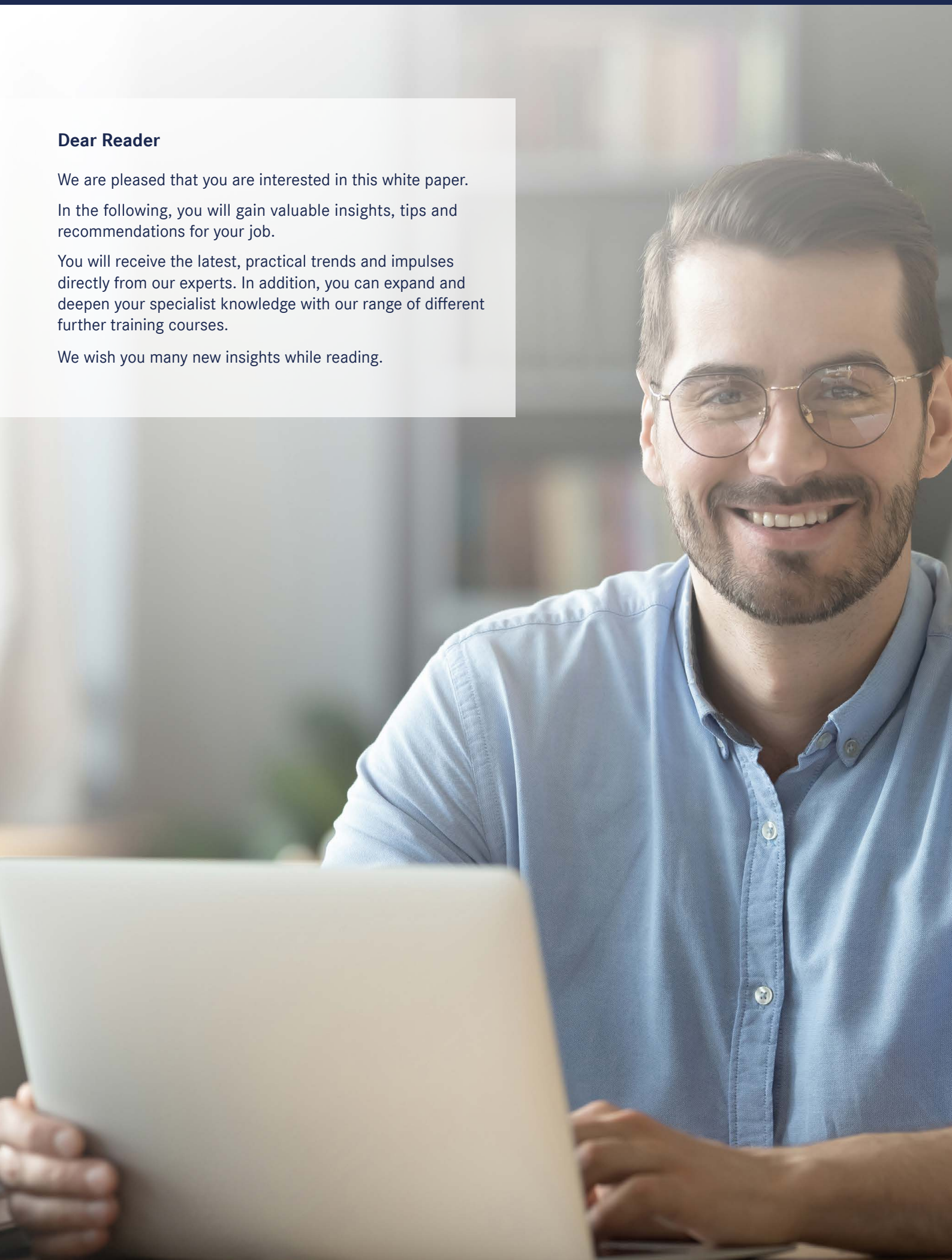
FORUM

MA and lifecycle management in Japan

Additions and differences to ICH requirements

Dr. Christina Juli



Dear Reader

We are pleased that you are interested in this white paper.

In the following, you will gain valuable insights, tips and recommendations for your job.

You will receive the latest, practical trends and impulses directly from our experts. In addition, you can expand and deepen your specialist knowledge with our range of different further training courses.

We wish you many new insights while reading.

About the author

Dr Christina Juli

Dr Christina Juli studied pharmacy at the University of Würzburg, Germany. She started her professional career as Senior Manager in the department of EU Regulatory Affairs Generic Maintenance. Since 2018, she is working at the manufacturing site for biopharmaceuticals of Boehringer Ingelheim Pharma GmbH & Co. KG in Biberach, Germany. In her role as Head of CMC Management CMB, she focuses on the CMC development for biologics and is responsible for the definition compilation and review of the CMC documentation for clinical trial and new drug applications as well as for post approval submissions worldwide.

Additions and differences to ICH requirements

You are working in Regulatory Affairs and dealing with affiliates or external partners in Japan?
You would like to get more confident understanding which documentation/quality data have to be included in addition into the global dossier and avoid typical mistakes when submitting in Japan?
This whitepaper describes what you need to keep in mind when it comes to specific Japanese CMC requirements for marketing authorisation and lifecycle management of a pharmaceutical product.
It includes details on small molecules and biologics.

CMC related sections of the J-CTD (M3 and M2)

FORUM

- **Module 3:**
  - Source documents for J-QOS
  - Submission in English language
  - 3.2.R: No specific requirements as for other ICH countries
  - Specifications and test methods acc. to Japanese Pharmacopoeia, if applicable
- **Module 2 (J-QOS):**
  - Primary review document for PMDA (usually more than 100 pages); J-QOS forms the basis for the approval decision
  - Summary of all critical data from Module 3
  - Discussion on every critical point ensuring quality of product to be included
  - Includes many figures and tables and detailed information
  - Items listed in the manufacturing process description require appropriate change control

→ Partial change application and minor change notification

CMC related sections of the J-CTD (S-Part)

- **Differences compared to EU and US:**

CTD	Japan specific requirements
S.1	• Submission of J-MAA with a new API: JAN (Japanese Accepted Name) has to be registered before in JAN database
S.2.2 S.2.4	• Process parameters identified according to minor change or partial change application • Storage considered as part of manufacturing
S.2.3	• Detailed method description
S.4.2	• Detailed method description (acc. to the guidance of drafting new JP monographs)
S.4.4	• Overview of all batches / results in one table
S.5	• Test items and acceptance criteria to be established for all references
S.7	• Shelf life based on real time data • Overview of all batches / results in one table

CMC related sections of the J-CTD (P-Part)

- **Differences compared to EU and US:**

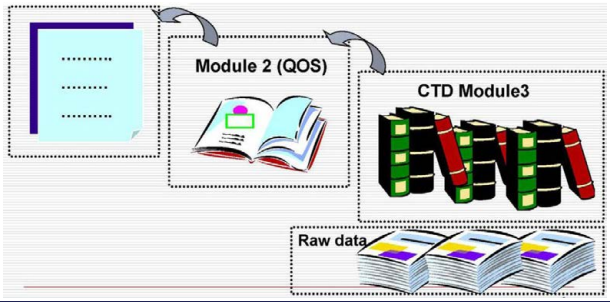
CTD	Japan specific requirements
P.3.3 P.3.4	• Process parameters identified according to minor change or partial change application • Secondary packaging process to be described • Storage considered as part of manufacturing • Final release site of DP has to be located in Japan
P.4.1 P.4.2	• Excipients to comply with JP (if not full list of specifications/ acceptance criteria, full descriptions, full range of validation and justification required)
P.5.2	• Detailed method description (acc. to the guidance of drafting new JP monographs)
P.6	• Test items and acceptance criteria to be established for all references
P.8	• Shelf life based on real time data • Overview of all batches / results in one table

CMC related sections of the J-CTD (M2/3 – Biologics)

- **Special requirements for biotechnological products**
  - Additional guidelines and requirements for Japan:
    'Minimum Requirements for Biological Products' (MRBP)
  - Detailed description of cell culture system
  - Intensive viral safety studies
  - Viral testing of MCB and WCB explained in detail
  - In-depth viral risk assessment
  - Biological products undergo product designation review
  - Classification of the product according to special precautions related to public health and safety → No risk to the health of the public
  - Stricter guidelines and rules for biological ingredients from human or animal sources

Japanese Approval Form (J-AAF)

- Included in Module 1
- Identification of critical information on the basis of M2/ J-QOS
- Legally binding document: this document has to be updated after approval; maintenance of J-QOS for PCA in specific cases
- All contents in J-AAF are regulatory relevant and any changes need a regulatory action:
  - PCA: Parameters which affect the quality of the product
  - MCN: Parameters which have no influences on the product quality



J-AAF – Lifecycle Management

- Introduction of Notification systems, Partial Change Application (PCA) and Minor Change Notification (MCN), by Japanese PAL revision in April 2005
  - Detailed descriptions of mfg. procedures and process controls were required.
  - PCA: Parameters which affect the quality of the product
  - MCN: Parameters which have no influences on the quality of the product
  - All parameters have to be distinguished by brackets.
  - **Example**: Stir 『1 kg』 of XYZ and 『2 L』 of methanol for "at least 1 hour". Heat to <<49ºC>> and then stir for not less than 2 hour.

Process parameters and standard charge-in amounts	PCA Item	MCN Item
Target / set values	Entered into << >>	Entered into 『 』
Other than target / set values	non-brackets	Entered into " "

J-AAF – Content

- **Manufacture of DS and DP**
  - Information of manufacturing sites such as name, address, FMA number incl. external warehouses and external labs.
  - Manufacturing flow schemes
  - Manufacturing procedures incl. IPC (Critical processes & critical intermediates also have to be indicated)
  - Material flow should be described clearly
  - Control of raw materials and intermediates
  - Information of bio-derived materials
- **Excipient**
  - Amounts and reference specifications
  - Specifications and test procedures (if non-compendial or EP/USP excipient is used)
- **Specification and Test Procedure** of DS, DP and Reference Standard
- **Storage Condition and Retest Period / Shelf-life** of DS and DP

Other offers:

Practical regulatory affairs and vigilance knowledge

Our regulatory courses and conferences provide practical information on the fundamentals and trends in marketing authorisation, regulatory maintenance and post-marketing surveillance. More information.

e-Learning – Click and learn

The FORUM Institut offers a flexible form of training with quality e-learning courses. You decide for yourself when and where to learn. Test free now.

In-house seminars – Tailored solutions

All our seminars are also perfect for in-house training. Request a personalised quotation now.

FORUM · Institut für Management GmbH · Vangerowstraße 18 · 69115 Heidelberg • Germany
Phone: +49 6221 500-500 · Fax: +49 6221 500-555 · www.forum-institut.com