Session 1
Transgene experience with the Clinical Trials Regulation (CTR) preparation

EMA webinar for SMEs and Academia on the Clinical Trials Regulation (CTR) and Clinical Trials Information System (CTIS)

November 29, 2021

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Agenda

Presentation: Transgene experience with the Clinical Trial Regulation (CTR) preparation

1. **INTRODUCTION**
2. **METHOD: STEPWISE CTR IMPLEMENTATION PREPARATION**
   - **Step 1: Identify**
   - **Step 2: Inform and Prepare**
   - **Step 3: Implement**
3. **EXPERIENCED COMMENTS AND CHALLENGES IN CTR ADOPTION**
4. **ADVICES IN CTR IMPLEMENTATION PREPARATION**

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Introduction

Transgene portfolio

- 150 employees
- Headquarter in Strasbourg (France), no EU affiliate
- Part of the Mérieux Group
- Mainly in-house clinical trial activities

Product	Indication	Target/Transgene	Design	Preclinical	Phase I	Phase II
MODIFIED VACCINIA VIRUS ANKARA-BASED (MVA) GTMPs						
TG4050 myvac / NEC	Ovarian cancer	Patient neoantigens				
	Head and neck cancers					
TG4001	Anogenital HPV+ cancers	HPV 16 E6 – E7				
ONCOLYTIC VIRUSES (OVs) GTMPs						
TG6002	Gastro-intestinal cancers (IV*)	5-FU chemotherapy				
	Colorectal cancer (IHA*)					
BT-001 invir io / BioInvent	Solid tumors	Anti-CTLA4 + GM-CSF				
OVs invir io	Solid tumors	Undisclosed				
5 OVs invir io		Undisclosed				

** IV: intravenous administration, IHA: intrahepatic artery administration, GTMP: gene therapy medicinal product*

Stepwise CTR implementation preparation

Step 1: Identify

<u>Global approach</u>: No complete overhaul of internal clinical trial management process; focus on needed adaptations

IDENTIFY

- **Identification of CTR preparation referent company member(s)**
- **CTR preparation Working Group established (i.e.: 1 member from Clinical Quality Assurance, Regulatory affairs, Clinical trial management)**
  - **Regular meetings**
  - **Coordinate actions and follow-up**

March 21

Nov 21

INFORM AND PREPARE

IMPLEMENT

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Stepwise CTR implementation preparation

Step 2: Inform & Prepare

IDENTIFY

INFORM AND PREPARE

- **Inform:**
  - **Initial training to detail CTR to clinical department as part of company QA training plan**
  - **Regular CTR status updates through monthly QA / regulatory watch bulletins and regular clinical department meetings**

IMPLEMENT

Jan 21

Nov 21

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Stepwise CTR implementation preparation

Step 2: Inform & Prepare

CTR Reference	Impact	Action	Responsible	Timelines & Status	Comment
Chap.XX, Art.XX	Y/N	XXXX	XXX, XXX	Ongoing,by Feb 2022	

IDENTIFY

INFORM AND PREPARE

- **Prepare:**
  - ➢ **Read and use EMA CTIS training and support material**
  - ➢ **Change control and Impact analysis: Procedures and clinical document template adaptations; etc**
  - ➢ **Company organization CTIS role mapping through user persona exercise**

Regulatory affairs manager (RAM)

CTIS activities:

- CTA (including RFI): Prepare administrative documents, Compile part I documents from eCRF, XXXX
- Amendment (including RFI): XXXX
- End of trial: XXXX

CTIS roles:

- Sponsor administrator, Part I preparer, Part I submitter, XXXX

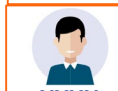
Pharmacovigilance manager (PVUR)

CTIS activities:

- Trial management: Prepare annual Development Safety Update Report, XXXX
- XXXX: XXXX

CTIS roles:

- Part I preparer, XXXX



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CTIS activities:

IMPLEMENT

March 21

Sept 21

Nov 21

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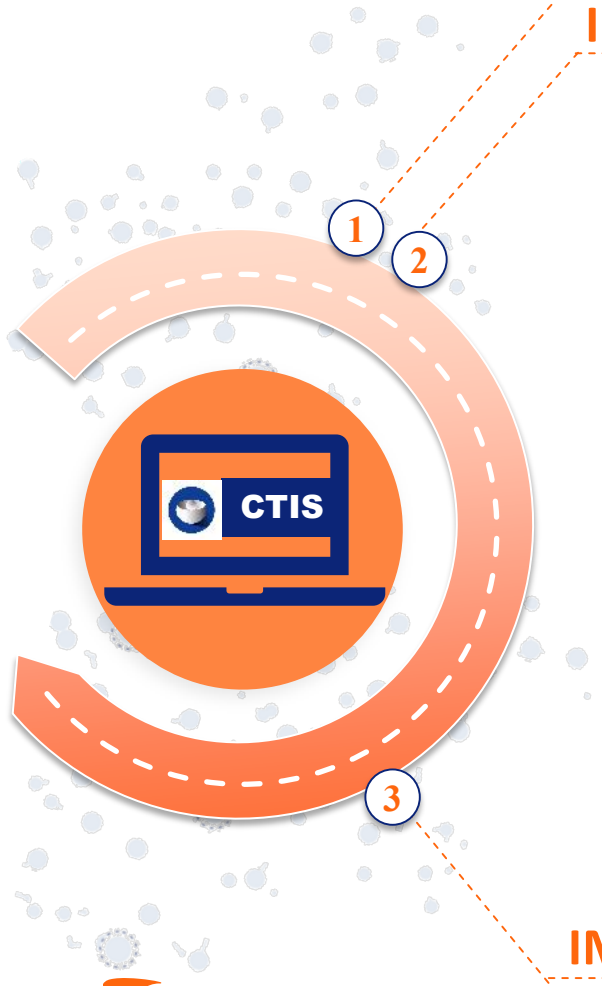
Stepwise CTR implementation preparation

Step 2: Inform & Prepare



IDENTIFY

INFORM AND PREPARE

- **Prepare:**
  - **Read and use EMA CTIS training and support material**
  - **Change control and Impact analysis: Procedures and clinical document template adaptations; etc**
  - **Company organization CTIS role mapping through user persona exercise**
  - **Organisation centric approach validation; CTIS sponsor administrators assignment**
  - **Response to EMA CTIS Sandbox access need survey**
  - **Company CTIS training plan & Clinical trials Directive to CTR transition timetable definition**
  - **Share information to future user of CTIS**

March 21

Sept 21

Nov 21

IMPLEMENT

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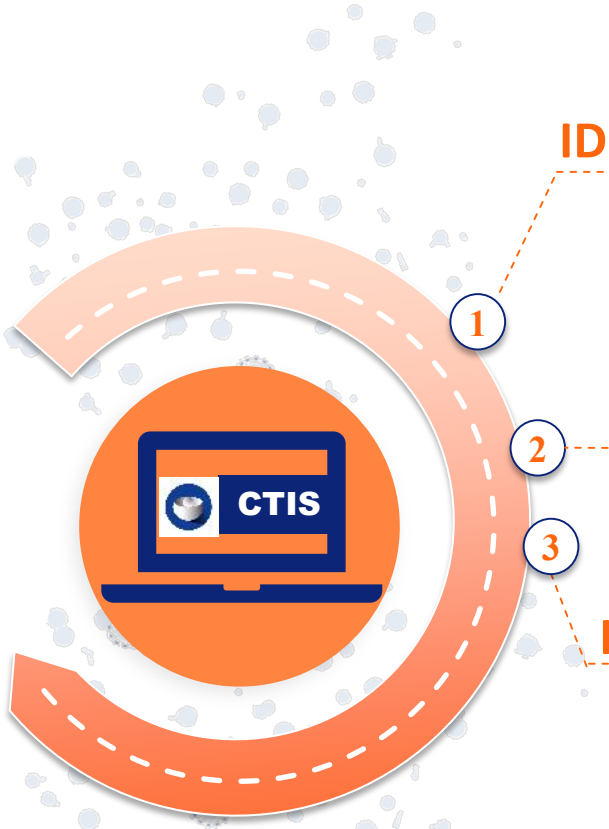
Stepwise CTR implementation preparation

Step 3: Implement



IDENTIFY

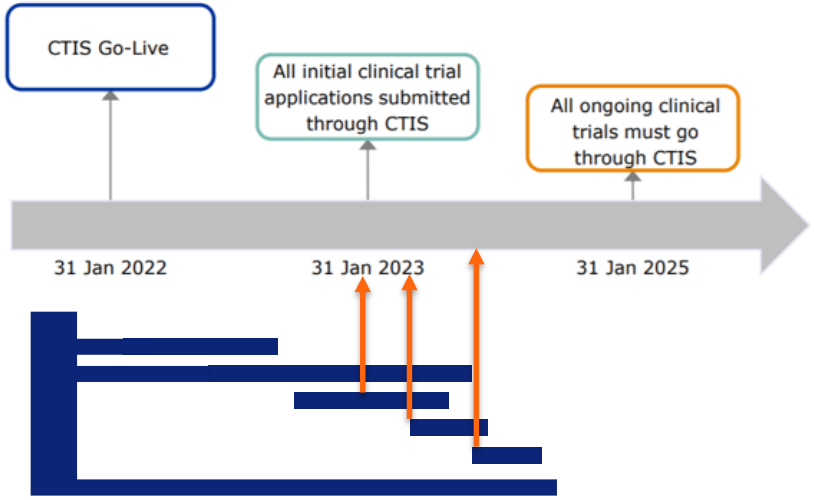
1

INFORM AND PREPARE

2

3

IMPLEMENT



- **Company CTIS training plan execution**
- **Transition new and ongoing clinical trials from Directive to CTR per timetable established**

Nov 21

2022

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Experienced comments and challenges in CTR adoption

Request of CTIS webportal testing option up to the go-live

- EMA phased rollout of a CTIS sandbox planned from mid-November 21.

Clinical trial portfolio features

- **Mainly early phase clinical trials with single or few numbers of participating countries**
- **Low number of clinical trials: all are critical, no priority level**

- No immediate transition of clinical trials from Directive to CTR; waiting period to have some real-life feedback before transition activation.
- CTIS number and figures regular reports from Feb 2022 would be appreciated in CTIS activation final decision making.

Amount of operational and planning work for transitioning ongoings clinical trials

- Consolidated protocol version (when applicable) through an amendment + CTIS transition submission = periods with no clinical trial amendment possible.
- Management of CT planned to end before February 2025: result posting still possible in EudraCT after transition period ends.
- 12 calendar days RFI response period challenge under CTR in case of whole application (Part I and II) for small project team.

Clinical development of investigational ATMPs containing GMO

- Not full all in one integrated submission; GMO Environmental risk assessment not coordinated in CTR review.
- ATMP assessment period extensions (e.g.: Potential CTIS transition timelines extension for ATMPs clinical trial transition dossier on top of the maximum 106 days period while it should be an administrative process)

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Advices in CTR implementation preparation

Even if you do not plan transition implementation from the beginning (i.e. Feb 2022), **the earlier** your CTR preparation starts, **the smoother** your CTR preparation should be.

Nominate **CTR specialist(s)** in your organization.

Massive high quality **training material offered** including some tailored for SMEs companies:

- EMA CTIS sponsor handbook
- EMA CTIS training programme Module 19 for SME and academia
- European Commission CTR No 536/2014 Questions & Answers document
- EMA CTIS highlights newsletter; Etc

Find the good **timing** for your **CTIS user training** plan activation considering your planned CTR activation timing.

Use experience and **processes already in place** for other Health Authority clinical trial webportal(s) when applicable (e.g.: EudraCT, clinicaltrials.gov)

Thank you for your attention

Session 1 - Stakeholders' experience with the Clinical Trials Regulation implementation – SME presentation

Upcoming Q&A session

Acknowledgements:

All Transgene Clinical and Quality colleagues involved in the CTR preparation and implementation.