CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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**Agenda Item 6** **CRD3**

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**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**

**FAO/WHO COORDINATING COMMITTEE FOR EUROPE**

***30th Session, 3 – 7 October 2016***
***Astana, Kazakhstan***

***COMMENTS SUBMITTED BY HEALTH FOR ANIMALS***

## Agenda item 6 CODEX WORK RELEVANT TO THE REGION

### Introduction

Zilpaterol hydrochloride (ZH) was put forward by the Delegation of the United States (U.S.) at CCRVDF 20. ZH met every requirement to be added to the priority list at CCRVDF 20, when only some or all of the criteria is required (Codex Procedural Manual, Section IV: Risk Analysis, 3.1.2- Establishment of Priority List, P. 150). ZH is now currently at Step 3 in the Codex processes and will be discussed at the upcoming CCRVDF meeting.

JECFA has evaluated ZH twice. The sponsor company provided a very comprehensive and complete toxicological and pharmacological data package including several studies where zilpaterol was used in humans. The 78th JECFA came to the conclusion to base the ADI on a human pharmacological study. The sponsor company then supplied additional data for the 81st JECFA which proposed draft MRLs for muscle, liver and kidney.

By establishing an ADI and proposed draft MRLs, JECFA has deemed ZH safe for human consumption.

### Zilpaterol Facts

- ZH is a beta-agonist used for feed efficacy in cattle. When consuming ZH, cattle gain weight through increased muscle without adding more fat to the animal or carcass.

- Before ZH was approved, the sponsor company worked with university and industry experts who conducted research on many aspects of the product to ensure its safety and effectiveness. The research confirmed ZH is safe and effective for cattle and has no negative impact on their well-being, when used according to label directions along with good animal care practices.

- The first country to approve ZH was South Africa in 1993 and it is currently used by most of the major cattle producers. Currently over 15 national competent authorities including Brazil, Canada, Costa Rica, Kazakhstan, Mexico and South Korea, have reviewed the extensive data package and found ZH safe. This also includes countries like Japan who have reviewed and established an import MRL for ZH as recently as 2014.

- Zilmax is a recognized feed supplement for helping farmers raise beef in a sustainable manner. The ability to raise more beef with fewer cattle also means less waste, and less use of land, water and energy. The use of just one bag of zilpaterol is the equivalent of saving 32,178 net gallons of water, saving $13,812 in feed costs at $300/ton (907.2 kg) of feed, decreasing 16 cattle equivalent of additional beef produced, can feed 164 additional United States consumers, conserves 2 semi-truck loads of feed**,** and creates 4,098 kg of beef.
  (http://www.zilmax.com/sustainability.aspx)

**Zilpaterol in the United States (U.S.) and Animal Well-being Concerns**

- While animal welfare is within the mandate of the World Organization for Animal Health (OIE) and not the Codex, animal welfare questions have been raised regarding ZH, specifically by one food company.

- The events that occurred in the U.S. (discussed further below) have led the sponsor company, leading universities and the U.S. Department of Agriculture to a significant amount of scientific understanding on potential animal welfare impacts of ZH. This understanding has concluded that there are **no negative animal welfare impacts related to the use of ZH**. In fact, it may be argued that there is more scientific understanding on the use of ZH related to animal welfare than on almost any other veterinary drug.

- The concerns in the U.S. began with questions raised by one company and has subsequently led to not only confirming the safety of ZH but has also led to a better understanding of cattle management practices, which benefits all those associated with managing the health and well-being of cattle whether ZH is utilized or not.

- In 2013 the company Tyson Foods noticed an animal welfare concern at their packing facilities. Some cattle were severely lame and their hooves were coming off. John Gerber, director of cattle procurement for Tyson Fresh Meats, Inc. said, *"We do not know the specific cause of these problems"* (http://beefmagazine.com/animal-welfare/tyson-says-it-won-t-buy-zilmax-fed-cattle-after-sept-6), but Tyson Foods decided to stop accepting cattle that had been fed ZH anyway.

- Subsequently, the sponsor company suspended sales of ZH in the U.S. and Canada to allow for additional scientific studies to be conducted in order to determine if there were any animal welfare related problems associated with ZH. It is important to note that there were never any food safety related concerns related to this voluntary suspension.

- Under the guidance of an industry advisory board, a five-step plan was prepared to address the questions. This plan included reinforcing checks and balances to ensure proper product use and the commitment to conduct additional research. Out of that plan came the Zilmax Quality Assurance (ZQA) program. ZH is one of the only products on the market that has its own quality assurance program and encourages producers to educate themselves on how to best utilize ZH for consumer, animal and worker safety.

- As a result of this, a significant amount of additional scientific understanding has been developed related to the use of ZH.
  - In March 2014, Dr. Guy Loneragan published "Increased Mortality in Groups of Cattle Administered the β-Adrenergic Agonists Ractopamine Hydrochloride and Zilpaterol Hydrochloride." Unfortunately, this study was based more on Dr. Loneragan's opinions and observational information. There is minimal biological effects even though there are statistical effects. It also appeared that days on feed had more of an effect on death rate than beta agonist exposure. Since this study, several Universities, using third-party experts, have done more than 30 studies, with 65,000 head of cattle where no increased death loss was seen between ZH fed cattle and the control group which was not fed ZH.

  - In May 2014, the American Veterinary Medical Association (AVMA) published a "Literature Review on the Welfare Implications of the Use of Beta-Adrenoceptor Agonists." The AVAM sited "multifactorial" possibilities for what was causing the lameness.

  - Dr.'s Daniel Thomson and Guy Loneragan published "Description of a novel fatigue syndrome of finished feedlot cattle fowling transport" in the Journal of the AVMA (July 1, 2015, Vol. 247, No. 1, Pages 66-72) in July 2015. This was the first study that indicated ZH was not to blame for the lameness seen in the feedlot cattle, and a new management issue termed "Fatigued Cattle Syndrome" (FCS) described the symptoms of the lame cattle arriving at the processing facilities.
- The researchers found cattle subjected to multiple stress factors including heat stress, higher body weights, loading and unloading, time spent standing, available shade, water cooling, pen surfaces, shipping, etc., could show signs of distress. Symptoms included labored breathing, reluctance to move, lameness, a stiff gait and lying down despite showing no signs of injury or disease. Specific indicators for stress also were identified from blood samples drawn from the animals. The researchers identified this distress in both cattle fed beta-agonists and cattle not fed beta-agonists. The research

concluded that Fatigued Cattle Syndrome is multifactorial and further concluded that ZH was not simply the cause of the welfare concerns.

- As recently as September 15, 2016, Dr. Daniel Thomson published two more studies further confirming that ZH does not cause any negative animal welfare impacts, but rather the cause is more directly related to improper management of cattle even if they have not been fed a beta agonist.
  - In "Effects of ractopamine hydrochloride and Zilpaterol hydrochloride on cardiac electrophysiological and hematologic variables" the researchers concluded that cattle fed ractopamine and ZH at U.S. Food and Drug Administration approved doses had no effect on arrhythmia rates, but caused an increased heart rate that remained within reference limits.

  - In "Cattle handling technique can induce fatigued cattle syndrome in cattle not fed a beta-adrenergic agonist" the study concluded that "aggressive cattle handling produces significant physiological responses, which can be detrimental to some animals." Finishing cattle need to be handled with care in order to prevent an animal welfare concerns, such as Fatigued Cattle Syndrome. The syndrome can be brought on simply by improper management even in cattle not fed a beta-agonist

- It is important to note that many, if not all, the indicators for Fatigued Cattle Syndrome listed above are addressed from an animal welfare perspective in the OIE Terrestrial Animal Health Code, Section 7 Animal Welfare, Chapters 7.1, 7.3, 7.5 and 7.9.

When used according to label directions along with good animal care practices, the results from the observations and additional studies all reaffirm ZH safety and conclude that it has no negative impact on the well-being of cattle.

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