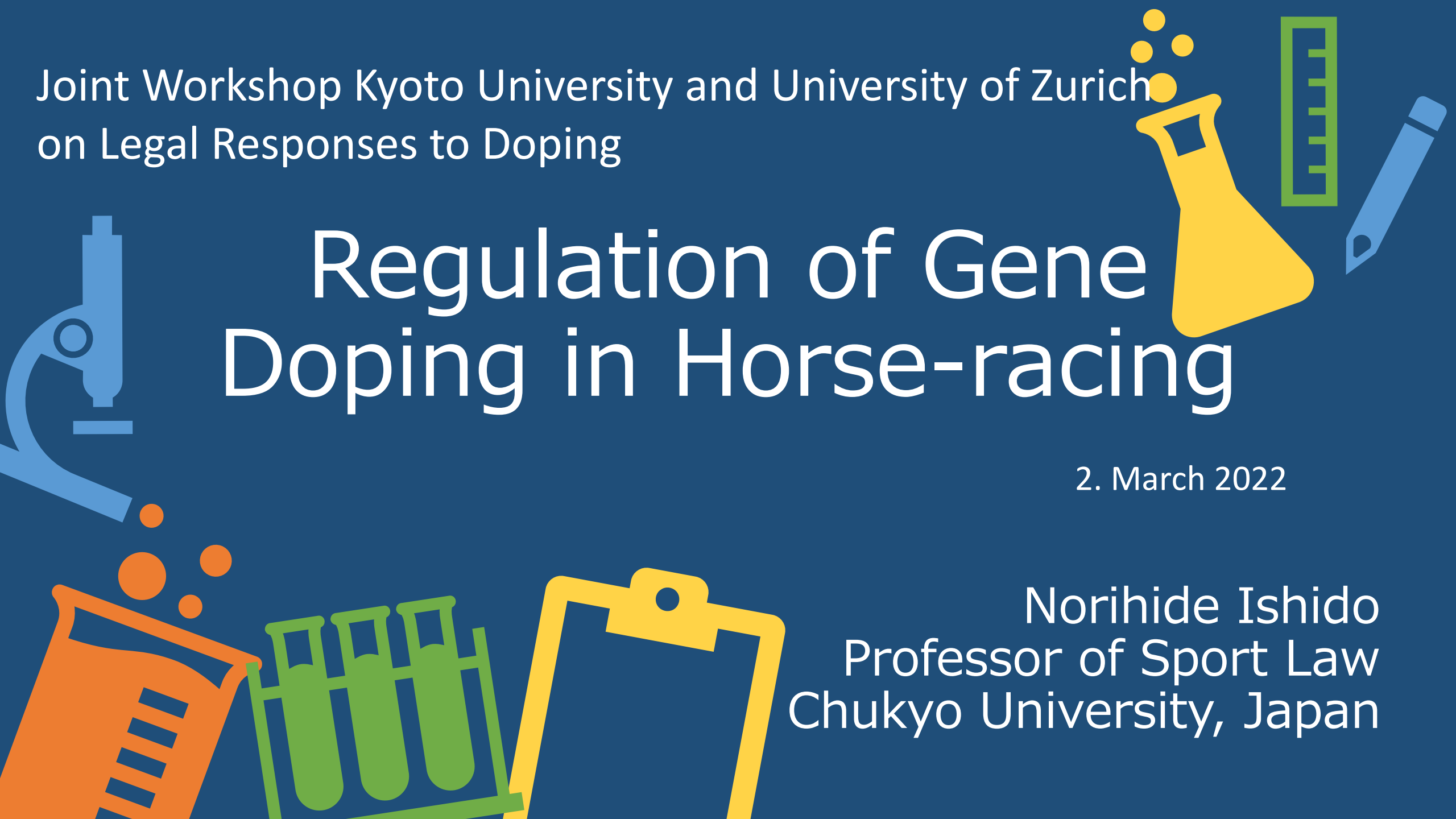


Joint Workshop Kyoto University and University of Zurich  
on Legal Responses to Doping

# Regulation of Gene Doping in Horse-racing

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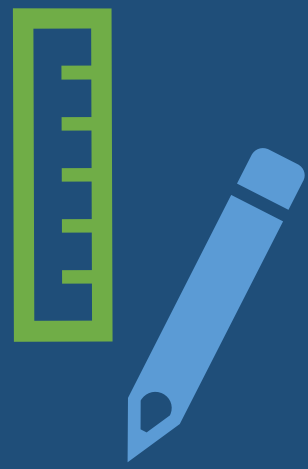


# Agenda

- Definition; What is Gene doping ?
- Gene doping detection
- Regulation of Gene doping
- Review the issues



# Definition; What is Gene doping?



# What is Gene doping ?

- Gene doping can take different forms; gene transfer, gene silencing and gene editing.
- Gene doping techniques are based on methods that have been developed by researchers for medical research, gene therapy and to improve selective breeding.
- Wilkin(2017), “over 2300 gene therapy clinical trials have been completed in humans focusing mainly on the treatment of cancer..”



# Gene transfer and Gene silencing

- Gene transfer; the insertion of genetic material into a cell
- Gene silencing; interruption or suppression of the expression of a gene at transcriptional or translational levels

# Genome editing and CRISPR-Cas9

- CRISPR-Cas9 is a unique technology that enables geneticists and medical researchers to edit parts of the genome by removing, adding or altering sections of the DNA sequence.

# Regulation of Gene-doping



# organizations

- International Stud Book Committee(ISBC)
- International Federation of Horseracing Authorities(IFHA)
- World Arabian Horse Organisation(WAHO)
- Federation Equestre Internationale (FEI)
- Thoroughbred Breeding Associations (IFTBA)
- World Anti-Doping Agency(WADA)





# What is a Thoroughbred?

- Article 12 (BREEDING) the International Agreement on Breeding and Racing Thoroughbred Stud Books  
– DEFINITION
- A Thoroughbred is a horse which is recorded in the Thoroughbred Stud Book of the country of its foaling



International Stud Book Committee

# Definition of A Thoroughbred:

A Thoroughbred is a horse which is recorded in the Thoroughbred Stud Book of the country of its foaling

- A: QUALIFICATION
- For a horse to be eligible to be recorded in an approved Thoroughbred Stud Book all of the following requirements must be satisfied:
- 1. STATUS OF SIRE AND DAM
- 2: SERVICE TO PRODUCE AN ELIGIBLE FOAL
- 3: GESTATION TO PRODUCE AN ELIGIBLE FOAL
- 4: RECORDING OF THE MATING AND RESULT
- 5: IDENTIFICATION & DESCRIPTION
- 6: PARENTAGE VERIFICATION

- 3.1 A natural gestation must take place in, and delivery must be from, the body of the same Mare in which the Foal was conceived. Any Foal resulting from or produced by the processes of Artificial Insemination, Embryo Transfer or Transplant, Cloning or any other form of genetic manipulation not herein specified, shall not be eligible for recording in a Thoroughbred Stud Book approved by the International Stud Book Committee.

# 6. Registration Systems

- 6.3.3 The SBA must require, in addition to the above, receipt of the following to complete a foal registration:
  - a) Covering certificate or covering, duly signed, or approved computerised equivalent
  - b) Foal identification certificate (see requirements under 'Identification')
  - c) Confirmation that the foal was not conceived by AI, embryo transfer or transplant, cloning or other genetic manipulation.
  - d) DNA profile/Bloodtype

# International Federation of Horseracing Authorities(IFHA)

- foundation in 1993
- In 1961, the Horseracing Authorities of the United States of America, France, Great Britain and Ireland decided to coordinate their action in order to protect the integrity of horseraces
- Their main objectives are:
- to coordinate and harmonize the rules of the member-countries regarding breeding, racing & wagering;
- to ensure the quality and fairness of racing in the interest of both the breeding and the public;
- to provide the organization on racecourses of the protection of the welfare of horses, jockeys and the people attending;
- to update the organization of horseracing on account of the technical, social and economical evolution;
- to update the International Agreement on Breeding, Racing and Wagering

# International Agreement

## Article 6 B (RACING): PROHIBITION OF GENETIC THERAPY, GENE EDITING AND GENOME EDITING

### 2. Prohibition on Gene Editing and Genome Editing

#### a. Definition of Gene Editing

- Gene Editing is defined as any process or treatment in respect of a horse which involves the insertion, deletion and/or replacement of DNA at a specific site in the genome of the horse.

#### b. Definition of Genome Editing

- Genome Editing is defined as any process or treatment in respect of a horse which involves the insertion, deletion and/or replacement of DNA in the genome of the horse.

**c. The use on, or administration or application to, any horse of Gene Editing or Genome Editing** is prohibited at all times.



Last update : JANUARY 2020

Fully signatory - agreed by:			
AUSTRIA	BAHRAIN	BELGIUM	CANADA
CHILE	CYPRUS	CZECH REPUBLIC	DENMARK
GERMANY	GREECE	HONG KONG SAR, CHINA	HUNGARY
INDIA	IRELAND	ITALY	KOREA
MACAU SAR, CHINA	MALAYSIA	MAURITIUS	NETHERLANDS
OMAN	PERU	QATAR	ROUMANIA
SAUDI ARABIA	SINGAPORE	SPAIN	SWITZERLAND
TURKEY	UNITED ARAB EMIRATES	UNITED STATES OF AMERICA	URUGUAY
VENEZUELA			
Partial signatory - by:			
AUSTRALIA	GREAT BRITAIN <i>working towards Full Signatory</i>	JAPAN <i>Currently there is no provision for gene doping, but now Japan is under consideration for the future revision of the regulations.</i>	NEW ZEALAND <i>Working towards prohibiting genetic therapy.</i>

# Regulation by Japan Racing Association

- Article 132 Prohibition of chemicals and drugs that affect racing ability
- Horses that are to be run in a race shall not use any chemicals or agents that temporarily increase or reduce their ability to race.
- 2 Even if it is something other than prohibited drugs, it should not be used for the purpose of temporarily improve or reduce the horse's racing ability for horses to be run in a race.



# Federation Equestre Internationale (FEI) 2022 Equine Prohibited Substances List BANNED METHOD

- **1. Manipulation of Blood and Blood Components (i.e. Blood Doping, ozone haemotherapy)**
- Withdrawal, manipulation and re-infusion of homologous, heterologous, or autologous, blood products or blood cells into the circulatory system with the exception of those performed for lifesaving purposes or the use of veterinary regenerative therapies for the treatment of musculoskeletal injury or disease.
- **2. Gene Doping**
- Any form of genetic modification



# World Arabian Horse Organization (WAHO)

- Genetic Modification Gene Editing and Gene Doping
- 1. It is a mandatory WAHO rule that any Arabian horse of any age which has been subjected to any form of genetic modification at the embryo stage or later must not be registered under any circumstances.
- 2. It is a mandatory WAHO rule that the progeny of any Arabian horse which was subjected to any form of genetic modification at the embryo stage or later must not be registered under any circumstances.
- 3. It is a mandatory WAHO rule that any Arabian horse of any age which has been conceived using genetically modified gametes must not be registered under any circumstances.
- 4. It is a mandatory WAHO rule that the progeny of any Arabian horse which was conceived using genetically modified gametes must not be registered under any circumstances.

# WADA, PROHIBITED METHODS

## M3. GENE AND CELL DOPING



- The following, with the potential to enhance sport performance, are prohibited:
- 1. The use of nucleic acids or nucleic acid analogues that may alter genome sequences and/or alter gene expression by any mechanism. This includes but is not limited to gene editing, gene silencing and gene transfer technologies.
- 2. The use of normal or genetically modified cells.

# WADA, Laboratory Guidelines Gene Doping Detection based on Polymerase Chain Reaction (PCR) Version 1.0, January 2021

Technical requirements on the application of  
direct PCR-based Analytical Methods



# Review the issues



# Review the issues

- Gene Testing⇒ Search for equine performance genes
- Spreading Cloning in Horse Industry
- TUE for gene therapy⇒Enlarge unintended gene editing
- Mutagenesis by gene editing⇒ Long term surveillance
- Cartagena Protocol on Biosafety⇒Alternative global regulation
- Sanction; Doping ≠ Gene Doping
- Period of limitation



# Candidates for Equine performance genes

- Genes that enhance muscle mass and strength
- Genes for oxygen regulation
- Angiogenic genes(blood flow increases)
- Energy metabolism genes
- Genes for overcoming pain and injury repair

(Wilkin,2017)



# Kheiron Biotech

- Kheiron Biotech: Argentine company breaks limits in technology for horse breeding
- By 2021, the Argentine laboratory had already generated more than 250 equine clones, testing the most precise breeding process ever developed.

# Spreading Cloning in the Horse Industry

Cloning boosts polo horse breeding in Australia,  
Clickpoloasia, Feb 13, 2021

Polo pony cloning is set revolutionise the sport at Argentina's  
Palermo Open, The Independent 30 October 2015

In July 2012 the Fédération Equestre Internationale (FEI) lifted a  
ban on cloned horses and their progeny competing in the  
Olympic Games.



# Review the issues

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# International Agreement

## Article 6 B (RACING)

### c. Exempted Genetic Therapy

- A Genetic Therapy may be used or administered to a specific horse with the express prior approval of a Racing Authority if that Genetic Therapy is used to treat an injury or disorder formally diagnosed by a veterinarian, and:
  - a. is not capable of modifying a horse's heritable genome;
  - b. does not pose a threat to the welfare of horse;
  - c. does not pose a threat to the integrity of racing, either by having the potential to enhance or harm the performance of a horse in a race.

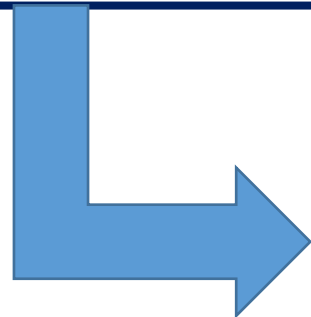
# International Agreement

## Article 6 B (RACING)

- **a. Definition of Genetic Therapy**
- A Genetic Therapy is defined as including any therapy, method or process which involves the use or administration of:
  - i. oligomers or polymers of nucleic acid
  - ii. nucleic acid analogues
  - iii. genetically modified cells
  - iv. gene editing agents which are capable, at any time, of directly or indirectly causing an action or effect on, and/or manipulating, gene expression in any mammalian body, including but not limited to gene editing agents with the capacity to alter genome sequences and/or the transcriptional, post-transcriptional or epigenetic regulation of gene expression.

# Therapeutic Use Exemptions (“TUEs”)

- WADA Code 4.4.1 The presence of a Prohibited Substance or its Metabolites or Markers , and/or the Use or Attempted Use , Possession or Administration or Attempted Administration of a Prohibited Substance or Prohibited Method shall not be considered an anti doping rule violation if it is consistent with the provisions of a TUE granted in accordance with the International Standard for Therapeutic Use Exemptions.



The possibility of TUE for gene editing?

# Cartagena Protocol on Biosafety

## the Convention on Biological Diversity



- The objective of this Protocol is to contribute to ensuring an adequate level of protection in the field of the safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health, and specifically focusing on transboundary movements.

# Act on the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms in Japan

- "Type 2 Use" shall mean use undertaken with the intention of preventing the dispersal of living modified organisms into the air, water or soil outside facilities, equipment or other structures

# Review the issues

- Gene Testing⇒ Search for equine performance genes
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# Thank You!

It is time to talk about Global Gene Doping Law



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