ISCP_10012023

י״ח טבת, תשפ״ג
11 ינואר, 2023

אל: בעלי הרישום

שלום רב,

הנדון: עדכון נהלי איכות של ארגון ה- ICH, VICH וסוכנות התרופות האירופאית European Medicine Agency (EMA) המאומצים ע״י המכון לביקורת ותקנים של חומרי רפואה

סימוכין: מכתבנו מתאריך 4.5.2016 ISCP_04052016 למעבר לחוזר
מכתבנו מתאריך 20.6.2018 ISCP_03062018 למעבר לחוזר
בהמשך לחוזרים שבסימוכין, להלן רשימה מעודכנת של נהלי האיכות המאומצים ע״י המכון:

נהלי ICH ו- VICH

1. **הנחיות בנושאי איכות של תכשירים הומניים-** הנהלים זמינים בקישור https://www.ich.org/page/quality-guidelines
   - 1.1. Q1A-Q1F Stability
     ראה גם נוהל המכון EX-007
   - 1.2. Q2 Analytical Validation
   - 1.3. Q3A-Q3D Impurities
   - 1.4. Q5A-Q5E Quality of Biotechnological Products
   - 1.5. Q6A-Q6B Specifications
   - 1.6. Q7 Good manufacturing Practice
     ראה גם תקנות הרוקחים תנאי ייצור נאותים לתכשירים התשס״ט-2008
   - 1.7. Q8 Pharmaceutical Development
   - 1.8. Q9 Quality Risk Management
   - 1.9. Q10 Pharmaceutical quality System
   - 1.10. Q11 Development and manufacture of drug Substance
   - 1.11. Q12 Life Cycle Management

2. **הנחיות בנושאי איכות של תכשירים וטרינריים-** הנהלים זמינים בקישור https://vichsec.org/en/guidelines.html
   - 2.1. VICH GL1, GL2 Analytical Validation
   - 2.2. VICH GL10 (R), GL11(R), GL18 (R) Impurities
   - 2.3. VICH GL8, GL4, GL3, GL5, GL45, GL51, GL58 Stability
     ראה גם נוהל המכון EX-007
   - 2.4. VICH GL39 Specifications
   - 2.5. VICH GL17, GL25, GL26, GL34, GL40 Biologicals

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3. הנחיות רב תחומיות (Multidisciplinary)- הנהלים זמינים בקישור
https://www.ich.org/page/multidisciplinary-guidelines

3.1. M4 Common Technical Document
3.2. M7 Genotoxic Impurities

<u>נהלי EMA</u>

1. Quality (Relevant to Chemistry and Biology products)

1.1. Active substance
- 1.1.1. Guideline on Active Substance Master File Procedure
- 1.1.2. Guideline on the chemistry of active substances
- 1.1.3. Investigation of chiral active substances
- 1.1.4. Guideline on Summary of requirements for active substances in the quality part of the dossier

1.2. Manufacturing
- 1.2.1. Guideline on manufacture of the finished dosage form
- 1.2.2. Guideline on process validation for finished products - information and data to be provided in regulatory submissions
- 1.2.3. Note for guidance on Start of shelf-life of the finished dosage form
- 1.2.4. The Use of ionizing radiation in the manufacture of medicinal products 3AQ4A

1.3. Impurities
- 1.3.1. Control of impurities of pharmacopoeial substances
- 1.3.2. Setting specifications for related impurities in antibiotics

1.4. Specification, analytical procedures and analytical validation
- 1.4.1. Specifications and control tests on the finished product
- 1.4.2. Use of near infrared spectroscopy (NIRS) by the pharmaceutical industry and the data requirements for new submissions and variations 9

1.5. Excipients
- 1.5.1. Excipients in the dossier for application for marketing authorization of a medicinal product
- 1.5.2. Guideline on the quality of water for pharmaceutical use

1.6. Packaging
- 1.6.1. Plastic primary packaging materials

1.7. Stability
- 1.7.1. Declaration of storage conditions for medicinal products particulars and active substances
- 1.7.2. In-use stability testing of human medicinal products

1.7.3. Maximum shelf-life for sterile products for human use after first opening or following reconstitution 6
1.7.4. Note for guidance on Start of shelf-life of the finished dosage form
1.7.5. Stability testing for applications for variations to marketing authorisation
1.7.6. Stability testing of existing active ingredients and related finished products

1.8. Pharmaceutical Development
1.8.1. Quality documentation for medicinal products when used with a medical device
1.8.2. Development pharmaceutics
1.8.3. Guideline on the sterilisation of the medicinal product, active substance, excipient and primary container
1.8.4. Pharmaceutical development of medicines for pediatric use

1.9. Quality By Design
1.9.1. Real time release testing
1.9.2. Use of near infrared spectroscopy (NIRS) by the pharmaceutical industry and the data requirements for new submissions and variations

1.10. Specific types of products
1.10.1. Medicinal gases: pharmaceutical documentation (including recommendation on non-clinical safety requirements for well-established medicinal gases)
1.10.2. Pharmaceutical quality of inhalation and nasal products
1.10.3. Quality of oral modified release products
1.10.4. Quality of transdermal patches
1.10.5. Radiopharmaceuticals

2. Biologics

2.1. Active Substance
2.1.1. Manufacture, characterization and control of the active substance
2.1.1.1. Allergen products: production and quality issues
2.1.1.2. Development and manufacture of lentiviral vectors
2.1.1.3. Development, production, characterization and specifications for monoclonal antibodies and related products
2.1.1.4. Gene therapy product quality aspects in the production of vectors and genetically modified somatic cells
2.1.1.5. Human cell-based medicinal products

2.1.1.6. Potency testing of cell-based immunotherapy medicinal products for the treatment of cancer
2.1.1.7. Process validation for the manufacture of biotechnology-derived active substances and data to be provided in the regulatory submission
2.1.1.8. Production and quality control of animal immunoglobins and immunosera for human use
2.1.1.9. Production and quality control of medicinal products derived by recombinant DNA technology
2.1.1.10. Quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells
2.1.1.11. Quality of biological active substances produced by stable transgene expression in higher plants
2.1.1.12. Quality of biological active substances produced by transgene expression in animals-Scientific guideline
2.1.1.13. Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products
2.1.1.14. Use of starting materials and intermediates collected from different sources in the manufacturing of non-recombinant biological medicinal products

2.1.2. Plasma-derived medicinal products
2.1.2.1. Investigation of manufacturing process for plasma-derived medicinal products with regard to variant Creutzfeldt-Jakob disease risk
2.1.2.2. Plasma-derived medicinal products
2.1.2.3. Replacement of rabbit pyrogen testing by an alternative test for plasma derived medicinal products

2.1.3. Plasma Master File
2.1.3.1. Requirements for plasma master file certification
2.1.3.2. Scientific data requirements for plasma master file
2.1.3.3. Epidemiological data on blood transmissible infections
2.1.3.4. Validation of immunoassay for the detection of antibody to human immunodeficiency virus in plasma pools
2.1.3.5. Validation of immunoassay for the detection of hepatitis B virus surface antigen in plasma pools

2.1.4. Vaccines
2.1.4.1. Adjuvants in vaccines for human use
2.1.4.2. Note for guidance on the development of Vaccinia virus based vaccines against smallpox

- 2.1.4.3. Influenza vaccines - quality module
- 2.1.4.4. Quality, non-clinical and clinical aspects of live recombinant viral vectored vaccines
- 2.1.4.5. Testing for simian virus 40 (SV40) in polio virus vaccines

2.2. Finished Product

2.2.1. Pharmaceutical development

- 2.2.1.1. Development pharmaceutics for biotechnological and biological products

2.2.2. Adventitious agent's safety evaluation

- 2.2.2.1. Adventitious agent safety of urine-derived medicinal products
- 2.2.2.2. Use of bovine serum in the manufacture of human biological medicinal products
- 2.2.2.3. Use of porcine trypsin used in the manufacture of human biological medicinal products
- 2.2.2.4. Virus validation studies: the design, contribution and interpretation of studies validating the inactivation and removal of viruses
- 2.2.2.5. Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products

2.2.3. Biosimilarity

- 2.2.3.1. Guideline on similar biological medicinal products
- 2.2.3.2. Similar biological medicinal products containing biotechnology-derived proteins as active substance: quality issues
- 2.2.3.3. Guideline on non-clinnical and clinical development of similar biological medicinal products containing low molecular-weight-heparins
- 2.2.3.4. Guideline on non-clinical and clinical development of similar biological medicinal products containing recombinant human insulin and insulin analogues

2.2.4. Cell based Therapy

- 2.2.4.1. Human cell-based medicinal products
- 2.2.4.2. Potency testing of cell-based immunotherapy medicinal products for the treatment of cancer
- 2.2.4.3. Guideline on the risk-based approach according to annex I, part IV of Directive 2001/83/EC applied to Advanced therapy medicinal products

2.2.5. Gene Therapy
- 2.2.5.1. Quality, Pre-Clinical And Clinical Aspects Of Gene Transfer Medicinal Products
- 2.2.5.2. Guideline on the quality, non-clinical and clinical aspects of gene therapy medicinal products
- 2.2.5.3. Quality, non-clinical and clinical aspects of medicinal products containing genetically modified cells
- 2.2.5.4. Development and manufacture of lentiviral vectors
- 2.2.5.5. Guideline on the risk-based approach according to annex I, part IV of Directive 2001/83/EC applied to Advanced therapy medicinal products

2.2.6. Herbal Medicinal Products
- 2.2.6.1. Good agricultural and collection practice for starting materials of herbal origin
- 2.2.6.2. Quality of combination herbal medicinal products/traditional herbal medicinal products
- 2.2.6.3. Quality of herbal medicinal products/traditional herbal medicinal products
- 2.2.6.4. Specification: test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products

3. Veterinary

3.1. Guideline on manufacture of the veterinary finished dosage form
3.2. Guideline on the chemistry of active substances for veterinary medicinal products
3.3. Development pharmaceutics for veterinary medicinal products
3.4. Excipients in the dossier for application for marketing authorisation for veterinary medicinal products
3.5. Declaration of storage conditions: 1. in the product information of pharmaceutical veterinary medicinal products, 2. for active substances In-use stability testing of veterinary medicinal products (excluding immunological veterinary medicinal products)
3.6. Additional quality requirements for products intended for incorporation into animal feeding-stuffs (medicated premixes)
3.7. Quality aspects of pharmaceutical veterinary medicines for administration via drinking water
3.8. Quality aspects of single-dose veterinary spot-on products
3.9. Quality of modified release dosage forms for veterinary use

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3.10. Inclusion of antioxidants and antimicrobial preservatives in medicinal products
3.11. Note for guidance on limitations to the use of ethylene oxide in the manufacture of medicinal products
3.12. Implementation of risk assessment requirements to control elemental impurities in veterinary medicinal products
3.13. Guideline on parametric release

4. אימוץ הנחיות המתייחסות ל-Nitrosamine impurities

ראה חוזר המכון בנושא פרסום מסמך הנחיות EMA לביצוע הערכת סיכונים לנוכחות ניטרוזאמינים.

4.1. Nitrosamine impurities in human medicinal products
4.2. European Medicines Regulatory Network approach for the implementation of the CHMP Opinion pursuant to Article 5(3) of Regulation (EC) No 726/2004 for nitrosamine impurities in human medicines

בכבוד רב,

ד"ר עפרה אקסלרוד
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