TAFS

INTERNATIONAL FORUM FOR TRANSMISSIBLE ANIMAL DISEASES AND FOOD SAFETY
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Recommended Risk Management Plan for Paratuberculosis

Introduction:

TAFS was founded in response to the world-wide crisis in the late 1990s that followed the confirmation that the outbreak of BSE in the U.K. had given rise to disease in humans. The scientific understanding of all TSE diseases and their prion basis was in a state of high uncertainty at the time, and continues to be so. Especially uncertain was the relationship between animal prion diseases, such as BSE, scrapie and CWD, and similar prion diseases (CJD) in human beings. Because of well-founded concerns about the potential risk that the BSE outbreak posed to human health, and because of the significant gaps in the scientific understanding of the diseases and the links between them, TAFS brought together leading scientists, government and industry food safety experts, and others skilled in risk assessment, management and communication, with the objective of providing science-based, but precautionary recommendations to governments and industry for the protection of animal and human health, where such advice was deemed necessary. Reassessment of existing risk management measures was key to the debate, as was the clarification of issues for those that remained confused by the multiple conflicting messages arising from political, scientific and media sources.

TAFS thus set about achieving several objectives, among which were the following:

1) To review the best and most current science relating to prion diseases and assess their implications for health risk,
2) To advise risk managers and the public on the most reasonable means of managing the diseases and the risks to human health while the gaps in scientific understanding were being filled in,
3) To identify the gaps in the scientific understanding of TSE's and propose areas of scientific research.

TAFS met these objectives through regular scientific meetings and conferences, the dissemination of position papers, and other means. As an independent scientific organization, TAFS was in a position to raise questions about food safety that, if raised by others, could result in unwarranted fears and/or severe economic repercussions in the food industry. TAFS was active in supporting precautionary measures that were previously controversial, but

which in retrospect have largely been judged to have been effective risk reduction measures. There have been other measures which have been debated as not necessary, however these were the most reasonable courses of action at the time.

Since the BSE crisis has abated, TAFS has expanded its scope to other transmissible animal diseases that are of concern to human health. It is particularly concerned with how to manage potential serious zoonotic diseases, like BSE, where lack of scientific certainty appears to compromise understanding of routes of exposure, and the willingness and ability of authorities to implement formal control plans. TAFS´ major objective is to adopt socially responsible, but scientifically founded, risk management options that can be taken to prevent infections in animal as well as protect public health. MAP is one particular organism where precautionary action appears appropriate. By recognizing the gradual accumulation of evidence, and acknowledging the possibility of a future confirmation of a link between MAP and human health, it aims both to minimize risk to consumers and to prevent a food related crisis before it arises.

Background:

Paratuberculosis (pTB[1]) is an animal disease that fits the profile outlined above. pTB has emerged as a common and economically significant infectious disease of food producing animals. Scientific evidence indicates that the cause of pTB, *Mycobacterium avium* subspecies *paratuberculosis* (MAP)[2] is spilling out of its natural host, ruminants, and into the environment and the food chain and thus resulting in exposure of humans. In humans, MAP has been associated with diseases such as inflammatory bowel disease (IBD) and type 1 diabetes mellitus (T1DM), but the extent to which MAP is a contributing factor, or cause, of any human disease remains unknown and is the subject of continuing scientific research.

The purpose of this position paper is to provide recommendations for risk management (mitigation) strategies that will serve to:
a) improve animal health and welfare;
b) promote sustainable agriculture;
c) lessen the burden of MAP in the food chain and consequent exposure of humans to MAP, as a precaution in case MAP is proven to be a human pathogen.

Principles:

- This document is a response to what TAFS considers as an important issue requiring imminent measures;
- The measures proposed are consistent with supporting a sustainable agriculture since interventions to control MAP will offer a long-term improvement in animal health and welfare as well as production profitability and sustainability;
- The measures proposed are based on the principle of placing as many cost-effective hurdles between the sources of MAP and consumers as economically feasible.

[1] pTB: paratuberculosis, also known as Johne's disease.

[2] MAP: *Mycobacterium avium* subspecies *paratuberculosis*

Facts upon which this risk management plan is based:

- MAP is an obligate animal pathogen, i.e., it is not able to replicate itself to any significant extent outside its host;
- The primary reservoir of MAP is infected domestic ruminants that serve as sources of food for humans.
- The prevalence of pTB at the animal and herd level[3] has increased wherever it has been studied in detail (USA based on USDA-APHIS-VS surveys) and is having a negative impact on agriculture.

Assumptions:

- Foods of animal origin, (e.g. milk and meat) are sources of MAP. MAP contaminated water, or fruits and vegetables exposed to such water, may also be sources of MAP exposure of humans;
- The implementation of on-farm pTB control[4] measures will result in lower MAP levels (bioburden) in raw food products such as meat and milk and contamination of the environment;
- On-farm pTB control measures are needed to help achieve sustainable dairy and beef farming because pTB decreases productivity and longevity of animals.
- On-farm pTB control measures serve also to control transmission of other fecal-oral transmitted pathogens;
- Existing food processing and manufacturing practices significantly decrease the level of viable MAP in food products; although surveys of food products, as well as laboratory studies simulating commercial milk processes, seem to indicate that sometimes survival is possible.

Uncertainties:

- The role of MAP in human disease is at this time a matter of scientific uncertainty, and this document should not be construed as implying that it has been established as the cause of any human disease;
- The routes by which humans are exposed to MAP, including non-food routes, are not known in their entirety and the relative importance of different exposure routes is also unknown;
- In case MAP is confirmed to be a human pathogen, the risk posed by organisms surviving the processing, if any, can at this stage not be evaluated as the minimal infectious dose of MAP is currently not known.

Risk management measures at the international level

The World Animal Health Organization (OIE) should update recommendations regarding pTB testing in relation to trade in livestock. Countries basing animal trade on herd-level tests for pTB should not be considered excessively restrictive, in comparison with those relying on single animal testing. There is also a need to facilitate the evaluation and standardization of tests to be used both for trade and herd management purposes. In order to ensure consistency

[3] Herd: a population of animals; synonymous with flock for sheep.

[4] Control: lower infection prevalence to acceptable levels.

of approach, there is also a need for guidance on the action to be taken in the face of positive test results.

Risk management measures at the national or regional level

1. Education programs or literature targeted to producers and veterinarians or other professional farm advisors should be offered on a regular basis by multiple methods, e.g. face-to-face courses, print and electronic-based materials. Educational materials should include the biology of pTB as well as the rules and regulations regarding national or regional pTB programs, and convey the understanding that effective pTB control takes many years;
2. Laboratory quality assurance programs should be maintained to ensure the integrity of the pTB testing programs;
3. A system for certifying herds as low risk for MAP infection should be established along with a mechanism for informing buyers of the availability of animals from such low risk herds.

Risk management measures at the herd level

1. Veterinarians or other farm advisors specifically trained with respect to the biology and control of MAP should perform an on-farm situation analysis and recommend changes to management practices, consistent with local conditions and animal husbandry practices, which limit opportunities for MAP transmission among animals and bring the producer in line with improved farming practices. The following management strategies are <u>essential</u> to control MAP infection:
    a. Birthing of animals in clean facilities.
    b. Hygienic collection of colostrum if fed to newborns manually; colostrum should be obtained from pTB test-negative animals; pooling of colostrum should be avoided.
    c. Ensuring that milk, feed and water supplied to young livestock are clean (i.e. free of manure contamination); ideally only pasteurized milk, such as milk replacer, should be fed to neonates until weaning;
2. A regular herd testing program should be implemented, using validated diagnostic tests in competent laboratories, when prescribed by a herd veterinarian or farm advisor, or where such testing is mandatory under local regulations. The testing program should be applied at least once per year to every adult animal in the herd. The tests do not need to be applied to every animal in the herd simultaneously. Rather, they can be applied to each animal at a particular stage in its production cycle, e.g., two weeks after giving birth. The testing program <u>must</u> be accompanied by a written plan of action developed in consultation with a herd veterinarian or farm advisor consistent with the farm situation analysis; and:
    a. Herd replacements or additions should come from low risk herds (see national risk management measures);
    b. Animals diagnosed with pTB by a veterinarian should be excluded from the herd as quickly as possible;

Risk management measures at the food processor level

1. Ideally and where feasible, milk and animals for meat should be sourced from herds of lowest possible risk for MAP infection.
2. Pasteurization of all milk for human consumption, including milk to be used for cheese, should continue;
3. Hygienic practices directed at limiting fecal contamination of raw foods should continue to be strengthened and promoted.

Key References

U.S. National Advisory Committee on Microbiological Criteria for Foods, 2007. Assessment of Food as a Source of Exposure to *Mycobacterium avium* subspecies *paratuberculosis* (MAP).
http://www.fsis.usda.gov/About_FSIS/NACMCF_Subcommittee_MAP/index.asp
(The final draft of the report for comment was issued September 24, 2007. A form of this report has been submitted for publication).

European Commission, 2000. Possible link between Crohn's disease and paratuberculosis. Report of the Scientific Committee on Animal Health and Animal Welfare. Adopted 21 March 2000. SANCO/B3/R16/2000.

Gould, G., Franken, P., Hammer, P., Mackey, B., Shanahan F., 2004. *Mycobacterium avium* subsp *paratuberculosis* (MAP) and the food chain. ILSI Europe Report Series, 2004. http://europe.ilsi.org/file/RPMAP.pdf

Health Canada's Bureau of Microbiological Hazards, 2008. Microbiological Risk Profile on *Mycobacterium avium* subsp. *paratuberculosis* (MAP) in Foods. Executive Summary. This report is to be provided soon on the Health Canada website:
http://www.hc-sc.gc.ca/index-eng.php

Nacy, C. & Buckley, M. 2008. *Mycobacterium avium paratuberculosis: Infrequent human pathogen or public health threat?* American Society for Microbiology, Washington DC, USA.
http://academy.asm.org/index.php?option=com_content&task=blogcategory&id=18&Itemid=53

IFL-IDF, 2004. Guide to Good Dairy Farming Practice. A joint publication of the International Dairy Federation and the Food and Agriculture Organization of the United Nations. Rome, January 2004.
http://www.fil-idf.org/docsharenoframe/NetServices/Documents/ViewPortalDocument.aspx?docid=4900

OIE Animal Production Food Safety Working Group, 2006. Guide to good farming practices for animal production food safety. Rev. Sci. Tech.- Off. Int. Epiz., 2006, 25 (2), 823-836. http://www.eau.ee/~viltrop/VPH_GFP.pdf

Additional selected references providing reviews and general background information relevant to this TAFS document.

Abubakar, I., Myhill, D., Aliyu, S.H., & Hunter, P.R. 2008. Detection of *Mycobacterium avium* subspecies *paratuberculosis* from patients with Crohn's disease using nucleic acid-based techniques: a systematic review and meta-analysis. *Inflammatory Bowel Disease*, 14 (3), 401-410.

Antognoli, M.C., Garry, F.B., Hirst, H.L., Lombard, J.E., Dennis, M.M., Gould, D.H., & Salmon, M.D. 2008. Characterization of *Mycobacterium avium* subspecies *paratuberculosis* dissemination in dairy cattle and its association with antemortem test results. *Veterinary Microbiology*, 127, 300-308.

Behr, M.A. & Kapur, V. 2008. The evidence for *Mycobacterium paratuberculosis* in Crohn's disease. *Current Opinion in Gastroenterology*, 24, 17-21.

Benedictus, A., Mitchell, R.M., Linde-Widmann, M., Sweeney, R., Fyock, T., Schukken, Y.H., & Whitlock, R.H. 2008. Transmission parameters of *Mycobacterium avium* subspecies *paratuberculosis* infections in a dairy herd going through a control program. *Preventive Veterinary Medicine* 83:215-227.

Brady, C., O'Grady, D., O'Meara, F., Egan, J., & Bassett, H. 2008. Relationships between clinical signs, pathological changes and tissue distribution of *Mycobacterium avium* subspecies *paratuberculosis* in 21 cows from herds affected by Johne's disease. *The Veterinary Record*, 162, (5) 147-152.

Feller, M., Huwiler, K., Stephan, R., Altpeter, E., Shang, A., Furrer, H., Pfyffer, G.E., Jemmi, T., Baumgartner, A., & Egger, M. 2007. *Mycobacterium avium* subspecies *paratuberculosis* and Crohn's disease: a systematic review and meta-analysis. *Lancet Infectious Diseases*, 7 (9), 607-613.

Grant, I.R. 2005. Zoonotic potential of *Mycobacterium avium* ssp. *paratuberculosis*: the current position. *Journal of Applied Microbiology*, 98, 1282-1293.

Grewal, S.K. Rajeev S., Sreevatsan S., Michel F.C., Jr. 2006. Persistence of *Mycobacterium avium* subsp. *paratuberculosis* and other zoonotic pathogens during simulated composting, manure packing, and liquid storage of dairy manure. Applied and Environmental Microbiology, 72 (1):565-74.

Griffith, M.W. 2006. *Mycobacterium paratuberculosis*. In Emerging Foodborne Pathogens, Edited by Y. Motarjemi and M. Adams. Woodhead Publishing Limited, pp 552-543.

Harris, N.B. & Barletta, R.G. 2001. *Mycobacterium avium* subsp. *paratuberculosis* in veterinary medicine. *Clinical Microbiology Reviews*, 14, 489-512.

Hermon-Taylor, J., Bull, T.J., Sheridan, J.M., Cheng, J., Stellakis, M.L., & Sumar, N. 2000. Causation of Crohn's disease by *Mycobacterium avium* subspecies *paratuberculosis*. *Canadian Journal of Gastroenterology*, 14, 521-539.

Juste, R.A., Elguezabal, N., Garrido, J.M., Pavon, A., Geijo, M.V., Sevilla, I., Cabriada, J.L., Tejada, A., Garcia-Campos, F., Casado, R., Ochotorena, I., Izeta, A., & Greenstein, R.J. 2008. On the prevalence of *M. avium* subspecies *paratuberculosis* DNA in the blood of healthy individuals and patients with inflammatory bowel disease. *PLoS ONE*, 3 (7), e2537.

Juste, R.A., Elguezabal, N., Pavó, A., Garrido, J.M., Geijo, M.V., Sevilla, I., Cabriada, J.L., Tejada, A., García-Campos, F., Casado, R., Ochotorena, I., & Izeta, A. 2009. Association between *Mycobacterium avium* subsp. *paratuberculosis* DNA in blood and cellular and humoral immune response in inflammatory bowel disease patients and controls. *International Journal of Infectious Diseases*, 13 (2), 247-254.

Kennedy, D.J. & Benedictus, G. 2001. Control of *Mycobacterium avium* subsp *paratuberculosis* infection in agricultural species. *Revue Scientifique et Technique – Office International des Epizooties*, 20 (1), 151-179.

Kudahl, A.B., Nielsen, S.S., & Ostergaard, S. 2008. Economy, efficacy, and feasibility of a risk-based control program against paratuberculosis. *Journal of Dairy Science*, 91 (12), 4599-4609.

Lu, Z., Mitchell, R.M., Smith, R.L., Van Kessel, J.S., Chapagain, P.P., Schukken, Y.H., & Grohn, Y.T. 2008. The importance of culling in Johne's disease control. *Journal of Theoretical Biology*, 254, (1) 135-146.

Nielsen, S.S., Bjerre, H., & Toft, N. 2008. Colostrum and milk as risk factors for infection with *Mycobacterium avium* subspecies *paratuberculosis* in dairy cattle. *Journal of Dairy Science*, 91, 4610-4615

Nielsen, S.S. & Toft, N. 2009. A review of prevalences of paratuberculosis in farmed animals in Europe. *Preventive Veterinary Medicine*, 88 (1), 1-14.

Olsen, I., Sigurgardottir, G., & Djonne, B. 2002. Paratuberculosis with special reference to cattle. A review. *Veterinary Quarterly*, 24, 12-28.

Ravva, S.V, Stanker, L.H. 2005. Real-time quantitative PCR Detection of *Mycobacterium avium* subsp. *paratuberculosis* and differentiation form other mycobacteria using SYBR Green and TaqMan assays. *Journal of Microbiological Methods* 63: 305- 317.

Rubery, E. 2001. A review of evidence for a link between exposure to *Mycobacterium paratuberculosis* (MAP) and Crohn's disease (CD) in humans. Food Standards Agency, UK. http://www.food.gov.uk/multimedia/pdfs/mapcrohnreport.pdf

Sechi, L.A., Rosu, V., Pacifico, A., Fadda, G., Ahmed, N., & Zanetti, S. 2008. Humoral immune responses of type 1 diabetes patients to *Mycobacterium avium* subsp. *paratuberculosis* lend support to the infectious trigger hypothesis. *Clinical and Vaccine Immunology*, 15, (2) 320-326.

Stephan, R., Schumacher, S., Tasara, T., & Grant, I.R. 2007. Prevalence of *Mycobacterium avium* subspecies *paratuberculosis* in Swiss raw milk cheeses collected at the retail level. *Journal of Dairy Science*, 90 (8), 3590-3595.

Turenne, C.Y., Collins, D.M., Alexander, D.C., & Behr, M.A. 2008. *Mycobacterium avium* subsp. *paratuberculosis* and *M. avium* subsp. *avium* are independently evolved pathogenic clones of a much broader group of *M. avium* organisms. *Journal of Bacteriology*, 190 (7), 2479-2487.

Turenne, C.Y., Wallace, R., Jr., & Behr, M.A. 2007. *Mycobacterium avium* in the Postgenomic Era. *Clinical Microbiology Reviews*, 20 (2), 205-229.

USDA-APHIS-VS. 2008. Johne's disease on U.S. dairies, 1991-2007. Info Sheet #N521.0408.

Uzoigwe, J.C., Khaitsa, M.L., & Gibbs, P.S. 2007. Epidemiological evidence for *Mycobacterium avium* subspecies *paratuberculosis* as a cause of Crohn's disease. *Epidemiology and Infection*, 135 (7), 1057-1068.

Waddell, L.A., Rajic, A., Sargent, J., Harris, J., Amezuzca, R., Downey, L., Read, S., & McEwen, S.A. 2008. The zoonotic potential of *Mycobacterium avium spp. paratuberculosis*: A systematic review. *Canadian Journal of Public Health*, 99 (2), 145-155.