Considerations for Production and Quality Control of Animal Derived Pharmaceutical Excipients

Chinese Pharmacopoeia Commission

Comprehansive Division
Dr. Xiaoxu Hong

ChP-EDQM Workshop on Pharmaceutical Excipients

18 September 2018， Strasbourg, France

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn

1

Main Contents

- Relevant Background
- Compendial Requirements
- Key Points for Quality Control
- Working Progress

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn

2

Importance of Pharmaceutical Excipients

The management provisions for nonactive materials are derived from the specifications for use of pigments in foods and drugs

➢1906, Pure Food and Drug Act

Seven (7) synthetic organic pigments may be used in an appropriate range

Any one using a pigment other than the 7 pigments will be prosecuted

➢1937, The "Sulfonamide Elixir Event" made the United States Congress to pass the "Food, Drug, and Cosmetic Act"

(To facilitate oral administration in children, Harold Wotkins, a chief pharmacist in a company in the United States, used diglycol as solvent instead of alcohol, leading to renal failure in 358 persons, and deaths of 107 persons)

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn

Animal source excipients in Chinese Pharmacopoeia

Serial No.	Species	Source	Serial No.	Species	Source
1	Taurine	Separated from bezoar; Terrestrial mammals have higher levels of liver and bile; marine animals such as cuttlefish, octopus, fish, and shellfish such as oysters and clams	11	shellac	Animal-derived fatty resin
2	Lanolin-free lanolin	Wool	12	Sodium caseinate	Cow, sheep
3	shellac	Animal-derived fatty resin	13	Sulfuric acid fish egg	Fish
4	Egg yolk lecithin	Egg	14	Lactose for inhalation	Animal milk
5	Cetyl	Whale	15	Heparin sodium	Pig
6	Egg yolk lecithin (for injection)	Wool	16	glycerin	Natural animal and vegetable fat refining
7	Cholic acid, sodium cholate	Pig bile	17	Lactic acid	Fermentation
8	cholesterol	Fresh animal offal, bone marrow and brain, wool grease	18	Capsule gelatin	Bovine bone, pork bone
9	Squalane	Shark liver (botanical)	19	Squalane	Shark liver (botanical)
10	Bovine serum	Fetal calf, newborn calf	20	Human albumin	Human plasma

Safety Events of Animal Derived Raw materials/Excipients

Time	Country	Events
2005	China	Capsules with out-of-limit Chromium
2008	China	Strengthen supervision and examination of Cerebroprotein Hydrolysate Injection
2008	American	"Heparin Sodium" Event
2010	Europe/ American	Porcine circovirus DNA was detected in oral rotavirus vaccine (Rotarix and RotaTeg)
2015	China	Deproteinized Calf Extract Injection was manufactured was not complied with the approved process
2016	China	CFDA stopped import of Cerebroprotein Hydrolysate Injection manufactured by a manufacturer

5

Legal requirements for control of animal-derived materials in China

Year	Requirements
2015	General Notices and Procedures for Cells, ChP edition 2015
Sept. 2008	General Rules for Technical Review and Evaluation of Viral Safety Evaluation of Biological Tissue Extraction Products and Eukaryotic Expression Products
2008	Technical Guideline of Live Vaccine Products for Prevention, with Virus as Vector
2008	General Rules for Technical Review and Evaluation of Cell Matrix for Vaccine Production
2008	Technical Methods for Viral Removal/Inactivation of Blood Products, and Technical Guidelines for their Validation
July 10, 2002	• Notice for Further Strengthening Supervision and Management of Bovine-derived Materials and Relevant Drugs, State Drug Supervision Registration No.[2002]238
March 20, 2003	• Technical Guideline for Production and Quality Control of Bovine Serum for Cell Cultivation

6

Gelatin for Capsules

- **Chinese Pharmacopoeia edition 2015 vol.II and vol.IV**
- Products from Purification after Incomplete Acid Hydrolysis, Alkaline Hydrolysis, or Enzymatic Degradation of Collagens in Animal Skin, Bone, Tendon, and Ligament
- **General Rules for Empty Capsules (draft)**
- Products from Purification after Incomplete Acid Hydrolysis, Alkaline Hydrolysis, or Enzymatic Degradation of Collagens in Health Animal Skin (pig or ox, etc.) or Bone (pig and ox), which are mainly derived from fresh bovine bone, pig skin, and bovine skin, and minorly derived from pig bone, etc.;
- The supplier for raw materials has a quarantine conformance certificate issued by a respective authority, and keeps relevant records, so that they are of traceable sources; bovine-derived materials are derived from animals in a district without prevalence of BSE.
- **EP 9.0**
- Gelatin is derived from solidified or nonsolidified natural or dissovable proteins derived from hydrolysis of animal skin or bone collagens
- For animal bone:
  - Skull and spinal bone are removed for collection of bovine bone as raw material, of any age\any country source
  - Vertebra are removed, derived from oxen aged more than 30 months
  - Bovine femur for production of medical capsules for gastrointestinal administration is obtained from a district without BSE or at controllable risk

7

Relevant requirements in the ChP

Chinese Pharmacopoeia edition 2015vol.II and vol.IV

➢Tissue Extract

•For drugs derived from extraction of animal tissues, the species of the animal used is clearly defined;

•The organ used is derived from healthy animals through quarantine inspection.

•The organ of bovine origin is derived from healthy cattle in a bovine spongiform encephalopathy-free area.

•For drugs derived from extraction of human urine, human urine is obtained from healthy persons.

•Viral inactivation process requirements and quality management requirements are clearly defined for the above drugs.

➢Biological Products

•For bacterial and viral strains used directly for production, human- and animal-derived cells, as well as DNA recombinant engineering bacteria and cells, the source is approved by the drug administration authorities of the State Council and complies with the relevant management requirements of our country.

中国药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn

8

Relevant requirements in the Chinese Pharmacopoeia

- *Chinese Pharmacopoeia*, edition 2015 VOL III

◆ Animals for Production and Verification

- Animal cells for preparation of injectable live vaccines are derived from animals without any specific pathogens (SPF grade); animal cells for preparation of oral vaccines and inactivated vaccines are derived from animals of clean grade or higher. All animals comply with the relevant requirements for microbiological and parasitological tests (General Rules 3602 and 3603).
- Bovine serum for cell cultivation is derived from healthy cattle in an area without bovine spongiform encephalopathy (BSE), with quality complying with the relevant requirements of the current edition of the Chinese Pharmacopoeia.
- As demonstrated, trypsin for cell digestion is free of any exogenous or endogenous viral contamination.
- Unless otherwise specified, eggs for preparation of chick embryo or chick embryo cells are derived from chicken flocks without specific pathogens.
- Horses for production comply with the requirements of the "Quarantine and Vaccination Procedures for Horses for Production of Immune Serum"
- Unless otherwise specified, animals with clean grade higher are used as animals for verification; mice are obtained from closed colony animals.
- SPF grade animals are used, where bacterial or viral strains have to be passed by animals.

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.org.cn

9

Quality Control Procedures for Raw & Auxiliary Materials and Excipients for Production of Biological Products

Grade of Exdcipient	Marketing authorization certificate (such as registration approval documents for drugs and excipients, and production license)	GMP certificate of the supplier for drug production	Registration or filing certificates for excipients	Ex-factory inspection report of the supplier	National lot release certificate	Full inspection in accordance with the national drug standard, or the internal control quality standards of the manufacturing enterprise for biological products	Tests for critical items (such as identification, microbial limit, bacterial endotoxin, and undue toxicity, etc.)	Test for eadventitious agnet	Further processing and purification	Evidence of source	Comply with the safety requirements for relevant animal-borne diseases (including TSE) in the country of origin and in China	Audit of Suppliers
Grade 1	√	√	—	√	Provide if available	—	√	—	—	—	—	√
Grade2	√	√	—	√	—	Spot-check (batches)	√	—	—	—	—	√
Grade 3	—	—	Provide for excipients for registration management or filing	√	—	√	—	—	If required	—	—	√
Grade 4	—	Provide where a non-injectable pharmaceuticl substance is used as an excpient of an injection	Provide where a non-injectable pharmaceuticl substance under registration management or filing is used as an excpient of an injection	√	—	√	—	Test if animal-derived	If required	Test if animal-derived	Test if animal-derived	√

委员会 chp.org.cn

10

International Relevant guidelines in the Europe and the United States

- USA The U.S. Department of Agriculture (USDA) regulations for veterinary products as specified in the 9CFR 113 regulations (9CFR). (FDA)
- FDA The Sourcing and Processing of Gelatin to Reduce the Potential Risk Posed by Bovine Spongiform Encephalopathy(BSE) in FDA-Regulated Products for Human Use Guidance for Industry
- ICH VIRAL SAFETY EVALUATION OF BIOTECHNOLOGY PRODUCTS DERIVED FROM CELL LINES OF HUMAN OR ANIMAL ORIGIN Q5A(R1)
- ICH Q6A Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances

Relevant Guidelines issued by EMEA

- Adventitious Agents Safety Evaluation
- Viral Safety Development of a Guideline on Viral Safety Evaluation of Biotechnological Products to be used in Clinical Trials(CHMP/BWP/124447/04)
- Guidance on the Use of Bovine Serum in the Manufacture of Human Biological Medicinal Products(CPMP/BWP/1793/02)
- Quality of Biotechnological Products: Viral safety Evaluation of Biotechnology Products derived from Cell Lines of Human or Animal Origin (CPMP/ICH/295/95 ICH Topic Q5A)
- Virus Validation Studies: The Design, Contribution and Interpretation of Studies validating the Inactivation and Removal of Viruses(CPMP/BWP/268/953AB8A)

Relevant Guidelines issued by EMEA

- Transmissible Spongiform Encephalopathies (TSE) (Animal and Human)

- Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products, Amendments to section 6.2 and 6.3.(EMEA/410/01 Rev. 2)
- Position Paper on Re-establishment of Working Seeds and Working Cell Banks using TSE compliant materials(EMEA/22314/02)
- Public Report on Risk and Regulatory Assessment of Lactose and other products prepared using Calf Rennet(EMEA/CPMP/BWP/337/02 Final)
- Joint CPMP/CVMP Note for Guidance on Minimising the Risk of Transmitting Animal Spongiform Encephalopathy Agents via Human and Veterinary Medicinal Products(EMEA/CPMP/BWP/498/01)
- Public Statement on the Evaluation of Bovine Spongiform Encephalopathies (BSE) - Risk via the Use of Materials of Bovine Origin in or during the Manufacture of Vaccines (EMEA/CPMP/BWP/476/01)
- Explanatory Note: Gelatin for Use in Pharmaceuticals (EMEA/430600/00)
- Position Statement on Polysorbate 80 (CPMP/BWP/1952/98)
- Position Paper on Production of Tallow Derivatives for Use in Pharmaceuticals(CPMP/1163/97)

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.org.cn

13

Relevant Requirements in the European Pharmacopoeia

EP9.0

Raw materials of biological origin for the production of cell-based and gene therapy medicinal producs

- Applicable Scope:

- Serum and Serum Replacements
- Recombinant Protein Products (growth hormone, cytokines, hormones, enzymes, and monoclonal antibody products)
- Proteins extracted from biological materials (enzymes and polyclonal antibodies)

- Including:

- Source
- Manufacturing Process (removing and inactivation process of exogenous factors，process validation，exogenous factor examination)
- Identification
- Examination

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.org.cn

14

Requirements for decreasing the risk of TSE transmission in EP

EP 9.0：Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products

- Transmissible Spongiform Encephalopathies,(TSE)
- Bovine Spongiform Encephalopathy (BSE) in cattle ,
- Scrapie in sheep and goats,
- Chronic wasting disease (CWD) in cervids (deer and elk),
- Transmissible mink encephalopathy (TME) in farmed mink,
- Feline spongiform encephalopathy in fields (specifically domestic cats and captive large cats), and
- Spongiform encephalopathy of exotic ungulates in zoos.

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.cn

15

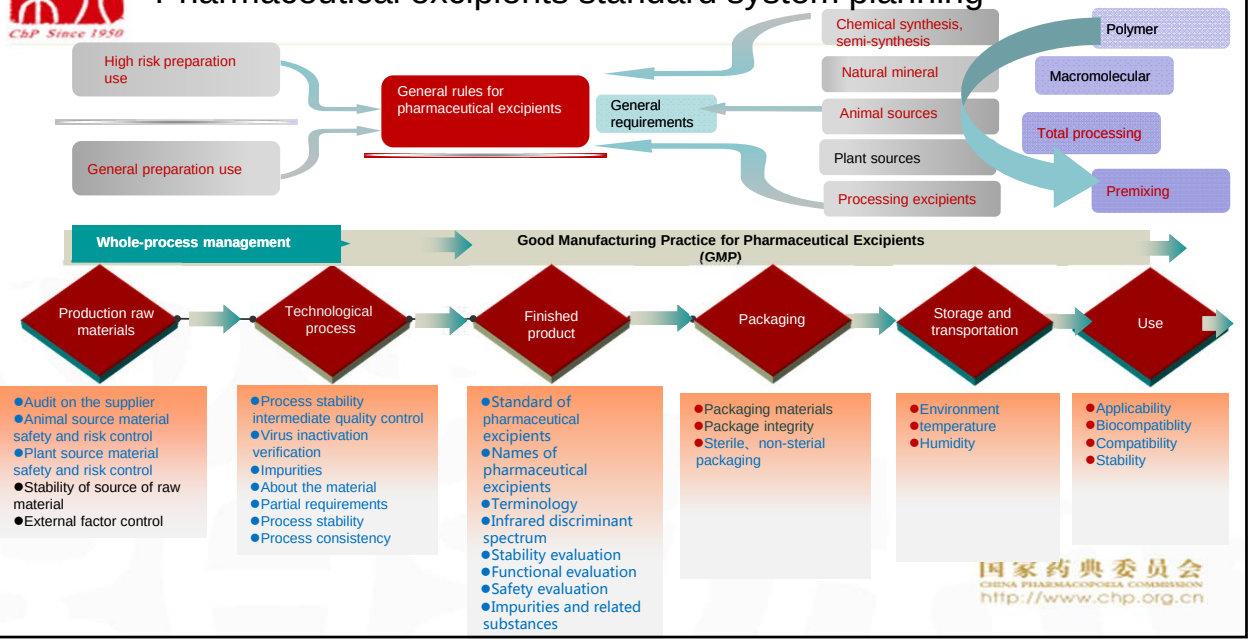
Key Considerations for High-risk Materials

- Collagen
- Gelatin
- Bovince Blood and Blood Derivatives
- Tallow derivatives
- Animal Charcoal
- Milk and Milk Derivatives
- Wool Derivatives
- Amino Acids
- Peptones

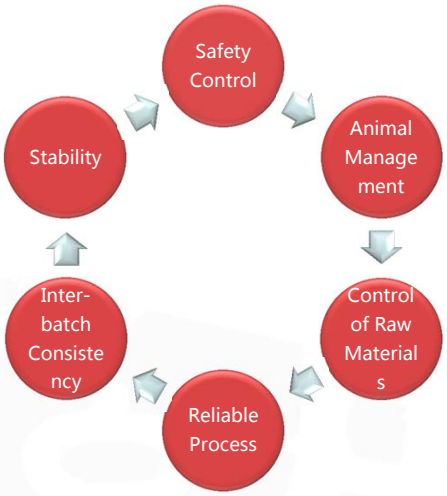
国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.cn

16

Pharmaceutical excipients standard system planning



Quality Control Key Points



国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn

18

Key points for control of animal-derived exipients

- Starting materials control

- Animal species, population health status
- Feeding facilities and environment, pathogen monitoring
- Organ extraction, collection, storage and transportation
- Screening before putting into production
- Adventitious agents screening (the minimum units)
- SOP for the pick up the organs of the animals
- Collect, storage, transport the organs
- Selected the organs before put into production
- Strengthen auditing of suppliers

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.org.cn

19

Key points for control of animal-derived exipients

- In-process Control

- Process Validation
- Stability
- Inter-batch consistency
- Determine key points for quality control of the process
- Establish relevant physical and chemical properties, to ensure effects of process treatment
- Strengthen test of intermediates for contamination of adventitious agents; in-process control may be more effective than finished product control
- Comply with the Good Manufacturing Practices (GMP) for drugs or excipients
- Avoid contamination /across contamination of any adventitious agents during preparation
- Prevent any potential risk for cross contamination between batches during production

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.org.cn

20

Key points for control of animal-derived excipients

- Establish a reliable viral inactivation process
- Establish an appropriate viral inactivation process, to maximize inactivation or removal of known or unknown adventitious agents
- Validation for effective viral inactivation
- Evaluation of viral inactivation effects
- Impact of the viral inactivation process on ingredients

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.cn
21

Key points for control of animal-derived excipients

- Control of ingredients
- Control of ingredients in the product
- Control of impurities/residual substances
- Test for at-risk substances, and establishment of the safety test limit
- Control for residual reagents used during process
- Stability control of ingredients
- Packaging
- Storage and transportation
- Establishment of the expiration date
- Potential impact during use

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.cn
22

Control of Adventitious Agents

1950's, Avian leukosis due to contamination of chick embryo for production of yellow fever attenuated live vaccine;

SV40 virus-contaminated metanephros cells for production of oral poliomyelitis vaccine attenuated live vaccine

Blood products contaminated with HIV/HCV

Human growth factors containing CJV

1940's, Stabilized human blood products contaminated with HBV

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.cn

23

Adventitious Agent Contamination Events

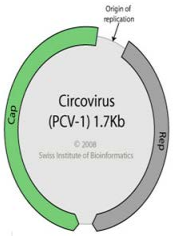
- Cache Valley Virus (CVV) –fermentors from multiple manufacturers have been infected. CVV, although not typically recognized as a bovine virus, is a multispecies virus with bovine host range.
- The operators of a manufacturing enterprise for biotherapeutic products were infected with Cache valley viruses
- Calicivirus 2117 [vesivirus]-facility contamination forced a costly facility shutdown resulting in product shortage that deprived patients of product .
- Production facilities contaminated with calciciviruses
- Multiple contaminations of fermentors with reoviruses, another virus family with wide host range.
- Fermentation tank contaminated with reoviruses
- Porcine circovirus type 1 and type 2 nucleic acid contamination of live rotavirus vaccines

国家药典委员会 CHINA PHARMACOPOEIA COMMISSION http://www.chp.cn

24

Events of pancreatin contaminated with exogenous factors

Porcine circovirus DNA found in Ro
7 MAY 2010



The US
recently
Glaxo Sr
protects
after an
the vacci
type 1. N
DNA in t

FDA rec
Co, Inc.
fragmen
porcine
vaccine.

Industry Alert
Rapid Communicat

Porcine Circoviru
in vaccine produ

FDA Issues Press Release
On March 22, 2010, the US FDA
"components of extraneous viru
infection. In the press release, th
risk associated with the contamir
inated by viable virus particles or
tion found is from *Porcine Circovir*
the temporary suspension of the

For more information, please visit t

Global Advisory Committee on Vaccine Safety

Porcine circoviruses and rotavirus vaccines

Extract from report of GACVS meeting of 16-17 June 2010, published in the WHO Weekly Epidemiological Report on 23 July 2010

GACVS reviewed new data on the fi nding of porcine circovirus DNA in Rotarix (GlaxoSmithKline) and RotaTeq (Merck & Co.), two oral vaccines for preventing rotavirus gastroenteritis. In March 2010, GlaxoSmithKline confirmed a report from academic investigators that Rotarix contained DNA from porcine circovirus type 1 (PCV1). GACVS met by teleconference on 25 March 2010 to discuss this finding, and issued interim advice regarding the safety of the vaccine. In May 2010, Merck reported that DNA from porcine circovirus type 2 (PCV2) had been found in RotaTeq.

Neither PCV1 nor PCV2 is known to infect or cause disease in humans. GlaxoSmithKline reported that PCV1 DNA has been identified in both the master cell bank and master viral seed used for vaccine production, and thus has been present in the vaccine throughout its clinical development, including in the vaccine used in prelicensure clinical trials. Initial data reported by GlaxoSmithKline suggest that Rotarix contains infectious PCV1, however PCV1 does not result in productive infection in human cell lines. Analysis of prevaccination and postvaccination serum samples from 40 infants who participated in clinical trials of Rotarix revealed no evidence of serological response to PCV1. DNA from PCV1 was detected in initial postvaccination stool samples (on days 3 or 7) in 4/40 infants; results were inconclusive on a stool sample from 1 additional infant. None of the infants had positive stool samples later.

Merck reported fi nding low levels of PCV1 and PCV2 DNA in bulk lots and fi nal-container lots of RotaTeq. The amount of PCV DNA found in RotaTeq is consistent with introduction from irradiated trypsin, and infectivity assays are under way.

Additional information on both products is expected from both manufacturers and from other investigators.

- PCF were detected in batches of the stock solution and the finished product
- The user population was under close observation
- Though PCF was detected in the products, there are no adequate clinical data suggesting that PCV, irrespective of PCV-1 or PCV-2, may result in human infections

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.cn

25

International Quality Control Requirements for Pancreatin

World Health Organization

ENGLISH ONLY
FINAL

Recommendations for the evaluation of animal cell cultures as substrates for the manufacture of biological medicinal products and for the characterization of cell banks

Proposed replacement of TRS 878, Annex 1

A.3.3 *Trypsin and other porcine-derived materials used for preparing cell cultures*
Trypsin used for preparing cell cultures should be tested for cultivable bacteria, fungi, mycoplasmas and infectious viruses, including bovine or porcine parvoviruses, as appropriate. The methods used to ensure this should be approved by the NRA/NCL.

In some countries, irradiation is used to inactivate potential contaminant viruses. If irradiation is used, it is important to ensure that a reproducible dose is delivered to all batches and the component units of each batch. The irradiation dose must be low enough so that the biological properties of the reagents are retained while being high enough to reduce virological risk. Therefore, irradiation cannot be considered a sterilizing process.

The quality of the trypsin, like serum, is the responsibility of the biologicals' manufacturer (see section A.4.2). Recombinant trypsin is available and should be considered; however it should not be assumed to be free of risk of contamination and should be subject to the usual considerations for any reagent of biological origin (see A.4.1).

Like serum batches that are derived from many animals, trypsin batches are prepared from the pancreases of many animals. Most batches of porcine trypsin contain genetic sequences of porcine parvovirus 1 and porcine circoviruses and should be therefore treated to inactivate any virus

Guidance for Industry

Characterization and Qualification of Cell Substrates and Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications

2. Trypsin

You should clearly identify the species from which the trypsin used in your vaccine production (including the production of the cell banks and viral seeds) is derived. If bovine trypsin is used, the concerns identified in Section IV.A.2.f, "Sourcing and Testing of Bovine-Derived Materials," apply. If porcine trypsin is used, it should be tested in accordance with the recommendations described in Section IV.A.2.g, "Testing of Porcine-Derived Reagents."

3. Amino Acids

You should document the source of the amino acids used in growth medium or in production.

WHO, FDA, and EMA have strict provisions for quality management and quality control of pancreatin for drug production

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 21 February 2013
2 EMA/CHMP/BWP/814397/2011
3 Committee for Medicinal Products for Human use (CHMP)

4 Guideline on the use of porcine trypsin used in the
5 manufacture of human biological medicinal products
6 Draft

Draft Agreed by Biologicals Working Party	December 2012

http://www.chp.cn

26

Control of bovine-borne advantitious agents

- Bovine Spongiform Encephalopathy (BSE)

  BSE is a progressive neurological disorder of cattle; its symptoms are similar to a disease of sheep, called scrapie. BSE has been called "mad cow disease". BSE and scrapie both result from infection with a very unusual infectious agent. As of July 2000, more than 176,000 cases of BSE were confirmed in Great Britain in more than 34,000 herds of cattle. The epidemic peaked in January 1993 at almost 1,000 new cases per week. The outbreak may have resulted from the feeding of scrapie-containing sheep meat-and-bone meal to cattle. There is strong evidence and general agreement that the outbreak was amplified by feeding meat-and-bone meal prepared from cattle to young calves.
  (For questions and inquiries call: 1-800-835-4709 or 1-301-827-2000.)

  Guidance for Industry: Revised Preventive Measures to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob Disease (CJD) and Variant Creutzfeldt-Jak

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn

Test methods for exogenous viruses

- ◆ Conventional method
- transmission electron microscopy
- in vitro infectivity
- biochemical assays
- in vivo assays
- ◆ Modern detection techniques
- PERT
- polymerase chain reaction (PCR) tests
- next generation sequencing (NGS)
- microarrays
- PCR paired with mass spectrometry

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn
28

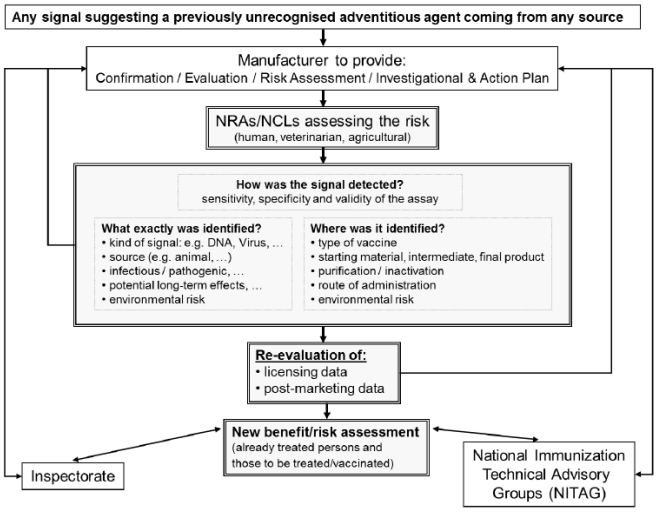
Evaluation of signals for detected adventitious

World Health Organization

WHO/RA_DRAFT/12 March 2013
ENGLISH ONLY

Regulatory Risk Assessment in the Case of Adventitious Agent Finding in a Marketed Vaccine

Scientific Principles to Consider



1

Viral inactivation/removal/process validation

Technical Methods for Viral Removal/Inactivation of Blood Products, and Technical Guidelines for their Validation (State Drug Supervision Registration No. [2002]160)

- ✓ Selection of Methods for Viral Removal/Inactivation
- ✓ Evaluation of Common Methods for Viral Removal/Inactivation
- ✓ Validation of Special Methods for Viral Removal/Inactivation
- ✓ Validation for Viral Removal/Inactivation Performance by the Manufacturing Process
- ✓ Revalidation of Methods for Viral Removal/Inactivation

Biological Activities

Adventitious agents inactivation

30

Viral Inactivation of Bovine Serum

- Method
  - Heat Inactivation
  - γ-ray irradiation (temperature, time, container, position, and dose)
  - Processing for 60 min at 37 ℃ (EDQM)
  - Ultrasonic Irradiation
- Selection of indicator viruses

Viral Characteristics	Enteroviruses		Reoviruses	Others
	Bovine diarrhea viruses	Infectious bovine rhinotracheitis viruses	Bovine adenoviruses	Porcine parvoviruses
Enveloped	Present	Present	None	None
Nucleic Acid	Single-stranded RNA	Double-stranded DNA	Double-stranded DNA	Single-stranded DNA

Summary

- ✓ High risk for the excipients derived from animals
- ✓ Whole prcoessing control is the base of the quality assurance
- ✓ Especially for the starting materials and prcessing control
- ✓ processing validation
- ✓ Set up the well establishment Viral inactivated processing
- ✓ adventitious agents testing method and the evaluation
- ✓ Storge situation for the excipients stability

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.cn

ChP Since 1950

Thank you for your attention!

国家药典委员会
CHINA PHARMACOPOEIA COMMISSION
http://www.chp.org.cn