VICH GL60
GOOD MANUFACTURING PRACTICE FOR ACTIVE INGREDIENTS USED IN VETERINARY MEDICINAL PRODUCTS

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- **Topics to be covered:**
- How the Quality Subgroup was formed
- Subgroup Membership
- Overview of Concept Paper: Why VICH GL60 is needed?
- Timeline/Status
- Key Sections/Topics covered by VICH GL60
- Examples
- Discussion & Revision
- Next Steps
- ICH vs VICH Quality Guidelines
- References

How the Subgroup was formed

- **Concept paper:**
  - Drafted by FDA/CVM and was first presented to VICH Steering Committee - Nov. 2019
  - Work did not start until March 2020
  - A new subgroup was formed within Quality Expert Working Group
    - SubGQual@vichsec.org
    - Topic Leader: FDA/CVM
    - Each region added additional members to the subgroup:
      - 1 lead member (Expert)
      - 1 advisor

Membership of the subgroup

Regulators

- EU:
  - Norbert Möller (Expert)
  - Gregory Verdier (Advisor-New Expert as of July 2024)
- JMAFF:
- Tomoko OGATA (Quality Chair)
  - Chikako Takahashi (Expert)
- US FDA:
  - Mai Huynh (Topic Leader)
  - Michael Kerrigan (Advisor)
- VMD:
  - Jason Todd
- APVMA:
  - Glen Edmunds
- Health Canada:
  - Neola Henry

Industry Representatives

- AHE:
  - Herve Fournel (Expert)
  - Martin Folger (Advisor)
- AHI:
  - Brandie Pies (Expert)
  - Claire Doyle (Advisor)
- JVPA:
  - Osamu Moriyama (Expert)
- CAHI:
  - Louise Labelle (Expert)
  - Ian Jarvis (Advisor)

Overview of Concept Paper-VICH GL60

Objectives:

- To adapt principles that have been established for years for Active Pharmaceutical Ingredients (APIs) for use in human drugs (ICH Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients).
- The ICH Q7 guideline which is incorporated in the Pharmaceutical Inspection Cooperation Scheme (PIC/S GMP) Part II has been referenced in PIC/S training program for APIs for the last several years. The goal of this training program is to raise awareness among global inspectorates in the relation to API manufacturers as well as their supply chain, especially for manufacturers located in countries subject to a Mutual Recognition Agreement (MRA) inspection review such as the US/EU MRA.

Overview of Concept Paper-VICH GL60-(cont.)

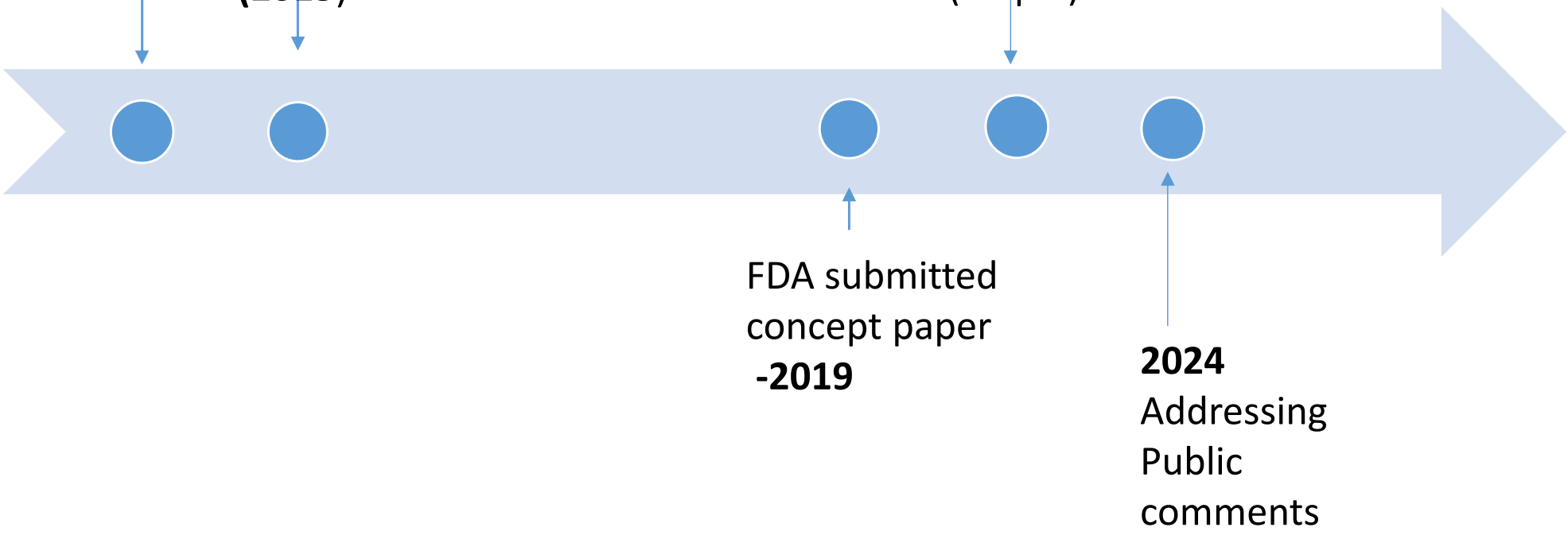
Objectives:

- The harmonized guideline will also provide manufacturers a framework to establish an appropriate quality system to manage the production of their products, which helps ensure that APIs meet the quality and purity characteristics that they purport, or are represented, to possess.

Importance of VICH GL60

It will be the first internationally harmonized Guideline for Good Manufacturing Practice (GMP) for Active Ingredients (APIs) used in Veterinary Medicinal Products (VMPs) developed jointly by industry and regulators.

Timeline


ICH Q7
(2000)
Q7 Q&As
(2015)
2023
Draft for
Public comment
(Step 4)
FDA submitted
concept paper
-2019
2024
Addressing
Public
comments

Timeline-(cont.)

- VICH GL60 reached Step 4 – September 2023
- Draft Guideline was posted both in each region and on VICH website for public comment since October 2023
- Comments were received at the end of the comment period (March 2024)
- Quality subgroup is in the process of addressing the comments

Key Topics in VICH GL60

- Introduction
- Quality Management
- Personnel
- Building and Facilities
- Process Equipment
- Documentation and Records
- Materials Management
- Production and In-Process Controls
- Packaging and Identification Labeling of APIs and Intermediates
- Storage and Distribution

Key Topics in VICH GL60- (cont.)

- Laboratory Controls
- Validation
- Change Control
- Complaints and Recalls
- Contract Manufacturers (Including Laboratories)
- Agents, Brokers, Traders, Distributors, Repackers, and Relabellers
- Specific Guidance for APIs Manufactured by Cell Culture/Fermentation
- APIs for Use in Clinical Trials
- Glossary
- References

VICH GL60-Key principles

1.3 Scope:

- This Guide applies to the manufacture of APIs for use in veterinary medicinal products. It applies to the manufacture of sterile APIs only up to the point immediately prior to the APIs being rendered sterile. The sterilization and aseptic processing of sterile APIs are not covered by this Guide, but should be performed in accordance with GMP guidelines for veterinary medicinal products as defined by local authorities.
- This Guide covers APIs that are manufactured by chemical synthesis, extraction, cell culture/fermentation, by recovery from natural sources, or by any combination of these processes.

Examples

Examples how this Guideline applies to API Manufacturing
(ref. Table 1, Section 1.3 in VICH GL60)

Type of Manufacturing	Application of this guide to steps used in this type of manufacturing				
Chemical Manufacturing	Production of the API starting material	Introduction of the API Starting Material into process	Production of Intermediate (s)	Isolation and Purification	Physical Processing And Packaging
"Classical" Fermentation To produce an API	Establishment Of cell bank	Maintenance of cell bank	Introduction of the Cells into Fermentation	Isolation and Purification	Physical Processing And Packaging

Increasing GMP requirements

Type of Manufacturing	**Application of this guide to steps used in this type of manufacturing**				
Chemical Manufacturing	Production of the API starting material	Introduction of the API Starting Material into process	Production of Intermediate (s)	Isolation and Purification	Physical Processing And Packaging
API derived from animal sources	Collection of organ, fluid or tissue	Cutting, mixing, and/or initial processing	Introduction of the Starting Material into the process	Isolation and Purification	Physical Processing And Packaging

Increasing GMP requirements

Type of Manufacturing	**Application of this guide to steps used in this type of manufacturing**				
Biotechnology: Fermentation/ cell cultures	Establishment of master cell bank and working cell bank	Maintenance of working cell bank	Cell culture and/or fermentation	Isolation and Purification	Physical Processing And Packaging
"Classical" Fermentation To produce an API	Establishment of cell bank	Maintenance of the cell bank	Introduction of the cells into fermentation	Isolation and Purification	Physical Processing And Packaging

Increasing GMP requirements

Discussion & Revision

- Sections where revisions were incorporated to tailor the production of APIs for use in VMPs:
  - **1.1. Objective:**
  - While animal welfare and environmental risk are not specifically covered by this Guide, international, national, and regional standards implemented in the country/region where the active substance is manufactured, where it is used in the production of a veterinary medicinal product and where such a veterinary medicinal product is marketed must be observed. Measures to prevent or minimize discharge of active substances into the environment should also be taken into account and relevant international, national, and regional standards implemented.

Discussion & Revision-(cont.)

1.2 Regulatory Applicability:

Special statement added for ectoparasiticides for veterinary use:

- In the case of ectoparasiticides for veterinary use, other standards than this Guide, that ensure that the material is of appropriate quality, may be used in some regions.
- In some regions, where the concept of “equivalent guidance” may not be applicable, adherence to the GMP concepts as described in this guideline is recommended.

Discussion & Revision-(cont.)

1.3 Scope:

This Guide excludes all vaccines, whole cells, whole blood and plasma, blood and plasma derivatives (plasma fractionation), and gene therapy APIs. However, it does include APIs that are produced using blood or plasma as raw materials. Note that cell substrates (mammalian, plant, insect or microbial cells, tissue or animal sources including transgenic animals) and early process steps may be subject to GMP but are not covered by this Guide. In addition, the Guide does not apply to veterinary medical gases, and bulk-packaged veterinary medicinal products.

Discussion & Revision-(cont.)

3.1 Personnel Qualifications:

- Clarification was provided to also include personnel responsible for packaging/labeling, testing and storage

4.3 Water

- Water quality? What standard to follow:
  - Clarification was added for water quality where a non-sterile API either intends or claims that it is suitable for use in further processing to produce a sterile veterinary medicinal product

Discussion & Revision-cont.

4.4. Containment:

- Dedicated areas or not?
  - Cleaning procedures are in place to prevent cross-contamination
- Shared facilities are allowed if:
  - Facility Quality System is effective
  - Quality risk management is in place to mitigate risk of cross-contamination

Discussion & Revision-cont.

11.20: Testing of Intermediates and APIs

- Biotechnology consideration: replaced reference to ICH Q6B to VICH GL40

- **19: APIs for use Clinical Trials**
  - Request to add “pivotal” clinical trials
- **19.8 Laboratory Controls:**
  - Should methods used to evaluate a batch of API be fully validated?
- **Glossary**
- Replacing reference to ICH Quality Guidelines to equivalent VICH Qs when one is available

Next Step(s)?

- The subgroup is currently reviewing the comments received from the draft (Step 4) issued for public comment.
- Can the subgroup reach a compromise to the questions/comments received?
- Would each region be open to create its own Question and Answers (Q&As) Guide to provide more clarity to the issues raised?
  - The US FDA is planning to issue a Q&As Guide once VICH GL60 is recommended for adoption.
  - The US FDA also recommends our stakeholders, when in doubt, to reach out to FDA/CVM (formally or informally) for further clarification on concepts described in any of the Quality Guidelines.

Next Step(s)?-cont.

- ICH has a Q7 Q&As document after Q7 was finalized, as well as training sessions to aid in the interpretation of ICH Q7
- VICH Quality can organize a workshop on GL60 once the guideline has been adopted for implementation to aid in the interpretation of concepts and principles included in the guideline. The workshop can be done virtually to encourage attendance.

- **ICH Quality Guidelines**
- Q7 Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
- Q8 Pharmaceutical Development
- Q9 Quality Risk Management
- Q10 Pharmaceutical Quality System
- Q11 Development and Manufacture of Drug Substance
- Q12 Life Cycle Management
- Q13 Continuous Manufacturing of Drug Substances and Drug Products
- Q14 Analytical Procedure Development

- **VICH Quality Guidelines**
- GL 60 (Q7 equivalent)-Draft
- GL 61 (Q8 equivalent)- Draft

There is no VICH GL equivalent to ICH Q9 – Q14

REFERENCES

- **ICH Q7:**
  - Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
- **ICH Q5A:**
  - Quality of Biotechnological Products: Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin
- **ICH Q5D:**
  - Quality of Biotechnological Products: Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products
- **VICH GL9:**
  - Good Clinical Practices
- **VICH GL40:**
  - Test Procedures/Acceptance Criteria for New Biotechnological/Biological Veterinary Medicinal Products

Thank You

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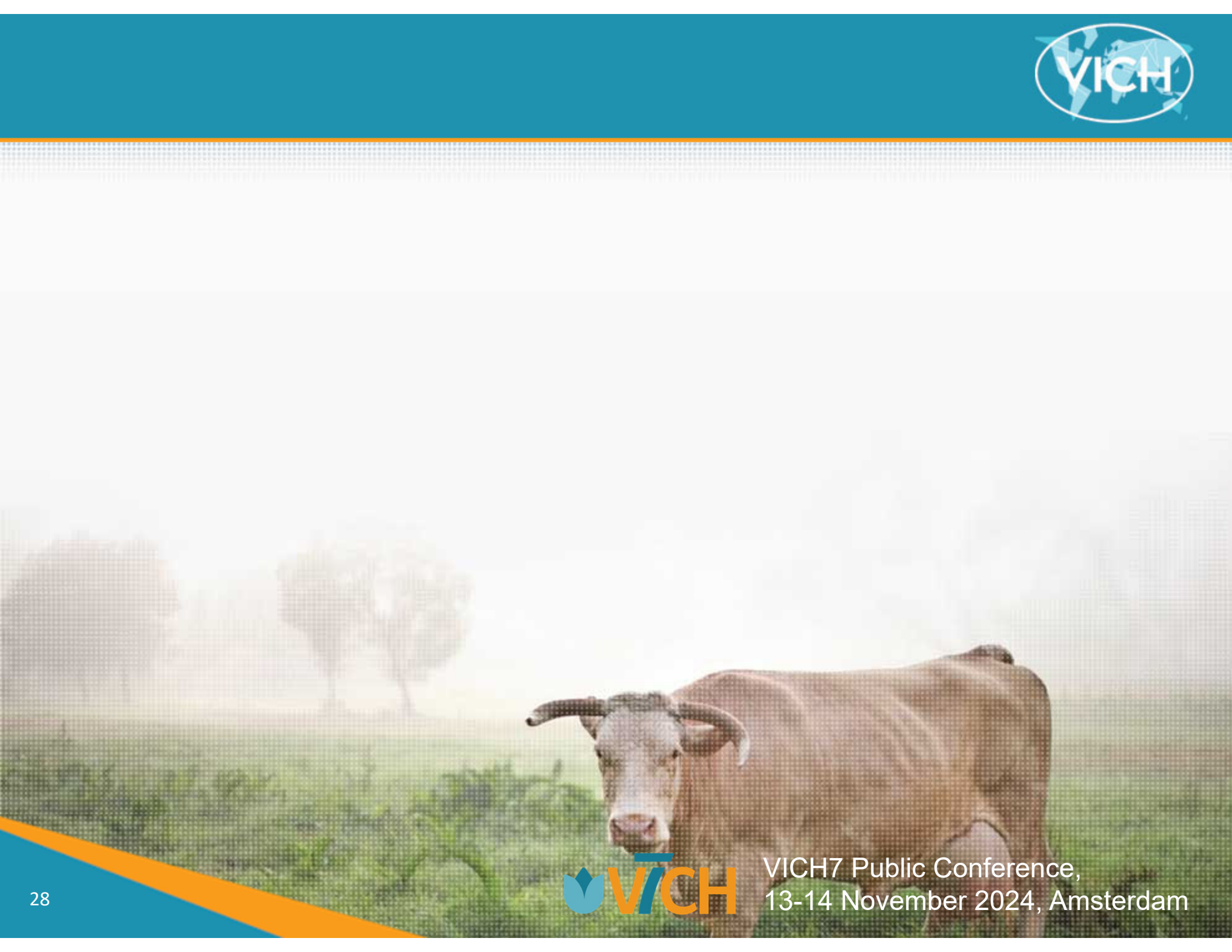

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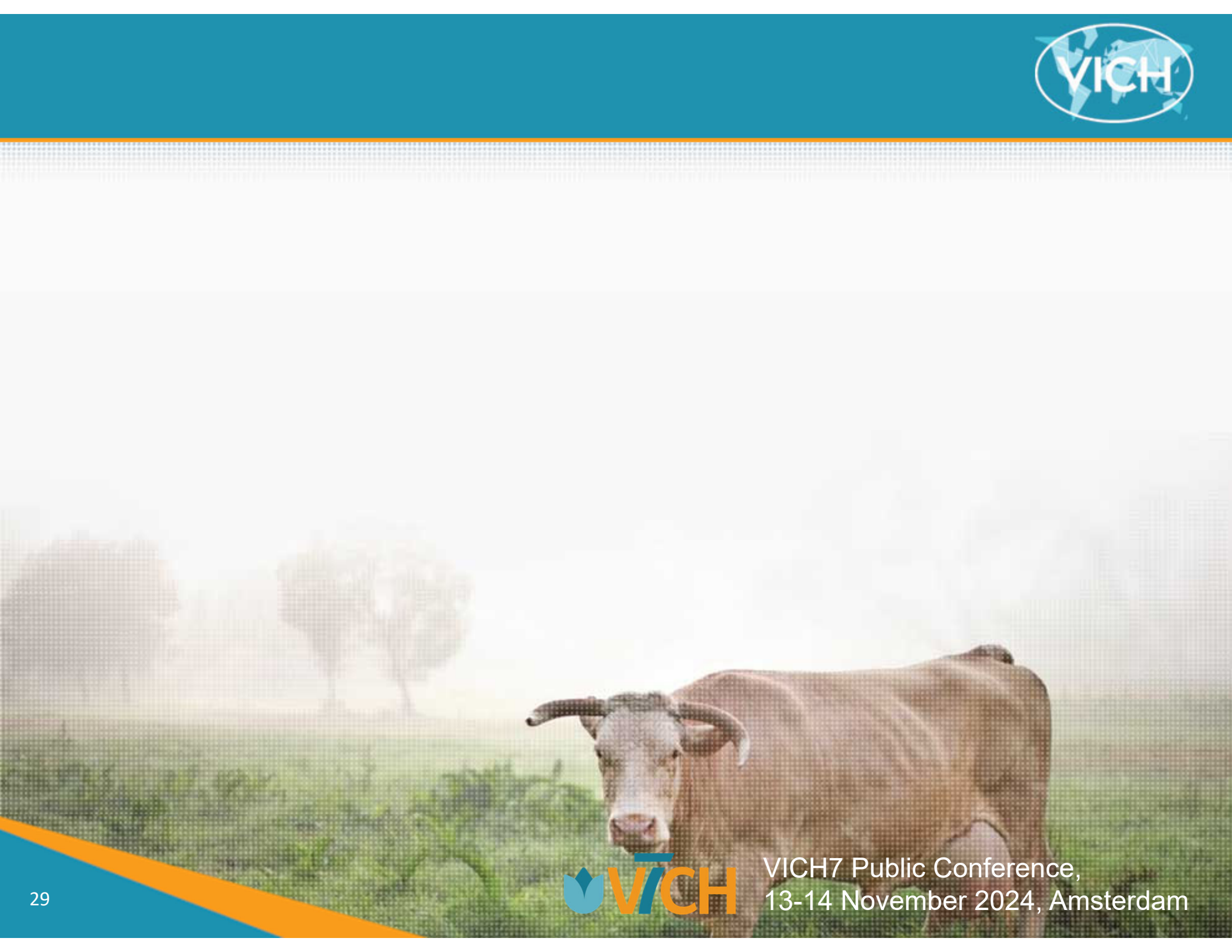

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