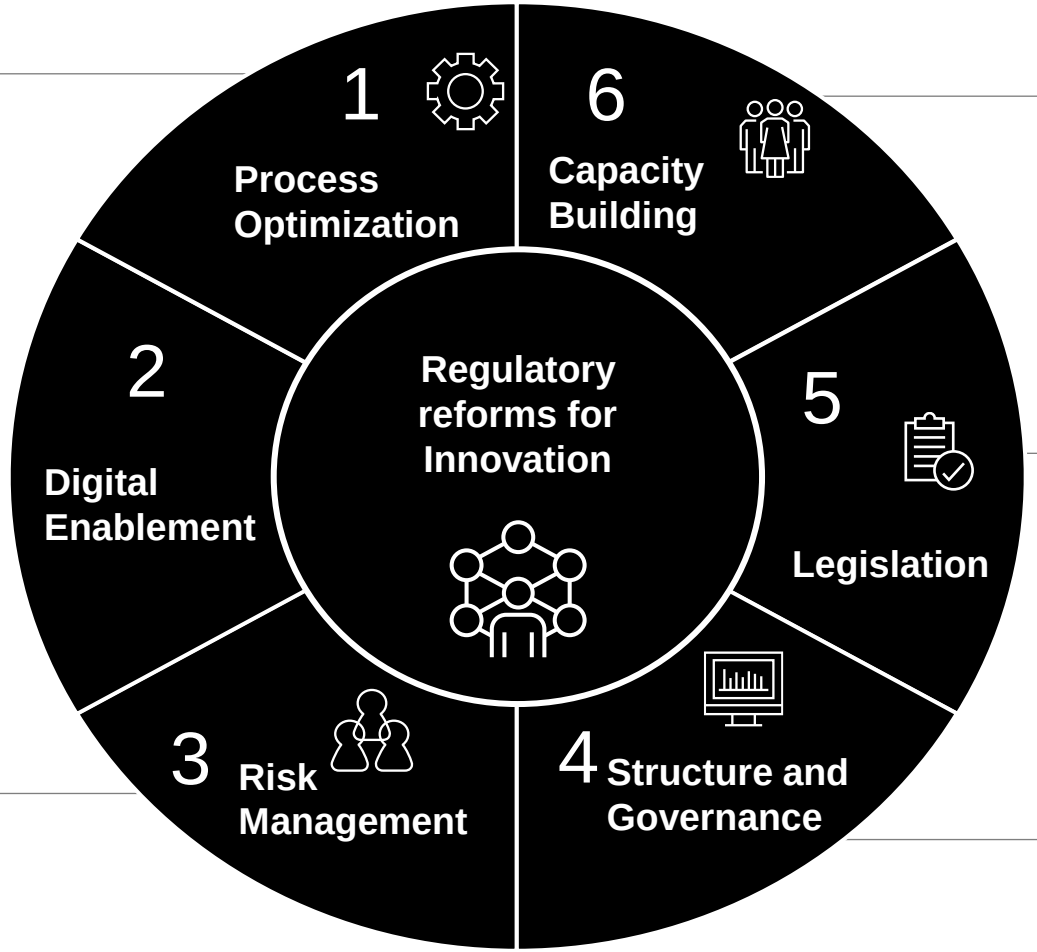
6 critical areas identified requiring immediate interventions to streamline regulatory ecosystem

Parallel processing of steps to minimize delay

Deemed approval (Time bound) and **Automatic approval (immediate)** for specific steps

Pre-defined **process checklists**

Pre-submission discussions for specific queries



Dedicated **project management office**

Build specific capacity (e.g. Empaneled labs for Diagnostics, Med Devices & Vaccines)

Onboarding of expert panels based on disease domains

Exemption of cultured and cultivated bio-resources from Biodiversity Act

Single End to End digital portal for seamless data **transfer and upload** to sub portals across departments and **automatic certificate generation** post step completion

Predefined procedural calendar for approval process

Electronic submission of documents and dossiers on a common portal

e-application status and tracking

Validation of submission for final review (checklist)

Risk based approach for regulatory efficiency

Risk mitigation approach through clinical and regulatory holds

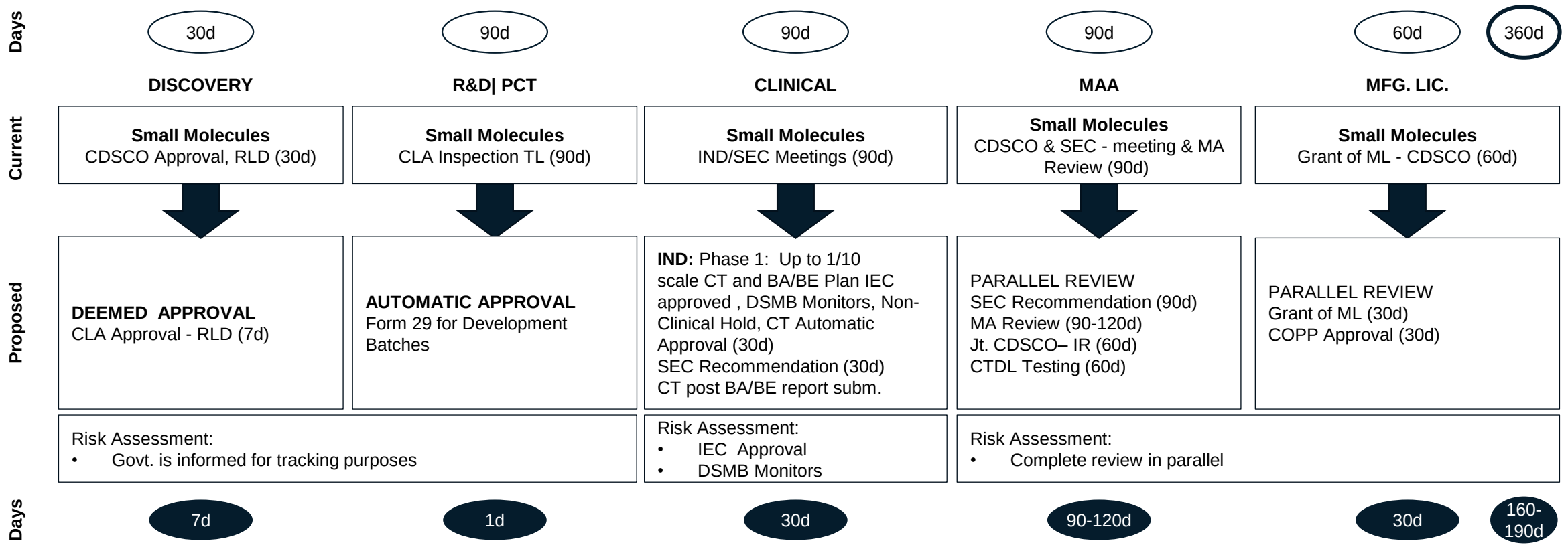
1,3: Process Optimization to reduce approval timelines

(NCE/Small Molecules, r-DNA products, Recombinant Vaccines, Non r-DNA vaccines, Products in Orphan drug/ Rare disease, Products for additional indication, Products in Restricted Emergency Use Authorisation (EUA) Stem cell, Cell Therapy Regenerative Medicines , Medical Devices)

Initiative	Detailed Description	Examples
Parallel processing	**Initiate parallel processing of critical steps that are not dependent on each other** to reduce the critical path for approval timelines	Parallel to RCGM, submit application in Form CT-04/CT-04A to DCGI to conduct CT Parallel to MAA, completion of Joint Inspection (if required) and submission of CTDL/NIB Testing report to CDSCO, HQ
	Reduction of overlapping approvals	For granting approval for initiation of research of biologics – Approval by IBSC and notification to RCGM
	Allow commercial manufacturing while application is under review	Allow commercial manufacturing of DS & DP under Form-29 license while drug is undergoing regulatory approval & permit marketing of these batches once manufacturing permission is received
Deemed approval (Time bound) and **Automatic approval (immediate)** for specific steps	**Deemed approval of steps post completion of pre-defined timelines**. i.e certain steps to be made deemed approval unless regulatory body finds an issue with the submission within stipulated time limit	CLA approval for RLD in 7 days Clinical trial initiation by CDSCO in 30 days RCGM clearance in 30 days
	Automated(immediate approval) for specific steps using risk based approach	Product already approved by Global regulator such as USFDA, EMA, PMDA, HC and TGA should be approved in India via automatic route Approval for import of cell lines and micro-organism strains for R&D work should be by automatic approval Phase IV studies (PMS studies/ RWEs/ Registry studies) conducted in approved labelled conditions (indication, dosage, dosage form and route of administration) should be allowed with an automatic approval from DCGI
Pre-defined Checklists and Pre-submission discussions	Create **detailed checklists for each submission step with digital capability to check completeness at the time of submission**	Separate checklist should be prepared for application for Phase I CT, Phase III CT and BA-BE studies (wherein extensive documents should not be required) Separate checklist for Phase I DS & DP should allow manufacturing under GMP-like conditions

Risk based approach for abbreviated regulations (e.g. Govt. is informed for tracking purposes during Discovery and R&D PCT stage)

Regulatory Pathway for NCE/Small Molecules: LAB TO LABEL



Efficiencies achieved through carrying out activities on-line, time bound deemed/automatic approvals and in Parallel reviews and inspections without any Compromises

Proposed Regulatory Pathway for NCE/Small Molecules: LAB TO LABEL

Parallel work

Timelines-160 - 190 Days

(Lab to Label)

1. Discovery
7 Days

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

7 days/Deemed Approval

2. R&D - PCT
1 Day

Grant of TL under **Form 29** to mfg. developmental batches – **Automatic Approval**

No CT-11 requirement (at Development & CT/consistency batches stages)

NCE: PCT will be conducted on both small and large animals based on IAEC approval, no other approval required. For large animals, CPCSEA and Dept. of Agriculture to be notified

3. CT and/or BA/BE
30 Days

Submit application in Form CT-04/CT-04A/CT-05 to DCGI to conduct CT and/ or BA/BE

IND / SEC meeting and recommendation (for 1st Applicant in India)

Form CT-06/ CT-04A/CT-07 from CDSCO to conduct CT or BA/BE- **30 days**, if not received within 30 days shall be deemed approval

Permission to start CT post submission of BA/BE report

Minor CT or BA/BE PAC - Protocol Amendments approved by DSMB/IEC and notification to CDSCO, HQ

4. MAA
90-120 Days

Application in Form CT-21 to CDSCO, HQ with CT and/or BA/BE report & CTD module for MAA

IND / SEC meeting and recommendation (for 1st Applicant in India)

Parallel to MAA, EIR & CDTL Testing report to CDSCO, HQ - **60 days**

Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) & Packaging (Label/Carton/PI)

Approval **90-120 days based on complexity and novelty.**

5. Mfg License
30 Days

Application in 24/27 for grant of mfg. license in Form 25/28

Grant of Form 25/28 30days

Application for COPP/WHO GMP Certificate

with PV/ consistency batches manufactured before MA Approval

COPP/WHO GMP Certificate Approval for Export registration 30days

2: Digital Enablement: Single End to End digital portal for seamless data transfer and upload

Initiative	Detailed Description
Single end to end digital portal	Creation of a single end to end digital portal used by different departments to be **hosted by CDSCO** **Interconnected portal** with automated transfer of data across departments and sub-departments (e.g. all data pertaining to RCGM would flow there, and automatic/deemed approval would be generated) Leverage **virtual platform** for all sponsor meetings
Online Submission of all applications	**All submissions to be made online with pre-defined checklists** (e.g. Shift of post approval changes applications to CDSO online portal SUGAM with defined timeline from current manual **Enable upload of all documents on integrated portal** (Some of the documents in particular sections cannot be uploaded. In SUGAM e.g. BE protocol - CRO center approval, Ethics Committee approval, No death declaration certificate In case of CTs, **streamline reporting of SAEs** by adopting uniform template and leveraging online platform
Online tracking of application status	**Live tracking of status** of application with current stage and timelines to be visible online **through password protected access** Detailed scientific reason to be provided for additional requirement through the online portal with timeline commitment
Automated Certificate generation	Requisite certificates post completion of different stages to be generated on online portal at every step Summary of approval with inputs from SEC, DSMB to be published publicly
Address SUGAM related issues	**Dedicated technical team for SUGAM**, to solve the issues on priority and timelines to be fixed for resolving the issue related to SUGAM

4: Structure and Governance: Setup governance mechanism to increase transparency

Initiative	Detailed Description
Pre-defined procedural calendar for each approval step	**Establish clear timelines** for each stage of process (e.g., responding to queries or protocol amendments) and ensure performance management on the agreed timelines to ensure no slippages
Enhanced Predictability and collaboration	Creating **visibility on review status** through the approval steps on online portal Actively **engage with industry to collect feedback** as FDA does through its quarterly meetings with the industry groups Appoint a **single point of contact** or project manager (similar to EMA's rapporteur) **Confidentiality of Sponsor and sponsor's data** to be ensured with access codes and password protection
Performance management	**Identification of key metrics;** tracking and quarterly publishing of performance on them **IND and SEC calendar to be published** on website, while ensuring adequate meeting frequency to meet approval timelines

5: Legislation: Exemption of cultured and cultivated bio-resources from Biodiversity Act and Empowering Institutional bodies for approving pre-clinical protocols

Initiative	Detailed Description
Exemption of cultured and cultivated bio-resources from Biodiversity Act	Products that are cultured and cultivated artificially under controlled conditions are essentially not impacting natural resources and effectively biodiversity of the country and hence should exempted from The Biological Diversity Act
Empower Institutional bodies for approving pre-clinical protocols	Institutional Animal Ethics Committee (IAEC) to be on par with Institutional Bio- Safety Committee (IBSC) to permit regulatory approvals for pre-clinical activities RCGM and CPCSEA both have nominees on IBSC and IAEC, so as to have the representation of CLAs to fulfil statutory requirement Thereby, for all pre-clinical studies, approval to be received from Institutional body (IAEC/IBSC) with notification to CPCSEA/RCGM IAEC should have authority to approve toxicity studies in large animals with notification to CPCSEA and Department of Agriculture
Reduce Repeated joint inspection for products within same facility	In case of Vaccines and Biologics for a particular class of product, joint inspection by CDSCO and State FDA and should be conducted only once, as parallel activity for marketing authorization Such activity should not be repeated for a new product within same class of drug manufactured within same facility, which has already been inspected before

5: Legislation: Facilitation of contract and clinical research, and Simplification of import and marketing of products

Initiative	Detailed Description
Facilitate contract and clinical research	Develop/ revamp process for Phase I CT for drugs developed outside India and for foreign funded trials Define guidelines for CT insurance based on industry best practices Permit automatic approval for coded molecules in early discovery stage, at a point where these are not recognized as drugs Permit automatic approval for import of animal tissue and other biological samples for conduct of in-vivo and in-vitro studies
Simplification of import and marketing permission	Current three-tier process for import and marketing permission can be made into a single tier process (one application and one approval) while bringing down the time from ~310 days to ~130 days
Exemption of animal toxicity and testing	In case of drugs approved in ICH countries and where complete data is available in public domain (FoI Act, Summary basis for approval), if the Sponsor's data meets Innovator specifications, then 4-week toxicology studies should be exempted

6: Capacity: Enhanced capacity of regulator to improve efficiency and reduce timelines

Initiative	Detailed Description
Project Management team	**Set up project management roles** in the regulatory body to act as single-point-window for industry (for NCEs and NBEs)
Empanelment of Labs	Build specific capacity through Empanelment of Labs for Diagnostics and Med Devices Class A & B Medical devices and may be certified by accredited labs notified by NABCB (both private & public) for approval by CDSCO
Capacity building collaboration and programs	**Dedicated capacity building program (**e.g. Center for regulatory excellence at NIPER's) **Improve level of collaboration with international agencies** to enhance experience/ exposure of Indian regulators on new drug approval Build **panel of internal experts** who can **evaluate and approve applications** which may not require an SEC opinion. The panel can have a mix of clinical and pre-clinical expertise

Outcomes to be targeted through pre-defined metrics

Product/ Permission type	Target duration of Approval in India (in days)	Percentage of approvals within time limits
NCEs/ Small Molecules	160-190	>90%
r-DNA products	160-190	>90%
r-DNA Vaccines	160-190	>90%
Non r-DNA Vaccines	160-190	>90%
r-DNA/NCE/Small molecules in Orphan/ Rare diseases	r-DNA : 110-140 NCE/Small molecules : 100-130	>90%
Additional indication of r-DNA/NCE/Small molecules	After Innovator : 7 Before Innovator :45	>90%
r-DNA/NCE/Small molecules in Restricted Emergency Use Authorisation (EUA)	r-DNA: 80-110 NCE/Small molecules : 70-120	>90%
Stem Cell, Cell Therapies Regenerative Medicines	160-190	>90%

CONCLUSION

If Indian R&D is to be globally competitive, we need to have a regulatory process that is simple, seamless, digital and above all, robust and in line with international practices

There is need for a centralised and harmonised regulatory platform that delivers uniform processes across states.

There is a need for enabling regulations for the rapid development of drugs, vaccines and medical devices driven by robust, reliable scientific and clinical processes that deliver safe, efficacious and high quality products.

Product already approved by Global regulator such as USFDA, EMA, PMDA, HC and TGA should be approved in India via automatic route

Drug regulations must leverage the benefits of digital platforms and technologies that enable a virtual single window, parallel processing and transparency through tracking and tracing as well as confidentiality

All submissions will be password protected for confidentiality

All Post Approval Changes that cover manufacturing, facility expansion, label extension and label changes must follow an expedited pathway.

Testing capacity needs to be expanded to accredited/ government labs

Contents

Snapshot of the process and timelines of regulatory approvals process in India

Product type	Duration of Approval in India	Duration of Approval in Regulated Markets
Recombinant Vaccines	29-53 months	24-36 months
Non-recombinant Vaccines	21-35 months	24-36 months
NCEs	33-63 months	12-18 months
NBEs	50-85 months	12-24 months
Biosimilars	34-75 months	12-24 months

Global agencies are working towards getting vaccines approved in 12-24 months

Source: Data from various Pharmaceutical companies

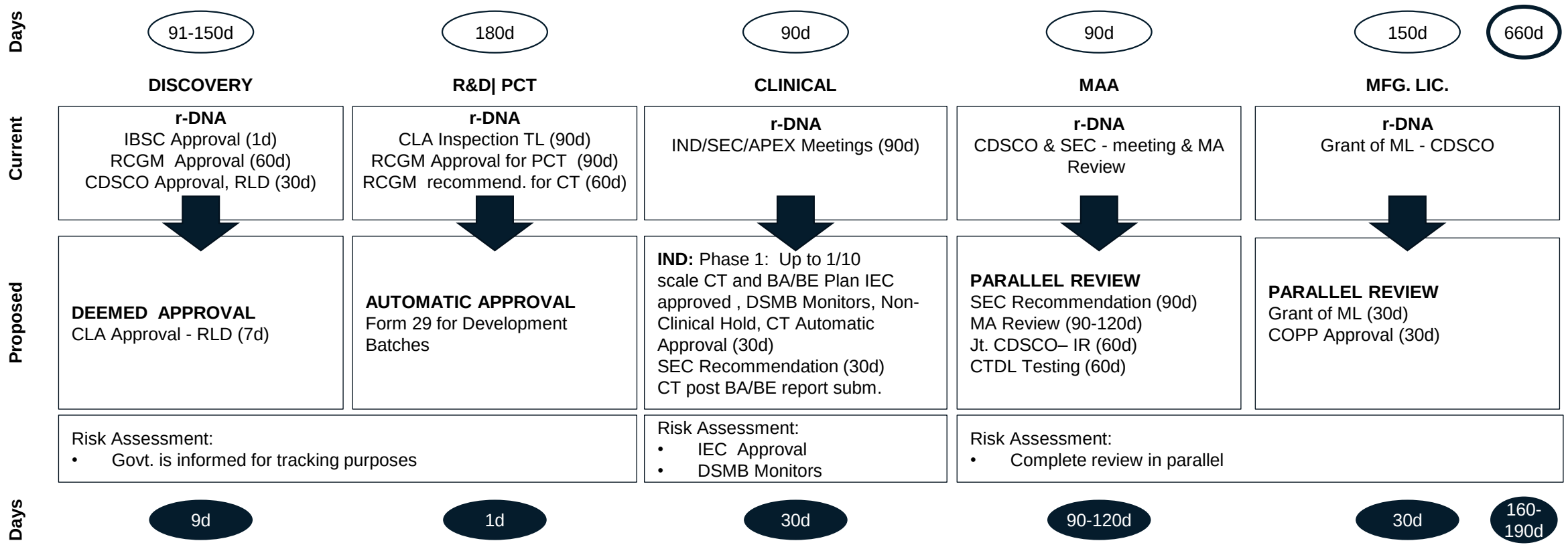
Global Examples: Best practices from leading countries in Innovation

Focus Area	Detailed description	USA	EU	Israel
Processes	**Duration of approval 30-50% less than India** (Details on previous page) driven by • Well-defined timelines for process – e.g., EMA takes 210 active days • Parallel processing of approval steps not linked with each other • Single body/portal for submission with automatic sharing and upload of data into sub-portals (e.g. USFDA) Regulators should provide clear timelines and clear target action dates			
Guidelines	600+ (in FDA) **detailed guidelines and pre-submission checklists** across several key areas (e.g., guidance on clinical study design);			
Predictability	**Detailed report shared** publicly and with applicant post approval/hold of a submission by USFDA Sponsor should be able to track the application in a predictable manner USFDA has a defined process to engage with Sponsors at every step for clarification in collaborative manner			
Regulatory Capacity	Leading regulatory bodies such as USFDA and Food & Nutrition Services of the Israel Ministry of Health have **dedicated project managers to act as single point of contact for industry** USFDA/EMA has therapeutic area wise in-house evaluation offices within FDA to build subject matter expertise			
Governance	**Commit and adhere to defined timelines for review and response** to provide a recourse (e.g. automatic approval) in case of no/delayed response **Metrics for performance management defined** (e.g., EMA provides procedural calendar)			

Appendix: Other Pathways

Process deep dive: r-DNA Products

Regulatory Pathway for r-DNA products: LAB TO LABEL



Efficiencies achieved through carrying out activities on-line, time bound deemed/automatic approvals and in Parallel reviews and inspections without any Compromises

Proposed Regulatory Pathway for r-DNA products: LAB TO LABEL

Parallel work

Timelines-160 - 190 Days (Lab to Label)

1. Discovery
9 Days

IBSC approval to import/ export /transfer/receive cell lines without quantity limit –

1 day RCGM approval not required for any quantity

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

7 days/Deemed Approval

IBSC recommendation for R&D initiation & notification to RCGM-Form C1

1 day /Automatic Approval

RCGM acknowledge in Form C-2 to initiate R&D activities-

(Automatic Approval)

2. R&D - PCT
7 Days

Based on IBSC recommendation, Grant of TL under Form 29 to mfg. developmental batches Automatic Approval– 1 day

No CT-11 requirement (at Development & CT/consistency batches stages)

Based on IBSC recommendation, PCT application in Form-C3 to RCGM as notification; approval not required

Submission of PCT report to RCGM for CT recommendation in Form C6 - **30 days**

RCGM parallel review of PCT report and send recommendation / query to CDSCO,HQ, CC to applicant

3. CT and/or BA/BE
30 Days

Parallel to RCGM, submit application in Form CT-04/CT-04A to DCGI to conduct CT

IND / SEC meeting and recommendation

Form CT-06/ CT-04A from CDSCO to conduct CT (Phase I, II & III) - **30 days**, if not received within 30 days shall be deemed approval (as opposed to 90 days in New Drug CT Rule 2019)

Minor CT Protocol Amendments to be approved by DSMB and notification to CDSCO, HQ . Currently, all protocol amendments require CDSCO & SEC approval

4. MAA
90-120 Days

Application in Form CT-21 to CDSCO, HQ with CT report & CTD module for MAA

IND / SEC meeting and recommendation

Parallel to MAA, EIR & NIB / CDTL Testing report to CDSCO, HQ - **60 days**

Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) &

Packaging (Label/Carton

/ PI) Approval **90-120 days based on novelty and complexity**

5. Mfg License
30 Days

Application in 27D for grant of mfg. license in Form 28D

Grant of Form-28D

30days

Application for COPP/WHO GMP Certificate

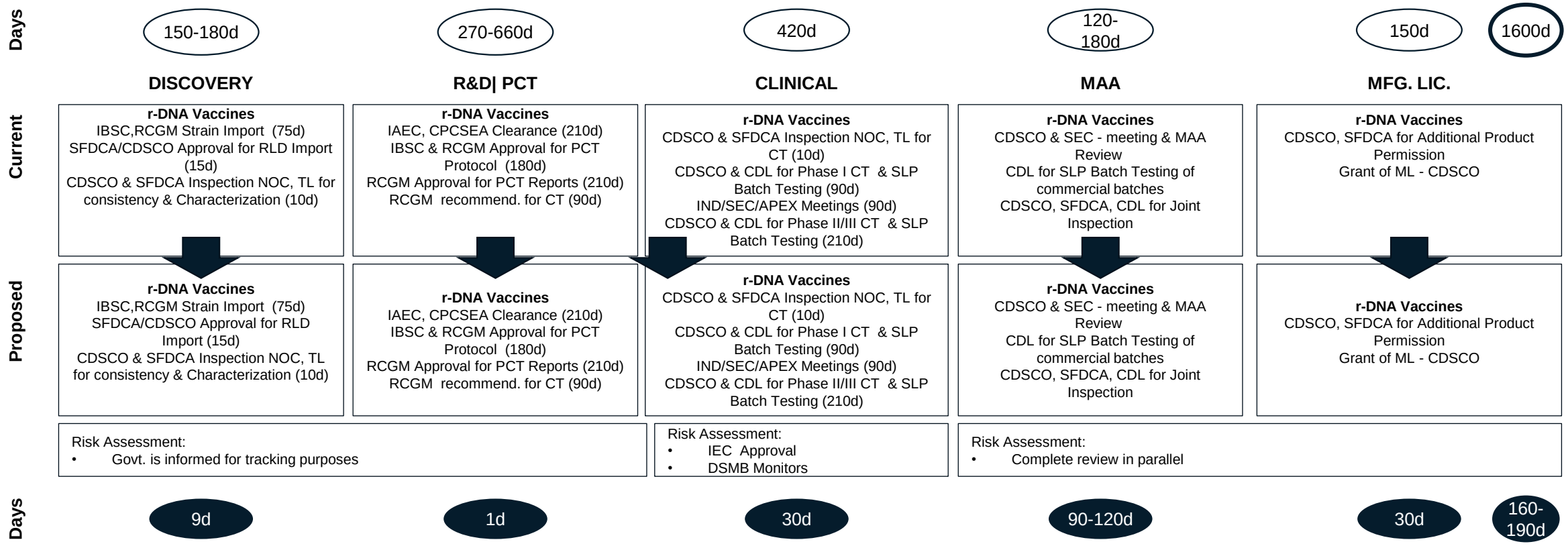
with PV/ consistency batches manufactured before MA Approval

COPP/WHO GMP Certificate Approval for Export registration

30days

Process deep dive: r-DNA Vaccines

Regulatory Pathway for r-DNA Vaccines: LAB TO LABEL



Efficiencies achieved through carrying out activities on-line, time bound deemed/automatic approvals and in Parallel reviews and inspections without any Compromises

Proposed Regulatory Pathway for r-DNA Vaccines: LAB TO LABEL

Parallel work

Timelines-160-190 Days (Lab to Label)

1. Discovery 9 Days

IBSC approval to import/ export /transfer/receive cell lines without quantity limit –

1 day RCGM approval not required for any quantity

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

7 days/Deemed Approval

IBSC recommendation for R&D initiation & notification to RCGM-Form C1

1 day /Automatic Approval

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Application in Form CT-21 to CDSCO, HQ with CT report & CTD module for MAA

IND / SEC meeting and recommendation

Parallel to MAA, EIR & NIB / CDTL Testing report to CDSCO, HQ - **60 days**

Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) &

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5. Mfg License 30 Days

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Grant of Form-28D

30days

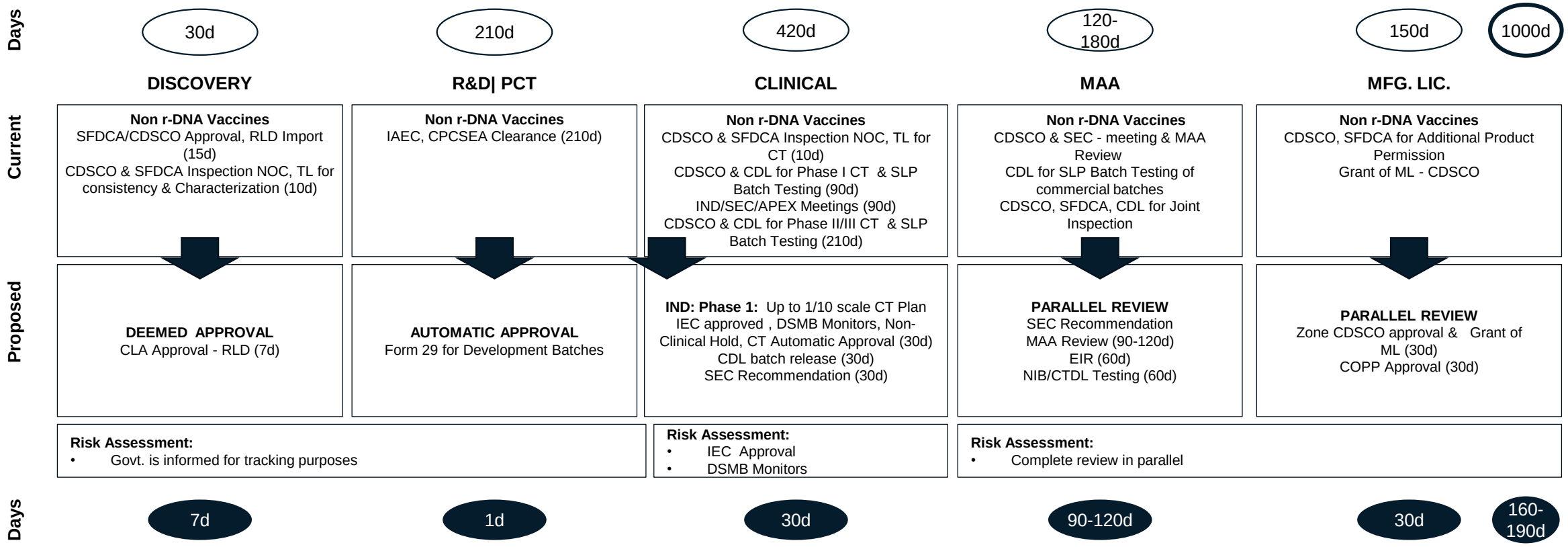
Application for COPP/WHO GMP Certificate

with PV/ consistency batches manufactured before MA Approval

COPP/WHO GMP Certificate Approval for Export registration **30days**

Process deep dive: Non r-DNA Vaccines

Regulatory Pathway for Non r-DNA, Vaccines : LAB TO LABEL



Efficiencies achieved through carrying out activities on-line, time bound deemed/automatic approvals and in Parallel reviews and inspections without any Compromises

Proposed Regulatory Pathway for Non r-DNA, Vaccines : LAB TO LABEL

Parallel work

Timelines-160-190 Days (Lab to Label)

1. Discovery 9 Days

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

7 days/Deemed Approval

2. R&D - PCT 7 Days

Grant of TL under Form 29 to mfg. developmental batches – Automatic Approval No CT-11 requirement (at Development & CT/consistency batches stages)

NCE: PCT will be conducted on both small and large animals based on IAEC approval, no other approval required For large animals, CPCSEA to be notified & no Dept. of Agriculture permission required

3. CT and/or BA/BE 30 Days

IND / SEC meeting and recommendation

Form CT-06/ CT-04A from CDSCO to conduct CT (Phase I, II & III) - 30 days, if not received within 30 days shall be deemed / automatic approval (as opposed to 90 days in New Drug CT Rule 2019)

Minor CT PAC - Protocol Amendments approved by DSMB/IEC and notification to CDSCO, HQ

CDL Batch release 30d

Currently, all protocol amendments require CDSCO & SEC approval

4. MAA 90-120 Days

Application in Form CT-21 to CDSCO, HQ with CT report & CTD module for MAA

IND / SEC meeting and recommendation

Parallel to MAA, EIR & NIB / CDTL Testing report to CDSCO, HQ - **60 days**

Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) &

Packaging (Label/Carton / PI) Approval **90-120 days based on novelty and complexity**

5. Mfg License 30 Days

Application in 27D for grant of mfg. license in Form 28D

Grant of Form-28D

30days

Application for COPP/WHO GMP Certificate

with PV/ consistency batches manufactured before MA Approval

COPP/WHO GMP Certificate Approval for Export registration

30days

Process deep dive: r-DNA/NCE/SM products in Orphan drug/ Rare disease

Proposed Regulatory Pathway for r-DNA/NCE/SM products in Orphan drug/ Rare disease

Parallel work

Timelines

(r-DNA)-110-140D

(NCE/SM) - 100-130D

(Lab to Label)

1. Discovery
9 Days

IBSC approval to import/ export /transfer/receive cell lines without quantity limit –

1 day RCGM approval not required for any quantity

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

7 days/Deemed Approval

IBSC recommendation for R&D initiation & notification to RCGM-Form C1

1 day /Automatic Approval

RCGM acknowledge in Form C-2 to initiate R&D activities-

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7 Days

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Submission of PCT report to RCGM for CT recommendation in Form C6 - **30 days**

3. CT and/or BA/BE
30 Days

Parallel to RCGM, submit application in Form CT-04/CT-04A to DCGI to conduct CT

Form CT-06/ CT-04A from CDSCO to conduct CT (Phase I, II & III) - **30 days**, if not received within 30 days shall be deemed approval (as opposed to 90 days in New Drug CT Rule 2019)

Minor CT Protocol Amendments to be approved by DSMB/IEC and notification to CDSCO, HQ . Currently, all protocol amendments require CDSCO & SEC approval

4. MAA
90-120 Days

Application in Form CT-21 to CDSCO, HQ with CT report & CTD module

for MAA

CTD will be reviewed by SEC and recommend to CLA for MAA

45-90 Days based on novelty & complexity

Parallel to MAA, EIR & NIB / CDTL Testing report to CDSCO, HQ - **60 days**

Grant of Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) &

Packaging (Label/Carton / PI) Approval

5. Mfg License
30 Days

Application in 27D for grant of mfg. license in Form 28D

Grant of Form-28D **30days**

Grant ofForm-25 (SM) **- 30days**

Provision for Batches manufactured under Form 29 Test or Trials may be used for commercial purposes on Approval

Process deep dive: Additional indication r-DNA/NCE/ Small molecules

Proposed Regulatory Pathway for additional indication r-DNA/NCE/Small molecules:

After innovator

Application to be submitted under PAC :

1. Approval of new indication from any NRA of innovator products will get automatic approval from CLA.

Label Extension with additional indication & Packaging (Label/Carton / PI) Approval **7 days**

7 d

Label Extension / additional indication Biosimilars/r-DNA/NCE/SM

Before innovator / novel r-DNA / BS/NCE/SM

Submit application in Form CT-04/CT-04A to DCGI to conduct CT for new indication **(not approved elsewhere)**

Form CT-06/ CT-04A from CDSCO to conduct CT - **30 days**, if not received within 30 days shall be deemed / automatic approval

Application under PAC with CSR, RMP, PI, Published literature

IND / SEC meeting and recommendation **10 d**

MA Approval with additional indication & Packaging (Label/Carton / PI) Approval **5 days**

45 d

Process deep dive: r-DNA/NCE/SM products in Restricted Emergency Use Authorisation (EUA)

Proposed Regulatory Pathway for NEW DRUG r-DNA/NCE/SM products in Restricted Emergency Use Authorisation (EUA)

Parallel work

Timelines

(r-DNA) 80-110D

(NCE/SM)-70-120 D

(Lab to Label)

1. Discovery
9 Days

IBSC approval to import/ export /transfer/receive cell lines without quantity limit –

1 day RCGM approval not required for any quantity

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

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Parallel to RCGM, submit application in Form CT-04/CT-04A to DCGI to conduct CT

Form CT-06/ CT-04A from CDSCO to conduct CT (Phase I, II & III) - **30 days**, if not received within 30 days shall be deemed approval (as opposed to 90 days in New Drug CT Rule 2019)

Minor CT Protocol Amendments to be approved by DSMB/IEC and notification to CDSCO, HQ . Currently, all protocol amendments require CDSCO & SEC approval

4. MAA
90-120 Days

Application in Form CT-21 to CDSCO, HQ with CT report & CTD module

for MAA

CTD will be reviewed by SEC and recommend to CLA for MAA

45-90 Days based on novelty & complexity

Parallel to MAA, EIR & NIB / CDTL Testing report to CDSCO, HQ - **60 days**

Grant of Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) &

Packaging (Label/Carton / PI) Approval

5. Mfg License
30 Days

Application in 27D for grant of mfg. license in Form 28D

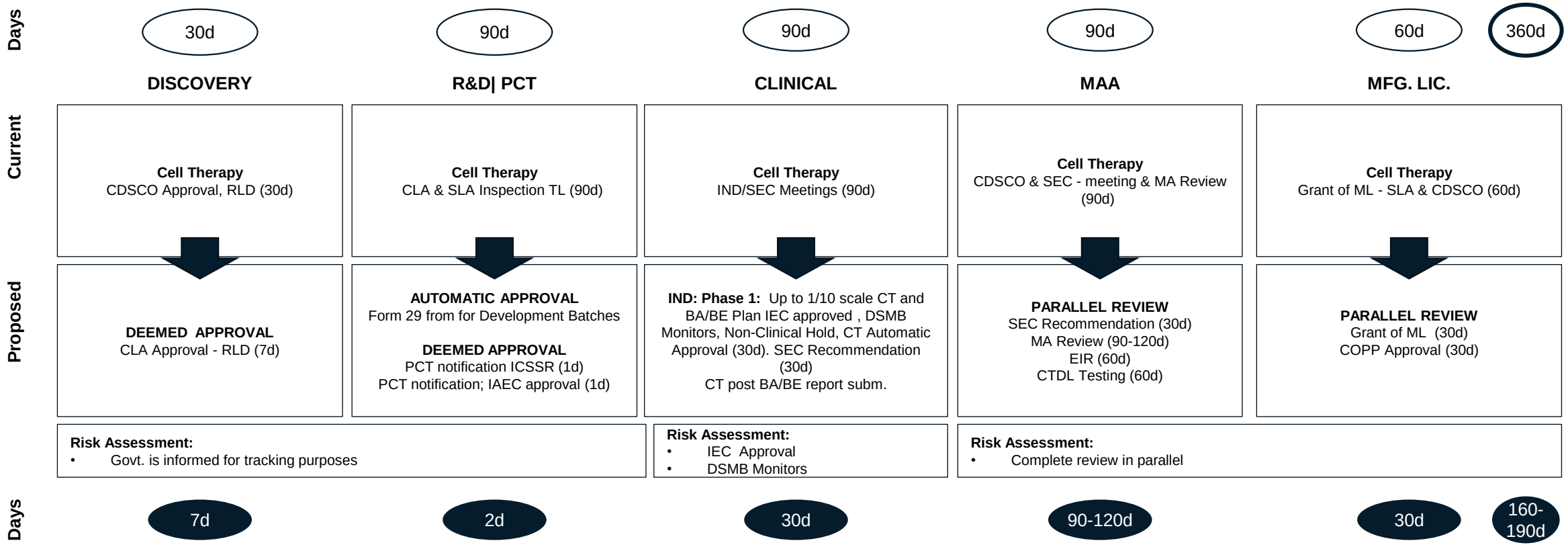
Grant of Form-28D **30days**

Grant ofForm-25 (SM) **- 30days**

Provision for Batches manufactured under Form 29 Test or Trials may be used for commercial purposes on Approval

Process deep dive: Stem cell, Cell Therapy Regenerative Medicines

Cell therapies; regenerative medicies



Efficiencies achieved through carrying out activities on-line, time bound deemed/automatic approvals and in Parallel reviews and inspections without any Compromises

Proposed Regulatory Pathway for Stem Cell, Cell Therapy Regenerative Medicines : LAB TO LABEL

Parallel work

Timelines-160-190 Days (Lab to Label)

1. Discovery 7 Days

RLD import license in Form CT-17 from CDSCO Zonal / sub zonal office

7 days/Deemed Approval

2. R&D - PCT 2 Days

Based on IBSC /equivalent committee, Grant of TL under Form 29 for mfg. developmental batches – Automatic Approval – 1day No CT-11 requirement

Submission of PCT application as Notification to Institutional Committee For Stem Cell Research (ICSCR) through online – 1day

PCT will be conducted on both small and large animals as per NDCT 2019 based on IAEC approval, no other approval required. For large animals, CPCSEA to be notified & no Dept. of Agriculture permission required

Comments 2

1 days/Deemed Approval

In Parallel

3. CT and/or BA/BE 30 Days

CBBTDEC meeting and recommendation

Form CT-06/ CT-04A from CDSCO to conduct CT (Phase I, II & III) - 30 days, if not received within 30 days shall be deemed / automatic approval

(as opposed to 90 days in New Drug CT Rule 2019)

Any CT PAC - Protocol Amendments approved by DSMB/IEC and notification to CDSCO, HQ

NCL Batch release 30d Currently, all protocol amendments require CDSCO & SEC approval

4. MAA 90-120 Days

Application in Form CT-21 to CDSCO, HQ with CT report & CTD module for MAA

Parallel to MAA, EIR & NIB / CDTL Testing report to CDSCO, HQ - **60 days**

Manufacturing Permission in Form CT-23 (DP)/CT-22 (DS) &

Packaging (Label/Carton

/ PI) Approval **90-120 days based on novelty and complexity**

5. Mfg License 30 Days

Application in 27D for grant of mfg. license in Form 28D

Grant of Form-28D

30days

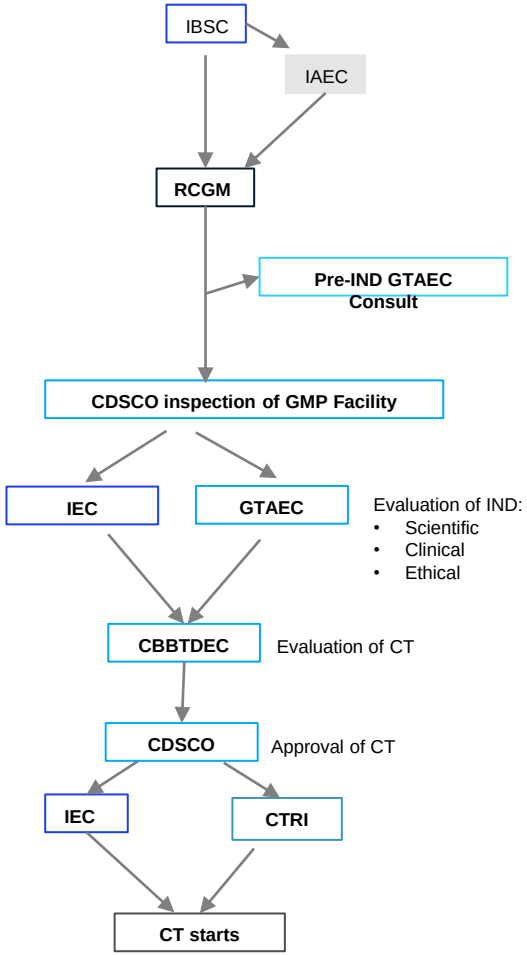
Application for COPP/WHO GMP Certificate

with PV/ consistency batches manufactured before MA Approval

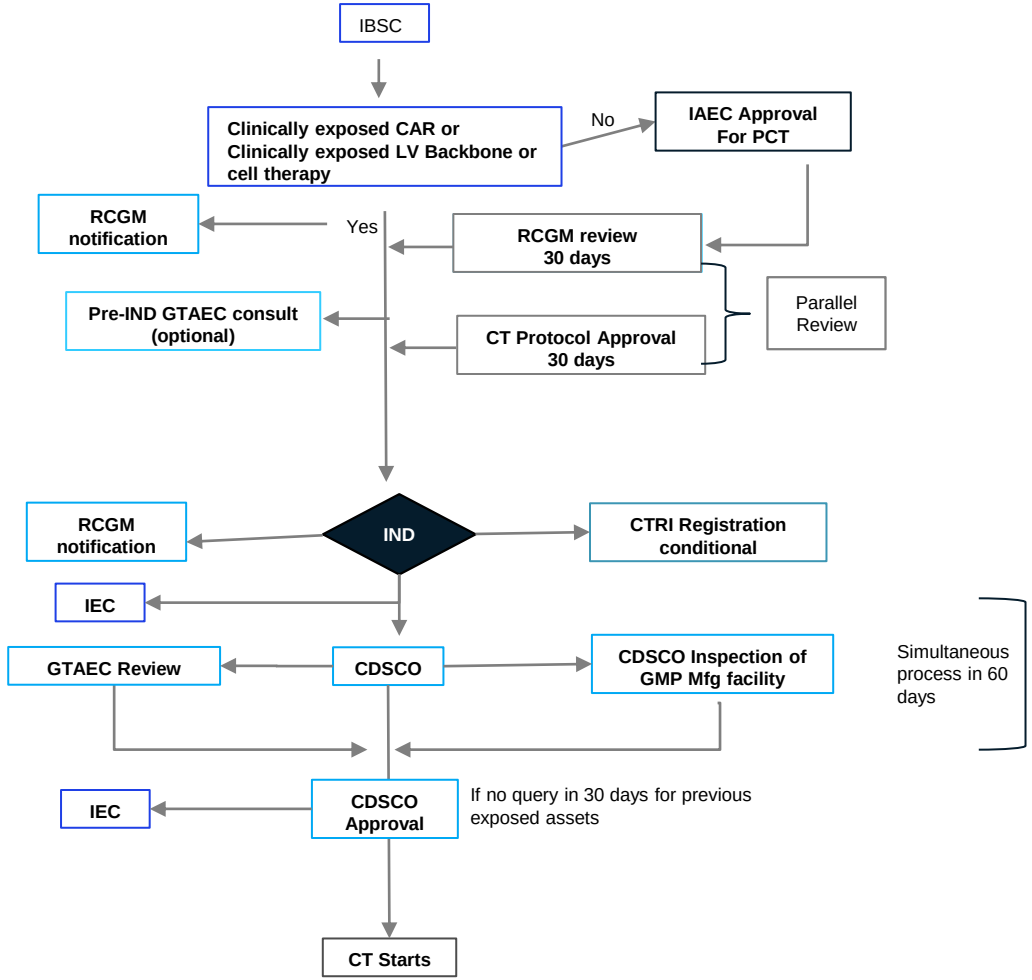
COPP/WHO GMP Certificate Approval for Export registration **30days**

Regulatory path for autologous car t therapy, cell therapy / regenerative medicine

Current



Proposed



Additional Changes & Rationale

Preclinical Testing (include only Efficacy and Pharmacology)

No Toxicology

- No relevant animal model for autologous therapy
- No toxicology studies were performed for the two approved CAR therapies (Kymriah & Yescarta)

Option for online/written pre-IND GTAEC consult

Manufacturing

Appropriate Range for Acceptance Criteria

Due to the autologous nature of the product, even in a validated process, inherent variability is acknowledged for

- % transduction
- dose
- Potency
- viability

Quality Control Testing

In vitro Potency should be used for product characterization and not as a release criteria

- In vitro potency does not correlate with Clinical efficacy

Clinical Trials

For First in Human studies - Dose escalation followed by dose expansion is needed. For assets with previous clinical exposure, a single study (abridged) may be considered sufficient, with post marketing commitment.

- Autologous/personalized therapy has minimal risk.

Process deep dive: Medical Devices

Medical devices - staging & time pathway: recommended regulations

Class of Medical Devices & Diagnostics	Current	Proposed	Proposed timeline from the application date
Class-A	Self-declaration	Self-declaration	15 days
Class-B	CDSCO	Third party notified bodies by NABCB & CDSCO	30 days
Class-C*	CDSCO	CDSCO	60 days
Class-D	CDSCO	CDSCO	60 days

Category C:

Includes Implants and critical medical devices which need to be evaluated and approved by CDSCO

Class B&C account for 80% of Medical Device Sector with > 40,000 devices.

Class A & B may be certified by accredited labs notified by NABCB (both private & public) for approval by CDSCO.

Key factors for Medical Technology for Governance

Empanelment of labs

Phasing by Product segments with prior intimation.

Category A&B should be regulated through notified testing centers.