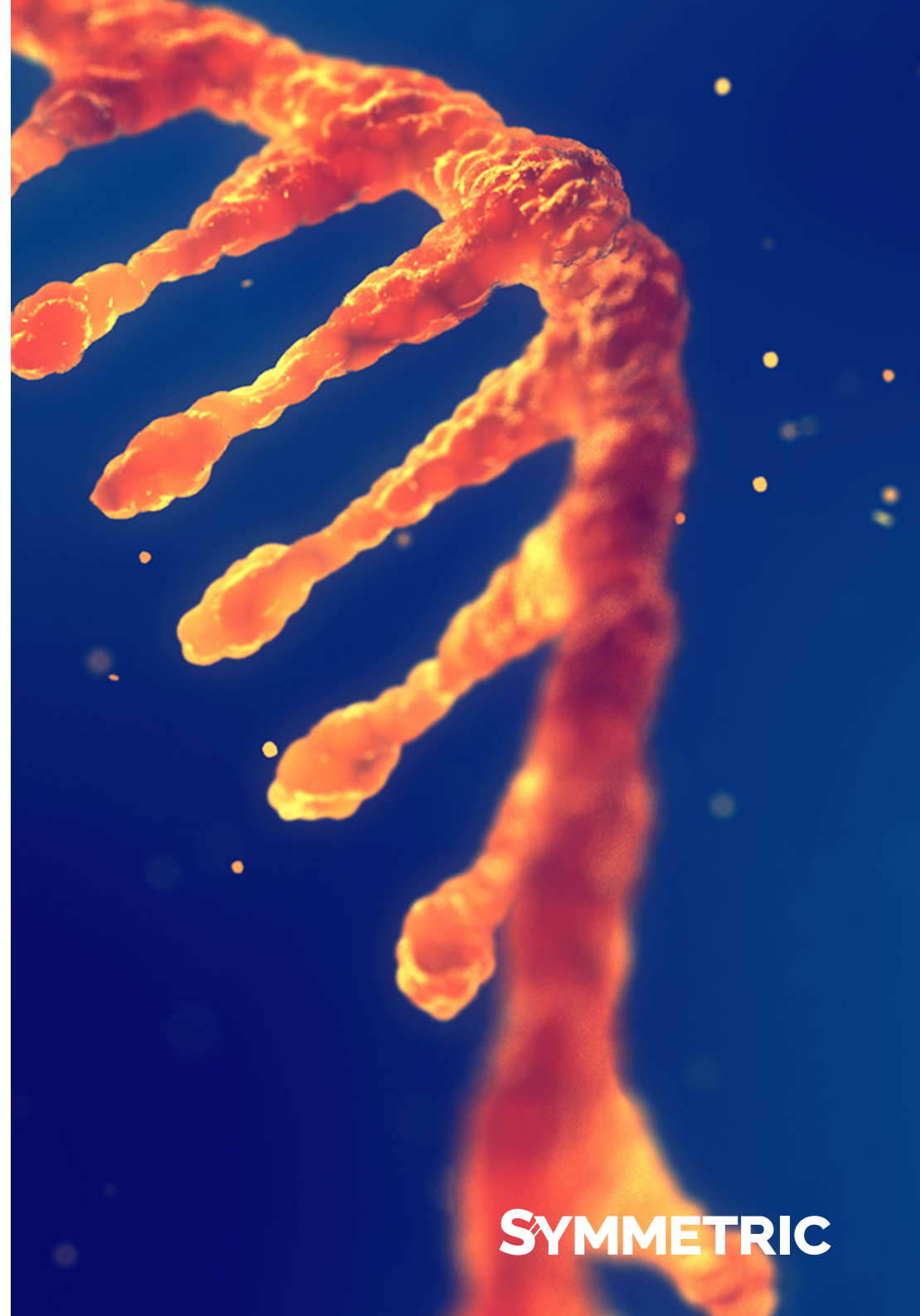


Sneak Peek

CMC/Regulatory Affairs for Nucleic Acids



Dr. Len Pattenden
CMC Expert and Independent
Consultant



SYMMETRIC

Conclusion on Classification

Know your drug!

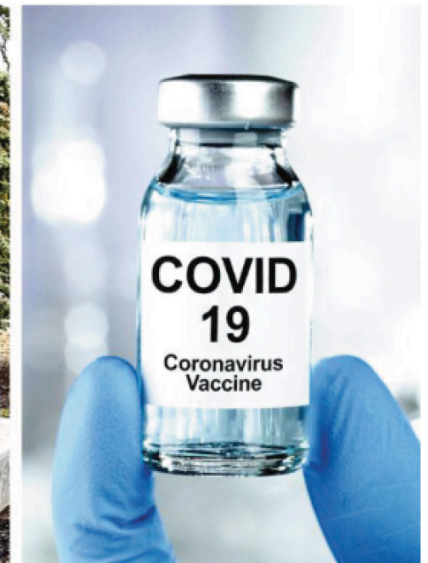
Definitions/classifications matter!

- Primarily about patient safety and related to:
 - How it is made and size of the Active Substance
 - Type of drug
 - Similarities for patient treatment
 - Adverse effects (management)
 - Disease being Treated
- inter-related**
- Your classification argument must consider**
- The landscape includes Pharmacopoeias, human tissue authorities, HSE/GMO authority
 - Along with Pharmaceutical Regulators govern end-to-end regulations and legals
 - Licensing required in many jurisdictions
 - Classification for minimal manipulations have relaxed approaches (mostly not of interest)
 - The US has complications of state & Fed legislation for neonatal and embryonic stem cells
 - Can influence facilities/operations and timelines at setup
 - Seek early and strategic engagement from the Regulators on classification of your Drug
 - Can gain significant assistance, timeline and reduced costs
 - Classifications will likely become even more diverse and distinct because of these factors and drivers to supply complicated cell therapies. This reflects the ever-expanding knowledge.

Regulatory Expectations Nucleic Acids



- ▶ Overall Development Plan
- ▶ CMC Plan
- ▶ Formulation Plan
 - Includes Development
 - Future changes predicted and planned
- ▶ Risk-based QbD
- ▶ Change Control & Management
- ▶ Continuous improvement planning
- ▶ Lifecycle Management
- ▶ Stability study planning & strategy
 - Including in-use stability
- ▶ Comparability



Impt: Overall filing strategy and eCTD considerations pf late-stage formulation development (Ph IV) which can be common for many drugs

What is a Control Strategy? Why is it important?



Important to CMC is ensuring the control strategy is in place

Control Strategy

- A planned set of controls to produce a drug based on an understanding of its production process.
- A control strategy ensures the process performs as it should and maintains quality. (ICH Q8, 9, 10)
- Starts from the patient (ICH Q9) and desired DP profile.
- Ensures the process performs at every stage and maintains quality and product attributes.



Typical Approach

- A planned set of controls to produce a drug based on an understanding of its production process.
- A control strategy ensures the process performs as it should and maintains quality. (ICH Q8, 9, 10)
- Starts from the patient (ICH Q9) and desired DP profile.
- Ensures the process performs at every stage and maintains quality and product attributes.

Special case mRNA Regulations (different or additional)?



Currently there is no guideline which reflects the quality requirements from regulators and industry on mRNA containing vaccines

mRNA is a new class of drugs - regulated as a vaccine - typical mRNA application work not ATMP

Other therapeutic mechanisms are emerging - not fully accounted currently! Some applications as GTMPs (self-replicating RNA)

Future classification may depend on the target or how the mRNA is made (chemically or biologically).

Many parts applicable criticisms to GTMPs (e.g. DNA template, formulation for PEI/LNPs).

There was a guideline consultancy due 30th [here](#).

There is a WHO document [here](#).

The WHO guidance document, Annex 3 "Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations", WHO technical 71 report Series, No.1039, 2022



1 22 June 2023
2 EMA/CHMP/ BWP/211968/2023
3 Committee for Medicinal Products for Human Use (CHMP)

4 Concept Paper on the development of a Guideline on the
5 quality aspects of mRNA vaccines
6
7

Agreed by Biologics Working Party	14 June 2023
Adopted by CHMP for release for consultation	22 June 2023
Start of public consultation	23 June 2023
End of consultation (deadline for comments)	30 September 2023

8
9
10 Comments should be provided using this EUSurvey [form](#). For any technical issues, please contact the [EUSurvey Support](#)

Keywords	Guideline, mRNA, Vaccine, Development and Manufacture, Starting Materials, Active Substance, Finished Product
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12

What are the Key Regulatory Points about ICH Q4

Q4B & Q4D

ICH Q4B Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions

Purpose: ICH Q4B is designed to promote harmonization in the interpretation and application of pharmacopoeial test methods to establish standards for the identity, quality, purity, and strength of drugs.

Key Points: The guideline provides a process for the evaluation and recommendation of pharmacopoeial texts to be used in the ICH regions (Europe, Japan, United States). It aims to facilitate mutual acceptance of pharmacopoeial standards.

Differences: Differences between the FDA and EMA in this context may arise in their specific pharmacopoeial requirements and acceptance criteria for certain tests.

Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Products

Purpose: ICH Q4D addresses the design of stability studies for new drug substances and products. Bracketing and matrixing are statistical experimental designs used to reduce the amount of stability testing needed (ICH Q1).

Key Points: The guideline provides principles and recommendations for the application of bracketing and matrixing designs to stability testing. It aims to ensure that the data generated are sufficient to support the proposed Aretest periods and shelf life. this

Differences: Differences between the FDA and EMA in the application of bracketing and matrixing designs may arise .S. due to specific regulatory interpretations or requirements.

Registration

Sneak Peek

CMC/Regulatory Affairs for Nucleic Acids



Mliekarenská 9, 821 09
Bratislava, Slovak Republic
ID: 47 068 124
VAT no: SK2023741973
Office: +421 948 262 346

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