

I. INTRODUCTION

BadgerBCG is authorised under a Limited Marketing Authorisation, under European Medicines Agency (EMA) guidelines for MUMS¹/Limited Markets. This type of Marketing Authorisation is intended for use where limited numbers of a product are expected to be sold, and where a need for a specific drug is required. Due to the nature of the use of such drugs, a full dossier meeting all requirements for the marketing of the drug is not required, provided that the safety, quality and efficacy of the product can be supported by available data, and a favourable benefit-risk profile is determined. There is a requirement for Periodic Safety Update Reports (PSURs) to be submitted for annual reassessment of this product. Moreover, results of any additional studies must be submitted to the Veterinary Medicines Directorate (VMD).

BadgerBCG is a live, freeze-dried vaccine prepared from an attenuated strain of *Mycobacterium bovis* (*M. bovis*) originating from a BCG Danish strain SSI (Statens Serum Institute) 1331. The vaccine is intended for use in badgers, and is to be given by intramuscular injection in order to reduce lesions caused by *M. bovis*. The reconstituted vaccine is a 1 ml solution containing 2-8 x 10⁶ CFU² BCG/ml. Badger BCG may be given to juvenile badgers emerging from the sett in addition to adults, and the onset of immunity is seventeen weeks. The duration of immunity is unknown. Annual vaccination on a population basis is recommended.

Badgers are a protected species under the Protection of Badgers Act of 1992, where it is an offence to kill a badger or to interfere with a sett without a licence from Natural England. There are strict limits to the use of badgers in clinical trials. These limitations have restricted the number of animals used in some studies, however this is acceptable for a Limited Marketing Authorisation.

II. QUALITY ASPECTS

Product Development and Composition

The original strain for the product was obtained from the Pasteur Institute and used by SSI for the manufacture of a liquid vaccine, which had a limited shelf life. In 1965, freeze-dried methods were employed, producing a more stable vaccine, which was placed in glass vials and stored at 2°C - 8°C. In 1988, rubber-stoppered vials were introduced, and thirty-one batches over six months were used to compare production. No differences were detected. In 1996, the freeze-drying process was transferred to a new facility, and since then, no significant changes in the production process have occurred. BCG was chosen as a candidate for use in badgers due to a long history of use in man and animals. The vaccine strain (1331) is considered to be among the most protective of BCG strains and the human product is already produced to GMP, avoiding the need to develop and validate alternative processes. The dose of vaccine was chosen based on developmental studies with the vaccine in the target species. The intramuscular route was selected because efficacy using this route was shown to be equivalent to the subcutaneous route, and the intramuscular route is more appropriate for use in badgers in the field.

The vaccine is produced in a traditional way by culturing the non-virulent BCG strain in culture flasks, and collecting these cultures to form a single batch. Manufacture is based on a Master Seed Lot system, and vaccine production is performed in dedicated areas where no other bacteria are prepared. The manufacture and sealing of Master Seed Lots is performed under GMP conditions. Bacteria used in production of the BCG vaccine do not exceed 8 passages

¹ MUMS. Minor Uses and Minor Species

² CFU. Colony forming units.

from the third passage from the master seed. In-process tests consist of analysis for contaminating organisms, pH, moisture content and total bacterial cell count. Equipment is sterilised prior to use, homogenisation of the culture is instigated followed by the aseptic filling of vials. Stoppers for the vaccine and diluent are steam-sterilised, and vials are stored frozen prior to shipping.

The applicant provided validation data in support of the sensitivity of the bacterial culture methods used to detect both BadgerBCG vaccine and wild type *M. bovis* during the safety, efficacy and field studies. These were considered satisfactory. The sensitivity of the cultural methods was dependent upon the sample tested. Samples such as faeces and rectal swabs had lowest sensitivity (approximately 200-300 CFU per sample). Sensitivity when testing other samples was higher and ranged between 2 to 40 CFU per sample.

A target animal safety study test is not performed on the finished product, as badgers are a protected species. This is additionally acceptable because the vaccine complies with European Pharmacopoeia (Ph. Eur) safety requirements. This was considered sufficient and the absence of a target species safety test was considered justified.

Vaccine Antigen

BCG Vaccine SSI contains *Mycobacterium bovis* (BCG), Danish strain 1331 (attenuated). The vaccine also contains sodium L-glutamate. There is no monograph for BCG for use in badgers, but there are monographs for use of BCG in humans as a vaccine and in immunotherapy. All BCG sub-strains originate from the Calmette/Guérin strain developed between 1908 and 1921. In 1931, SSI received the BCG culture from the Pasteur Institute, and the line for the current vaccine originated from this culture. Freeze drying of the strain was performed in order to preserve the genotype of the mycobacteria, and ampoules of Master Seed Lot are stored at < -20 °C. Currently, production is based on a primary and secondary seed lot system. Seed lots have been tested to be negative for virulence, and no vaccine production exceeds the eighth passage from the primary seed lot. Generally, the seed lot used is three or four passages from the secondary seed lot, which equates to three passages from the primary seed lot.

Other Substances

Excipients in the diluent are as follows: sodium L-glutamate, magnesium sulphate heptahydrate, dipotassium phosphate, citric acid monohydrate, L-asparagine monohydrate, ferric ammonium citrate, glycerol and water for injection. All excipients are listed in the Ph. Eur. With regard to transmissible encephalopathies, all ingredients now used in the production of the vaccine and the diluent are of non-animal origin. Ox bile used in the original Master Seed Lot is unlikely to be remaining in the subsequent seed lots. Ox bile was used in media during production of product before 1960, after which no ruminant materials have been used during production.

Packaging Materials

The vaccine is contained in amber glass vials, and the solvent, Diluted Sauton SSI is contained in colourless glass vials. The glass vials are Type I, in compliance with specifications stipulated in the Ph. Eur. Rubber stoppers also conform to Ph. Eur requirements, and the vials are closed with an aluminium seal, covered by a cap.

Manufacture of the Finished Product

The Secondary Seed Lot is used as the Working Seed Lot for the manufacture of BCG Vaccine SSI. The batch is prepared from the Master Seed Lot as three passages on from Sauton, and the common principles of vaccine manufacture are employed. Tests are performed on the identity of the Secondary Seed Lot, the absence of virulent bacteria is checked, and the product is checked for sterility and dermal reactivity.

Finished Product Quality Control

Control tests performed on the finished product are analysis of bacterial concentration, tests for absence of virulent bacteria, viability count, bacterial and fungal contamination, temperature stability, bacterial concentration, identification and the presence of residual moisture.

Stability of the Product

Vaccine Antigen

Storage as packaged for sale

Parameters analysed for stability of the vaccine as packaged for sale were: number of viable bacterial units, and appearance and presence of residual water. Stability testing was performed over thirty-six months.

In-use shelf life

The product was tested with regard to viability four hours after reconstitution, giving appropriate data for the product as it will be used in the field. Results were satisfactory.

Finished Product

Results from three batches of the product were analysed and found to be satisfactory. The shelf-life of the product as packaged for sale is eighteen months.

In-Use

The shelf-life of the product after reconstitution is four hours. BadgerBCG should be protected from the light and stored at 2°C – 8°C.

CONCLUSIONS ON QUALITY

The manufacturing process for BadgerBCG is supported by a long history of the product as being safe for use and of consistent quality. Data supporting the limit of detection of the culture methods have been provided, and culture methods have been shown to provide adequate sensitivity. The quality of the product has therefore been shown to be satisfactory.

III. SAFETY ASPECTS

Introduction

The vaccine contains *Mycobacterium bovis* Bacille Calmette Guérin (BCG), Danish strain 1331 and is recommended for use in badgers by intramuscular injection from the age at which they emerge from the sett.

Laboratory Tests

Safety and efficacy studies have been conducted in specialised facilities where the natural environmental of the badger is maintained under secure conditions, which are considered to be equivalent in principle to laboratory studies. Studies were conducted under licence from Natural England in accordance with Protection of Badgers Act of 1992.

Two studies were conducted in naïve badgers to investigate the safety and efficacy in badgers vaccinated with either a standard dose or a sub-standard dose of commercial BCG vaccine given by the intramuscular route, against challenge with *M. bovis*. A suitable number of badgers were allocated to either a vaccination or control group. Badgers were vaccinated with BCG by the intramuscular route with either a standard dose or a sub-standard dose. Seventeen weeks after vaccination, the badgers were challenged by the intrabronchial delivery of *M. bovis*. Twelve weeks post-challenge, all badgers were examined at post-mortem, and lesions caused by *M. bovis* or BCG were examined. Infection with *M. bovis* and/or presence of BCG in tissues was confirmed by culture and histopathology. At regular intervals during the study, the badgers were examined under anaesthesia.

The blood was sampled to monitor peripheral immune responses. The clinical samples were taken after challenge until post-mortem and submitted for culture to detect excretion of *M. bovis* by vaccinated and control badgers. Twelve weeks after challenge, the badgers were humanely euthanized and a detailed post-mortem examination was conducted. Visible lesions were recorded. A large range of tissues were sampled for culture of *M. bovis* and for histopathology. In addition, differential culture for BCG/*M. bovis* was conducted in tissues taken at post-mortem, in order to establish the extent of the persistence and dissemination of BCG in the vaccinated animals.

Vaccination with BCG was confirmed by immune response detectable by ELISPOT₃ developing post-vaccination. Two females were lactating at the time of vaccination. Their cubs were tested for cellular response to BCG/*M. bovis* (by ELISPOT) on two occasions but no PPD-B response was measured which suggested that there was no transmission of BCG from mother to cubs. The blood parameters measured for haematology and haematochemistry remained normal at all points. The rectal temperature remained between 37°C and 40°C. None of the animals presented any skin ulceration post-vaccination. In some animals vaccinated with the sub-standard BCG dose, mild scratches were observed on the skin shaved around the point of vaccination. Some badgers developed intra-muscular nodules at the point where the vaccine was delivered. Five badgers vaccinated with the standard BCG dose and five badgers vaccinated with the sub-standard BCG dose presented a nodule post-vaccination. The largest nodule was 25 mm diameter, 25 weeks post-vaccination. The majority of the nodules developed post-challenge. No granuloma or acid fast bacteria were observed in the lumbar muscle of any vaccinated badger when examined by histology.

Safety of one administration of an overdose:

The study was conducted to investigate safety in naïve badgers vaccinated with either an intramuscular or subcutaneous vaccination with an overdose of commercial Bacille Calmette Guérin (BCG) at a dose that exceeded a 10 times the proposed maximum. A second administration of a single dose was subsequently administered to investigate safety of a

³ The Enzyme-linked immunosorbent spot (ELISPOT) assay is a common method for monitoring immune responses in humans and animals.

repeated administration. The study was conducted in accordance with the principles of GLP⁴. A suitable number of badgers was divided into control and test groups. One test group of badgers was vaccinated by the proposed intramuscular route and another test group was vaccinated by the subcutaneous route. The badgers were vaccinated twice. An overdose was given on week 7 and a single dose was given on week 22. The animals were observed for these parameters: local injection site reaction, haematology, biochemistry, weight, temperature and behaviour.

Additional samples were taken on some occasions to detect excretion of BCG from tracheal aspirate, saliva, urine and faeces. The IFN- γ test⁵ was also done to determine immunological response. The study concluded that vaccination did not influence haematological parameters, blood chemistry parameters, body weight, temperature and behaviour. The local reactions following intramuscular vaccination with an overdose of BCG were resolved by 48 days after injection. No local reactions were observed in any badger following the second intramuscular (IM) vaccination with a single dose of BCG. Other than localised swelling, no discernable reactions were observed following intramuscular vaccination. The local reactions following subcutaneous administration were more persistent. The largest reactions recorded followed subcutaneous vaccination of an overdose and gave reactions up to 27 mm in diameter. Visible reactions were transient following IM vaccination and were all resolved by 48 days after vaccination. No reactions were seen in badgers following the second vaccination. The samples of saliva, faeces and urine were taken at intervals during the study. At no point was BCG recovered from the samples. None of the control animals, which acted as sentinels, became IFN- γ test positive to BCG, indicating that shedding had not taken place.

Examination of reproductive performance:

The applicant has submitted very limited data for use in captive badgers. The data indicated that there were no undue concerns for the use of the vaccine during pregnancy but these data were not sufficient to allow a specific recommendation. Therefore, the following statement is included in the Summary of Product Characteristics (SPC):

- 4.7 Use during pregnancy and lactation
No information available.

Special requirements for live vaccines

Spread of the vaccine strain and dissemination in the vaccinated animal

The applicant has submitted a risk assessment assuming a worse case based on the limits of detection for the range of samples taken. The analysis assumed that shedding of between 200 and 300 CFU of Badger BCG could occur from wounds or other means i.e. faeces, urine, and tracheal exudate. This level of sensitivity was based on validation of the level of detection in faeces and rectal samples. Sensitivity of detection from other samples was more sensitive and ranged from 2 to 40 CFU. It is stated that BCG does not survive for prolonged periods in the environment and that survival time is markedly less than that of wild type *M. bovis*. The published studies indicated that levels of BCG in faeces would decline rapidly. In addition, BCG is known to be labile at low pH and therefore survival if ingested by other badgers or non-target species would be very poor. The studies indicated that when large doses of BCG are given to a variety of mammalian species no evidence of disease or exacerbation of pre-existing tuberculosis have been found. Consideration has also been given to worse case for exposure of cattle to shed BCG. The published literature indicated that cattle experimentally exposed to 10⁸ CFU BCG by the oral route did not become positive in the comparative skin test as used in the

⁴ Good Laboratory Practice

⁵ Gamma Interferon Test. Gamma interferon is an immunological hormone that is produced after the stimulation of blood cells with antigens such as bovine tuberculin

UK. This dose is well above the level of exposure that is presented in the worse case. Therefore, the risk of BCG spreading and dissemination is effectively negligible.

Reversion to virulence of the attenuated vaccines

The applicant stated that more people have been vaccinated with BCG than any other vaccine. During this extensive use no reversion to virulence has been reported. The complications associated with human vaccination are linked to deficiencies in the host immune system. The studies on BCG recovered from individuals with infections caused by BCG have shown that the recovered BCG is no more virulent in guinea pigs and rabbits than the original strain used for vaccination. The published literature indicated that deficiencies within the BCG genome are such that a reversion event is effectively impossible. This is supported by studies which showed that complementation of deficient regions cannot restore virulence. The genetic divergence of BCG strains has been as a consequence of in vitro growth under differing growth conditions during the 80 years the vaccine has been available. The divergence consists of a series of gene deletions and not insertions, therefore there is considerable evidence that genetic transfer of information does not occur. There is no evidence of reversion from the use of BCG in a wide range of species. In the case of badgers the published literature and data presented by the applicant conclude that onward transmission of BCG from a vaccinated badger to other animals is highly unlikely. In the unlikely event that transmission to other badgers occurred the mutation rate of 1×10^6 CFU for BCG would mean that there would not be sufficient organisms transmitted to allow for selection of mutant organisms. The genetic basis for attenuation of BCG is such that there is effectively no possibility for reversion irrespective of the fate of BCG. Analogous studies in New Zealand have found no evidence of reversion to virulence from the use of BCG in a wildlife species. The BCG is sensitive to environmental factors and also the acid environment of the gut which provide an additional barrier to any potential passage of BCG through sequential hosts. In view of the extensive scientific studies reviewed which conclude that reversion to virulence is effectively impossible, it was considered that the potential risk of reversion to virulence was adequately addressed.

Biological properties of the vaccine strain

The applicant has submitted a review of the origins and nature of BCG, including a review of the development of the vaccine, the vaccination studies in a wide range of species, the behaviour of BCG in vivo and genetic studies to understand the basis of attenuation. This has provided sufficient information on the extensive information available concerning the biological properties of BCG.

Field Trials

The applicant has submitted two reports which contain data from different phases of one study. The field trial was conducted to investigate safety in, and shedding from, badgers of a commercial Bacille Calmette Guérin (BCG) vaccine when given parenterally to badgers in the field and to investigate the immunogenicity and efficacy of BCG in badgers. This trial was conducted according to the principles of GCP₆ at well defined locations identified by ordinance map grid reference covering a large area. In the first phase of the trial, badgers were surveyed and examined for immunological or cultural evidence of exposure to *M. bovis*. Badgers live in social groups (typically numbering 5-10 individuals) and for this trial the allocation to vaccine and control groups was done at a social group level with the trial having a cluster-randomised design.

Vaccinated badgers were given an intramuscular injection of BCG vaccine according to the recommended schedule. All animals (both vaccinated and control) were monitored for body temperature over 24 hours post vaccination (in the case of controls 24 hours post trapping and examination). Two weeks later body temperature and local reactions were measured. The

⁶ Good Clinical Practice

clinical samples collected were submitted for culture. Badgers found dead in the study area were submitted for post mortem examination including examination for any local reaction at site of vaccination. During the 24 hours immediately following vaccination the temperature of both vaccinated and control badgers ranged between 30.2°C to 40.5°C. Although temperature readings fluctuated immediately after vaccination it was noted that by 24 hours post vaccination the temperatures of both vaccinated and control animals had stabilised and were within the normal range. All badgers were monitored on recovery from anaesthesia and were not released at site of capture unless they were fully recovered. There were no adverse reactions noted prior to release. It was noted on clinical observation during recovery and prior to release that vaccinated badgers behaved indistinguishably from control animals. Badgers were re-trapped two weeks after vaccination and local reactions were measured. The data were collected from a suitable number of badgers that had been vaccinated two weeks previously. Of these, 5 had small intramuscular swellings and none exhibited skin ulceration. The largest swelling measured 16.84 mm. This badger had tested negative by both IFN-gamma test and Stat-Pak (serology) and was negative for *M. bovis* culture on the day of vaccination and again when re-trapped. These local reactions were restricted to animals which were all negative for *M. bovis* culture and *M. bovis* cellular immunity (IFN-gamma test). The vaccination injection site reactions appear minor during 2 weeks following vaccination and there was no evidence of more severe reactions in animals already infected with *M. bovis*.

In the second phase of the study, badgers were trapped twice, two weeks apart. A suitable number of badgers were divided into vaccinate and control groups. The vaccinated group was injected intramuscularly with BCG vaccine. The control group was left untreated. If a control group had merged with a vaccine group the merged group was subsequently allocated as a vaccinated group. All animals were observed for local reactions. The clinical samples collected were submitted for culture. Badgers found dead in the study area were submitted for post mortem examination including examination for any local reaction at site of vaccination. The study concluded that most of the vaccinated badgers had no local reaction at the vaccination site. Intramuscular swellings were found in some badgers with the swellings measuring between 6 and 23 mm. Rarely the local injections site reactions may persist for at least 2 years, although in most cases the reactions had resolved when next observed (approximately 8 months). No lesions were found at the site on post mortem of dead badgers. No reactions at the vaccination sites were seen with repeated vaccination, which was up to 3 vaccinations. No skin ulceration was observed in any of the badgers re-examined.

The specific information concerning safety in the youngest possible aged badger is difficult to obtain in view of the wild nature of the target species and for welfare concerns. Therefore, the applicant has reviewed data from the field trial and published data which indicated that the product is safe in badgers weighing 1.9 kg to 7.9 kg (average 3.9 kg), at the stage of development when emergence from the sett is expected. Therefore, the following statement is included in the SPC:

4.2 Indications for use, specifying the target species

For use in badgers from the age at which they emerge from the sett.

CONCLUSIONS ON SAFETY

Conclusions on User Safety

The applicant has confirmed that product will only be administered by trained and accredited personnel screened by FERA⁷. The operator warnings included in the SPC and product literature are equivalent to the user warnings for the human product. These are:

- BadgerBCG should not be handled by persons receiving systemic corticosteroids or immunosuppressive treatment including radiotherapy, those suffering from malignant conditions (e.g., lymphoma, leukaemia, Hodgkin's disease or other tumours of the reticulo-endothelial system), those with primary or secondary immunodeficiencies, those with HIV-infection. The reaction to self injection and infection with Bacille Calmette Guérin (BCG) may be exaggerated in these persons, and a generalised BCG-infection is possible.
- In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- To the physician:

BadgerBCG is a 1ml dose of the identical Statens Serum Institut SSI BCG product which is licensed for human use at a dose of 0.1ml. Overdose above 0.1ml increases the risk of suppurative lymphadenitis and may lead to excessive scar formation. Gross overdosage increases the risk of undesirable BCG complications. Expert advice, including that of a chest physician, should be sought regarding the appropriate treatment regimen for the management or prophylaxis of systemic infections or persistent local infections following self injection with BCG.

- Antibiotic sensitivity of the BCG strain:

Minimum inhibitory concentrations (MIC) for selected anti-tuberculous drugs for the BCG Danish strain 1331 (as determined by Bactec 460).

Drug	Minimum Inhibitory Concentration (MIC)
Isoniazid	0.4 mg/l
Streptomycin	2.0 mg/l
Rifampicin	2.0 mg/l
Ethambutol	2.5 mg/l

The MIC for isoniazid is 0.4 mg/l. There is no consensus as to whether *Mycobacterium bovis* should be classified as susceptible, intermediately susceptible or resistant to isoniazid when the MIC is 0.4 mg/l. However, based on criteria set for *Mycobacterium tuberculosis*, the strain could be considered to be of intermediate susceptibility.

Conclusions on Environmental Safety

The applicant has submitted an Environmental risk assessment which concluded that the overall risk to the environment is effectively zero.

IV. EFFICACY ASPECTS

⁷ Food and Environmental Research Agency

Laboratory Tests

Safety and efficacy studies have been conducted in specialised facilities where the natural environment of the badger is maintained under secure conditions, which are considered to be equivalent in principle to laboratory studies. Studies were conducted under licence from Natural England in accordance with Protection of Badgers Act of 1992.

Two studies were conducted in naïve badgers to investigate the efficacy (and safety) in badgers vaccinated with either a standard or sub-standard dose of commercial Bacille Calmette Guérin (BCG) vaccine given by the intramuscular route, against challenge with *M. bovis*. A suitable number of badgers were allocated to either a vaccination or control group. Badgers were vaccinated with BCG by the intramuscular route with either a standard dose or a sub-standard dose. Seventeen weeks after vaccination, the badgers were challenged by the intrabronchial delivery of *M. bovis*. Twelve weeks post challenge, all badgers were examined at post-mortem, and lesions caused by *M. bovis* or BCG were examined and their severity quantified. The infection with *M. bovis* and/or presence of BCG in tissues was confirmed by culture and histopathology.

At regular intervals, the badgers were examined under anaesthesia. The blood was sampled to monitor peripheral immune responses. The clinical samples were taken after challenge until post-mortem and submitted for culture to detect excretion of *M. bovis* by vaccinated and control badgers. The protective efficacy of BCG was assessed experimentally by comparing the severity of the pathology caused by *M. bovis* in vaccinated badgers with non-vaccinated controls, following experimental challenge with *M. bovis*. Twelve weeks after challenge, the badgers were humanely euthanized and a detailed post-mortem examination was conducted. The visible lesions were recorded. A large range of tissues were sampled for culture of *M. bovis* and for histopathology. The differential culture for BCG/*M. bovis* was conducted in tissues taken at post-mortem, in order to establish the extent of the persistence and dissemination of BCG in the vaccinated animals.

Suitable numbers of badgers were allocated to either a vaccination or control group. The vaccination with BCG was confirmed by immune response detectable by ELISPOT developing post-vaccination. The response to antigen PPD-B was higher in animals vaccinated with the standard BCG dose. The response to *M. bovis* specific antigens post-vaccination was indistinguishable from the controls response. Post-challenge, all animals produced high levels of IFN γ to PPD-B, and CFP-10/ESAT-6, for approximately 10 weeks. The response decreased subsequently. The blood parameters measured for haematology and haematochemistry remained normal at all time-points, and did not vary significantly between vaccinated and controls post-vaccination. The badgers did not present any clinical signs following vaccination with BCG nor challenge with *M. bovis*. The food uptake was good and general behaviour was normal. The badger did not show any clinical sign of respiratory insufficiency. The breathing rate appeared normal and no coughing was observed. The visible lesions were observed in all the animals with varying degree of severity. The majority of lesions were described at post-mortem, but additional visible lesions were also found in fixed lungs. *M. bovis* was cultured from tissues with both macroscopic and microscopic lesions, but also from tissues without any lesions. All tissues collected for culture were weighed, and the number of bacteria recovered per gram of tissues was calculated. Compared with non-vaccinated controls the vaccinated badgers showed significant reductions in lesions in both the lungs and lymph nodes. The severity of these lesions and the numbers of *M. bovis* within the lesions and in other clinical samples was also significantly reduced in vaccinated badgers. In addition, the total bacterial count was reduced in badgers vaccinated with both doses of BCG, compared with the non-vaccinated controls. However, the geometric mean bacterial load in the vaccinated groups was not significantly lower than the non-vaccinated group.

The applicant presented a detailed analysis of an in depth investigation into the cellular and humoral response of badgers following vaccination and subsequent challenge. These data confirmed that vaccination induces an immune response. Annual vaccination on a population basis is recommended in view of the estimated 30% rate of turnover including new cubs and badger movement.

Field Trials

No field trials have been presented. The applicant has stated that field data supporting efficacy will be provided when the study is completed.

No data have been provided in support of duration of immunity and efficacy of booster. This is considered acceptable for a Limited Marketing Authorisation.

Conclusion on efficacy

The applicant has provided data from a detailed study investigating the immunology and protective efficacy of BCG administered to naïve badgers. The limited efficacy claim and the onset of immunity of 17 weeks are considered acceptable. There are no data in support of duration of immunity. This is considered acceptable for a Limited Marketing Authorisation. The principle of a protective effect of the product in badgers has been established using vaccine as recommended for use.

PART V. OVERALL CONCLUSION ON THE PRODUCT

The data submitted in the dossier demonstrate that when the product is used in accordance with the Summary of Product Characteristics, the benefit-risk profile for the target species is favourable and the quality and safety of the product for humans and the environment is acceptable.

POST-AUTHORISATION ASSESSMENTS

The SPC and package leaflet may be updated to include new information on the quality, safety and efficacy of the veterinary medicinal product. The current SPC is available on the Product Information Database of the Veterinary Medicines Directorate website.

(WWW.GOV.UK/CHECK-ANIMAL-MEDICINE-LICENSED)

The post-authorisation assessment (PAA) contains information on significant changes which have been made after the original procedure which are important for the quality, safety or efficacy of the product.

The PAA for this product is available on the Product Information Database of the Veterinary Medicines Directorate website.

(WWW.GOV.UK/CHECK-ANIMAL-MEDICINE-LICENSED)