Experiences with PEI in ATMP development

Best Practice Examples

HOW SCIENTISTS SEE THE AUTHORITIES

Slide © Vuk Savkovic, Universität Leipzig

A JOURNEY TO MORDOR?

Overview

- Scientific Advice
- Experiences with PEI
- Q&A

No discussion of other counselling formats

WHAT YOU GET AND WHAT YOU DON'T

NO APPROVAL

You get advice and a «positive quote», but no approval!

CHANGE OF MIND

PEI can change their opinion.
State of the art can change.
→ «The Hobbit or **There and Back Again**»

CLEAR PATH

Often not the easiest way, but you actually know what to do.

SCIENTIFIC ADVICE

DEADLINES, PROCEDURE, APPLICATION, AND PREPARATION

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–4 Months

APPLICATION

- Topics
- Number of participants
- Appointment requests
- Question form: «Does PEI agree that ...?»
- Form on PEI website

GENERAL

APPLICANT

CONTACT PERSON

AREA OF MEDICINAL PRODUCT

ATMP

JOINT SCIENTIFIC ADVICE

MEDICINAL PRODUCT

Name of the medicinal product and of the active substance(s)

Therapeutic indication

Short description of key manufacturing steps

Short description of the mode of action respectively the effect of the medicinal product

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MEDICINAL PRODUCT

Name of the medicinal product and of the active substance(s)

Therapeutic indication

Short description of key manufacturing steps

Short description of the mode of action respectively the effect of the medicinal product

SCOPE OF THE SCIENTIFIC ADVICE

Quality

Viral safety

Microbiological safety

Non-clinic

Clinic

Biostatistics

Procedural issues

Paediatric indication

Not clearly stated that the questions should be asked now, but you may be asked to submit them later.

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SCOPE OF THE SCIENTIFIC ADVICE

- Quality
- Viral safety
- Microbiological safety
- Non-clinic
- Clinic
- Biostatistics
- Procedural issues
- Paediatric indication

ADDITIONAL INFORMATION

- Objectives of the advice
- Preferred dates
- Number of participants
- Some formal aspects

SCIENTIFIC ADVICE

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–4 Months

SCHEDULING

–3 Months

APPLICATION

- Topics
- Number of participants
- Appointment requests
- Question form: «Does PEI agree that ...?»
- Form on PEI website

BRIEFING DOCUMENT

- ≤ 40 pages + attachments
- Summarizing questions and your own position
- Detailed supportive evidence for your own argumentation

SCIENTIFIC ADVICE

DEADLINES, PROCEDURE, APPLICATION, AND PREPARATION

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–3 Months

BRIEFING DOCUMENT

- ≤ 40 pages + attachments
- Summarizing questions and your own position
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RECOMMENDATION

IMPD FORM

QUESTIONS AND APPLICANT'S POSITIONS

Question 1: Does PEI agree …?
Applicant's position: …

No open questions!

PAY ATTENTION TO EVERY SENTENCE

ANNEXES

Only supportive (e.g., raw data)

THIS IS PROBABLY THE MOST IMPORTANT WORK YOU DO FOR YOURSELVES

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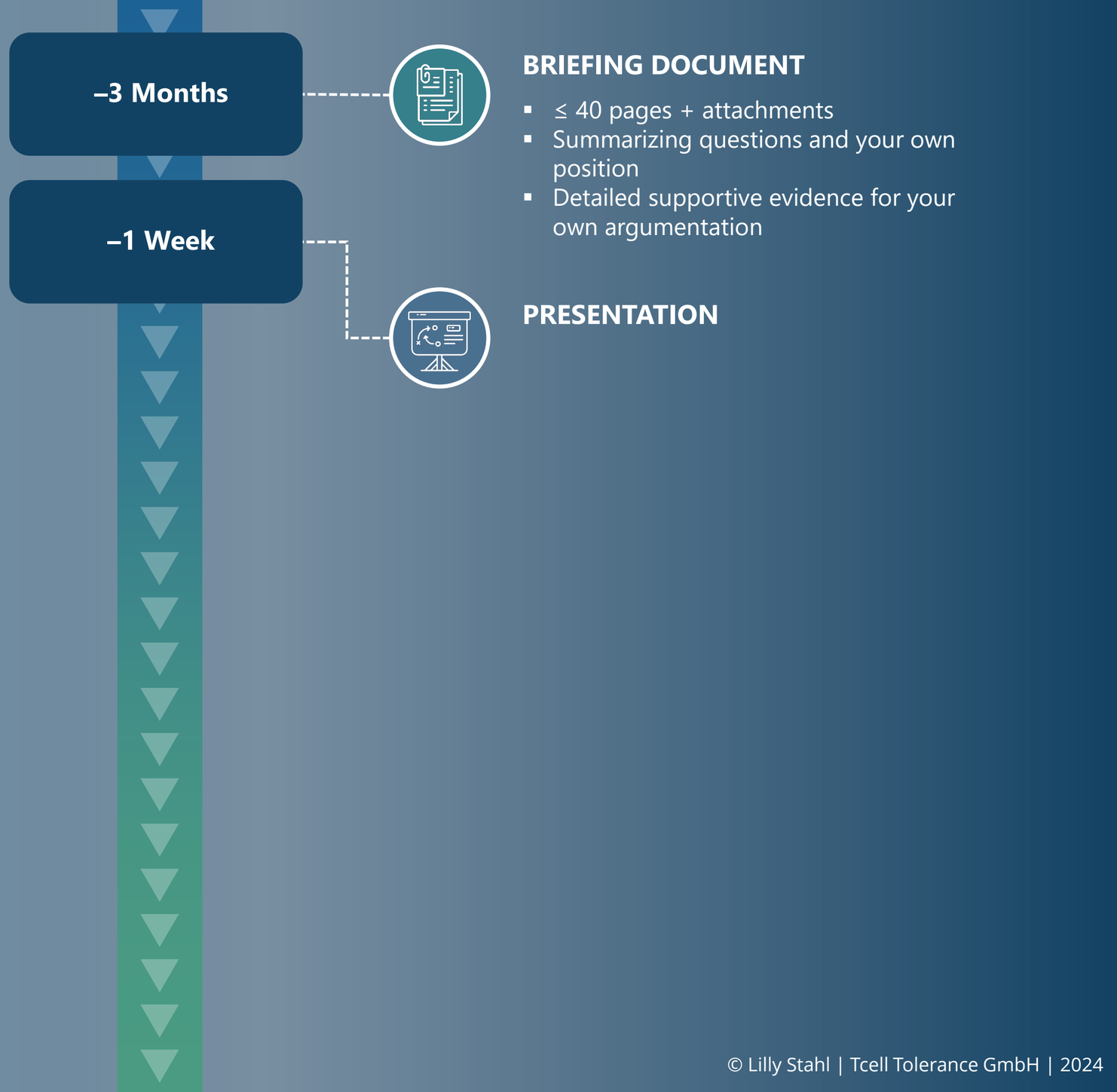

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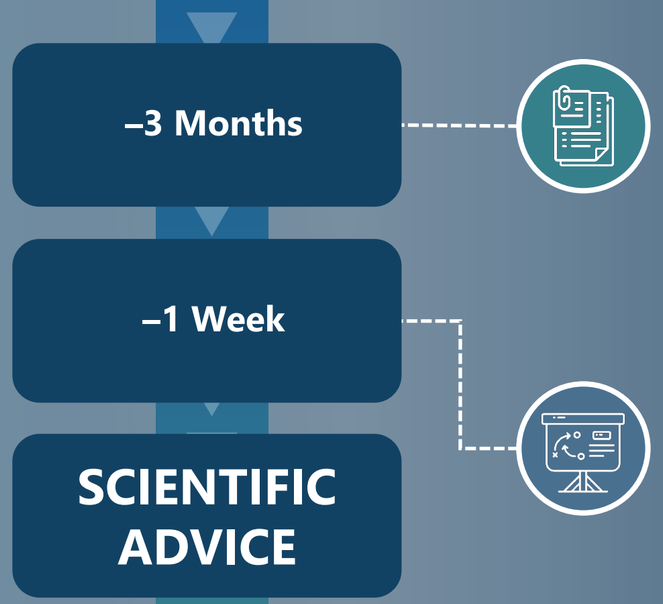

BRIEFING DOCUMENT

- ≤ 40 pages + attachments
- Summarizing questions and your own position
- Detailed supportive evidence for your own argumentation

PRESENTATION

SCIENTIFIC ADVICE

DEADLINES, PROCEDURE, APPLICATION, AND PREPARATION

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SCIENTIFIC ADVICE

PREPARATION

REHAERSAL

Pay attention to every sentence

Use notes, if necessary

CONSULTATION

Now: Online

PEI interrupts the presentation for questions
→ Encourage them to do so at the beginning

NOTES FOR PROTOCOL

Take someone to the consultation who can write quickly, ideally quotes

KEEP IN MIND:

YOU are the experts about your product.
PEI is not all-knowing.

SCIENTIFIC ADVICE

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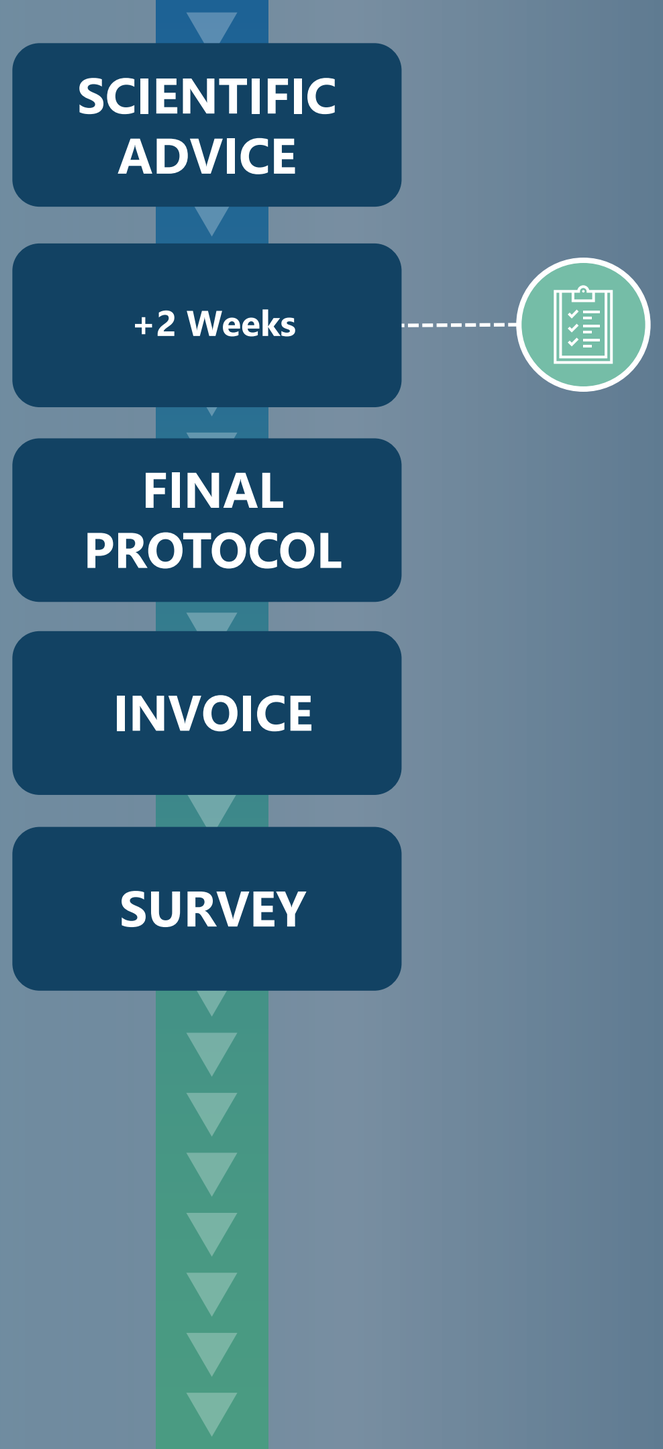
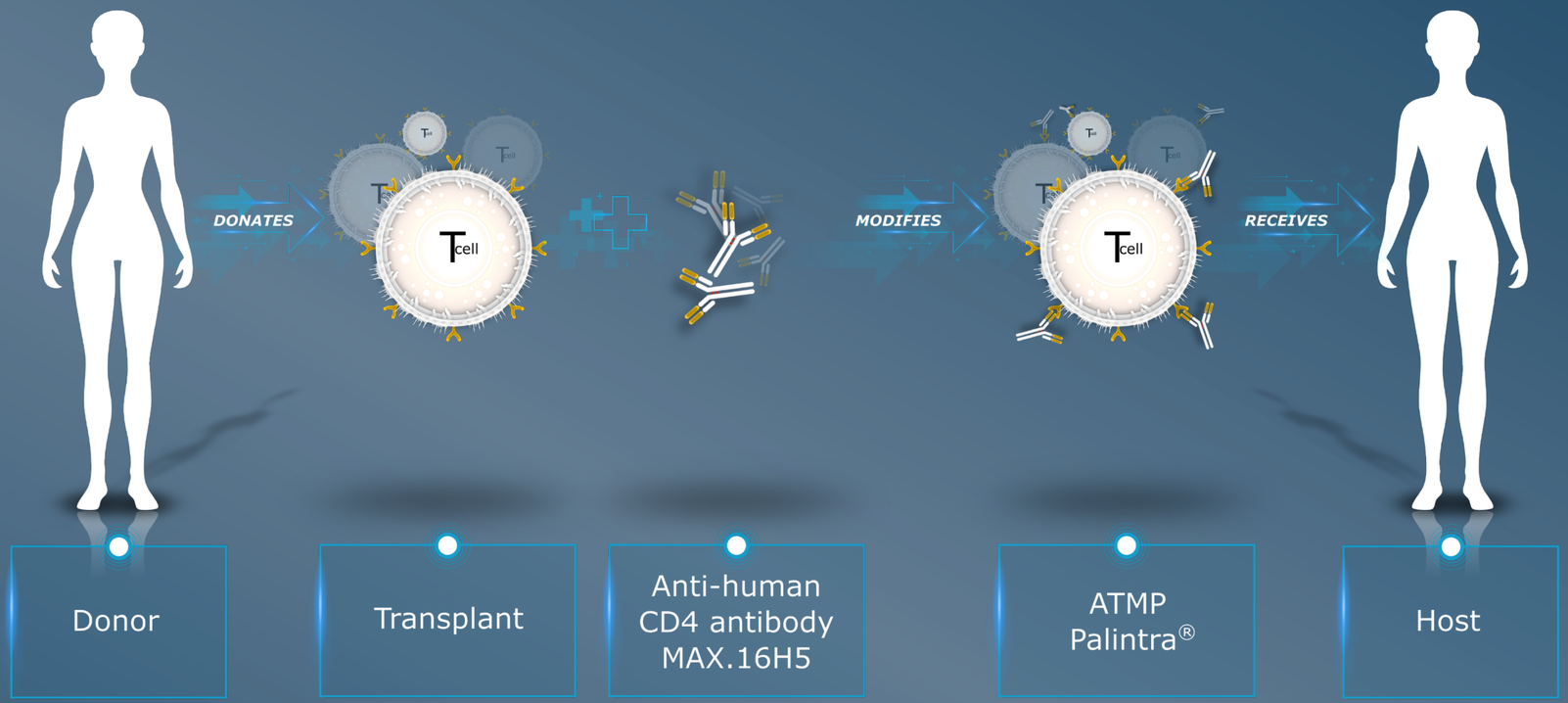


DRAFT PROTOCOL

- Take someone to the consultation who can write quickly, ideally quotes.
- Write what you hope for (in accordance with the consultation, of course)



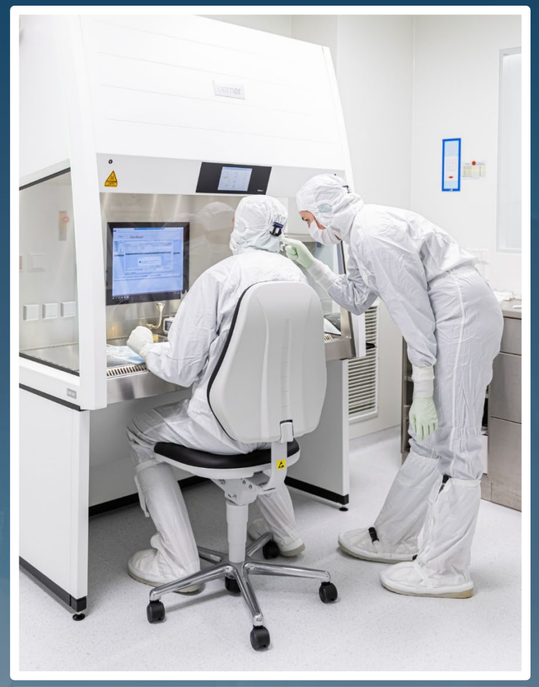
OUR CASE
ATMP PALINTRA®

CHALLENGES

- Short shelf life
- Decentralised Manufacture
- Who is the Manufacturer (German: PU)?
- Approval of antibody or ATMP or antibody as starting material for ATMP manufacture or …?

TOPICS SCIENTIFIC CONSULTATIONS WITH PEI

2017 until 2023



Early-Stage Development Regulatory advice on authorisation

Nonclinical Development & Synopsis Clinical Development

Nonclinical Development & Development/Validation ATIMP Manufacturing Process

Change in ATIMP manufacturing process and resulting change in nonclinical development

...

FIRST SCIENTIFIC ADVICE

Why it is important

- Preparation process: To summarise all you know about your product
- Clear picture («Fakten schaffen»): Are your marketing authorization ideas sustainable?

EARLY-STAGE DEVELOPMENT

REGULATORY ADVICE ON AUTHORISATION

OUR EXPERIENCES

- Aim: Only a few expensive nonclinical GLP experiments
  → Months of research for old data in dusty archives (supportive safety evidence)
  → PEI: «This data is not relevant.»

Write a review article.

FIRST SCIENTIFIC ADVICE

Why it is important

- Preparation process: To summarise all you know about your product
- Clear picture («Fakten schaffen»): Are your marketing authorization ideas sustainable?

EARLY-STAGE DEVELOPMENT

REGULATORY ADVICE ON AUTHORISATION

OUR EXPERIENCES

- The person who was supposed to give the presentation was admitted to hospital one day before departure

Have a back-up!

FIRST SCIENTIFIC ADVICE

Why it is important

- Preparation process: To summarise all you know about your product
- Clear picture («Fakten schaffen»): Are your marketing authorization ideas sustainable?

EARLY-STAGE DEVELOPMENT

REGULATORY ADVICE ON AUTHORISATION

OUR EXPERIENCES

- Detailed questions on data in the annexes

Take someone with you who actually knows the experiments.

FIRST SCIENTIFIC ADVICE

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- Preparation process: To summarise all you know about your product
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EARLY-STAGE DEVELOPMENT

REGULATORY ADVICE ON AUTHORISATION

OUR EXPERIENCES

- At that time no regulation for our case
  → PEI: Guideline on non-substantially manipulated ATMPs
  → PhD student asked:
  What ist that? Never heard about it.
  → PEI: Of course not, the draft is not public yet. But you can get it from us afterwards.

Take someone with you who does not lose face when he/she asks «stupid» questions.

FIRST SCIENTIFIC ADVICE

Why it is important

- Preparation process: To summarise all you know about your product
- Clear picture («Fakten schaffen»): Are your marketing authorization ideas sustainable?

EARLY-STAGE DEVELOPMENT

REGULATORY ADVICE ON AUTHORISATION

OUR EXPERIENCES

- Scheduled: 2 hrs, ended after 1:40 hrs
  → Withdrawn question on clinical trial design was asked (open form)

Asking open questions can end well but is NOT recommended.

SECOND SCIENTIFIC ADVICE

Why it is important

- Positive vote for your nonclinical development plan
- IMPD form

NONCLINICAL DEVELOPMENT

SYNOPSIS CLINICAL DEVELOPMENT

OUR EXPERIENCES

- Accomodation costs + costs for vendor
  → Now: Online Meetings
  → Cost-effective and time-saving

SECOND SCIENTIFIC ADVICE

Why it is important

- Positive vote for your nonclinical development plan
- IMPD form

NONCLINICAL DEVELOPMENT

SYNOPSIS CLINICAL DEVELOPMENT

OUR EXPERIENCES

- Unexpected (and incorrect) opinion that stem cells bear CD4
  → Although we knew better, no disagreement in the consultation
  → Literature study and additional experiments in preparation for the next SA

Take someone with you who does not lose face when he/she asks «stupid» questions.

SECOND SCIENTIFIC ADVICE

Why it is important

- Positive vote for your nonclinical development plan
- IMPD form

NONCLINICAL DEVELOPMENT

SYNOPSIS CLINICAL DEVELOPMENT

OUR EXPERIENCES

- PEI wanted extended nonclinical development plan

Homework for 3rd SA

THIRD SCIENTIFIC ADVICE

Why it is important

- Positive vote for your nonclinical development plan
- Positive vote for the ATIMP manufacture process development & validation plan
- IMPD form

NONCLINICAL DEVELOPMENT

DEVELOPMENT/VALIDATION ATIMP MANUFACTURING PROCESS

OUR EXPERIENCES

- PEI reduced the proposed extended nonclinical development plan

PEI is also subject to inspection by the animal welfare authorities.

FOURTH SCIENTIFIC ADVICE

Why it is important

- Positive vote for your nonclinical development plan
- Positive vote for the ATIMP manufacture process development & validation plan
- IMPD form

CHANGE IN ATIMP MANUFACTURING PROCESS

RESULTING CHANGE IN NONCLINICAL DEVELOPMENT

OUR EXPERIENCES

CHANGE OF MIND

- PEI: Old data is supportive safety evidence
- PEI: Absolute quantifiers
  (3rd SA they wanted relative quantifiers)

Homework for IMPD

A JOURNEY TO MORDOR?

WHAT I LEARNED

- Reading guidelines is very interesting
- Disillusionment with research articles
- Keep asking stupid questions

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