

## Foot and Mouth Disease Summary

### Introduction

1. This note provides a brief summary of an analysis undertaken by a DISCONTTOOLS group of experts on Foot and Mouth Disease (FMD). They reviewed the current knowledge on the disease, considered the existing disease control tools, identified current gaps in the availability and quality of the control tools and finally determined the research necessary to develop new or improved tools. Full details of the analysis can be downloaded from the web site at <http://www.discontools.eu/> by selecting Disease Database, then the specific disease and highlighting the variables of interest. This is completed by selecting “create a report” which can then be downloaded as either a PDF or Excel spread sheet.

### Disease profile

2. FMD is widely distributed with only the exporting countries of Northern Europe, North America and Australia/New Zealand being completely free while many developing countries in Asia, the Middle East and in Africa, in particular, have significant problems with endemic FMD. Positive progress with eradication has continued in South America where no new cases have been reported since 2012. OIE and FAO have launched a global initiative to support regional and national control.

3. FMD is an important animal disease with a considerable impact on livelihoods and trade for many developing countries with endemic infection as well as major trade implications when outbreaks occur in a previously free region. The economic impact is significant and prolonged for countries or regions with endemic FMD while epidemics, such as those that occurred in Japan and the Republic of Korea since 2010, are extremely costly in terms of disease control, proving freedom from infection and in terms of short or long term trade implications.

4. FMD has been studied for many years, but despite this there are still significant areas of uncertainty in relation to pathogenesis, immunology, vaccinology, epidemiology and control. This is partly due to the limited number of locations where such research can be performed under suitable containment conditions as well as limited field investigations in endemic areas. Consequently, significant research contributions are still needed to ensure that rational disease control, including vaccination, can be optimised. More research is now being done in economically emerging countries such as China and India.

### Risk

5. FMD is closely associated with poverty and is widespread in many developing countries severely reducing animal productivity and reducing the value of affected animals. Control of FMD in such settings will provide a significant economic boost to both the local animal keepers as well as the countries in general. The pressures for movements of people and products brought about by political instability and continuing globalisation enhance risks for international spread of the disease. Therefore, it is of utmost importance to bring FMD under control in these settings, taking into account the wildlife situation, as the reduction of infectious virus in these areas will provide a significant reduction in the risk of introduction of FMD virus to previously free areas.

### Diagnostics

6. Commercialisation of diagnostics for FMD is constrained by lack of resources in developing countries and uncertain demand in developed ones that are mostly FMD free. Diagnostics for FMD are only available from a small number of commercial suppliers. The main reagents used can only be obtained from the OIE/FAO Reference Laboratory in Pirbright or produced for local use in National or Regional Laboratories. The main commercial reagents include serology kits for NSP testing while commercial kits for structural antibodies are highly limited and often focused on rather old methods, such as the liquid phase blocking ELISA. New commercialised tests for antibodies and for virus and tests that can type across all the variants within serotypes have become recently available from the National and OIE Reference Laboratory for FMD in Brescia, Italy.

7. Faster diagnostics and field pen side tests are required along with the development of more effective and specific differential tests. Lateral flow devices for virus detection are now available but not yet for distinguishing between all seven serotypes. Prototypes exist for portable units that detect viral RNA with high sensitivity. The development of improved rapid and inexpensive diagnostic assays would assist in surveillance. A constraint is the lack of sufficient panels for test validation across all serotypes and species.

8. Assays to distinguish between vaccinated and infected animals with improved sensitivity are available, but lack of knowledge about virus transmission and persistence in vaccinated populations creates uncertainty about reliability of these tests to detect undisclosed infection.

### **Vaccines**

9. Support for fundamental immunology and for animal studies is essential. Current vaccines are quite efficient provided that they are applied before exposure to live virus (at least 1 week before exposure), that the vaccine strain has been carefully selected to match the outbreak strain, that sufficient amount of intact antigen is included in the vaccine and that the vaccine is of good quality. There are disadvantages with the current vaccines which include the dangers inherent in their large-scale production from virulent virus, the heat labile nature of the vaccine, necessitating provision of a cold chain and the short duration of protection elicited. Not all strains of FMD virus are covered fully by the limited number of vaccine strains commercially available and new variants emerge periodically.

10. The need to either know the antigenic characteristics of the outbreak virus strain or instead adding multiple antigens to the vaccine, thereby increases the costs of vaccination significantly. Lack of knowledge on circulating isolates in endemic regions may impact on the efficacy of vaccination campaigns by the incorrect selection of the antigens in endemic settings. In addition, the need for regular booster vaccinations is a major constraint to maintaining protective levels of immunity,

11. In the USA, adenovirus vectored vaccines have become commercially available for some serotypes with a reduced risk for FMD virus escape during production or from incomplete inactivation. Another promising line of research is the development of recombinant empty capsids which may have enhanced stability and could be produced without the need to handle live FMD virus.

### **Pharmaceuticals**

12. There may be some potential for the use of antivirals in FMD control but there would be considerable challenges in both developing and licensing such products. Some compounds with in vitro antiviral activity have been identified but problems such as safety, oral effectiveness and avoidance of virus resistance remain to be overcome.

### **Knowledge**

13. Research is needed to fill gaps in the understanding and knowledge about the disease especially in relation to pathogenesis, immunology, vaccinology and epidemiology many of which are closely linked to the research requirements to develop more effective tools for the control of the disease. For example, the development of longer lasting and more broadly cross-protective vaccines. Full details of the gaps are shown in the Disease and Product Analysis for Foot and Mouth Disease on the DISCONTTOOLS website.

### **Conclusions**

14. Increased studies of FMD leading to improved vaccines, diagnostics, treatment or disease control, are likely to result in significant progress in terms of reducing the presence of endemic FMD worldwide and in reducing the risk of introduction to previously free regions. Some differences in approach are required for FMD control in the free countries and the endemic countries.

15. The main obstacle for effective prevention and control, in particular in the developing world, are the availability of high quality and affordable vaccines that have been accurately selected and matched to the circulating virus strains.



16. Significant funding for the above activities will clearly improve the understanding of FMD epidemiology and control and will have a good chance of leading to improved disease control. There are prospects for new recombinant vaccines and commercial diagnostic kits in the next 5 years whilst ongoing research will provide a better background for using current vaccines and diagnostic methods.