Toxoplasmosis
Summary

Introduction
This note provides a brief summary of the Disease and Product analysis prepared by a DISCONTOOLS group of experts on Toxoplasmosis. 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 are available on the web site at http://www.discontools.eu/.

Disease profile
The apicomplexan protozoan *Toxoplasma gondii* is the etiologic agent of toxoplasmosis, a relevant zoonotic disease of humans and homoeothermic vertebrates. Felids, including domestic cats, are definitive hosts that can shed oocysts with their faeces, thus causing environmental contamination. In addition to infections that occur by accidental oral uptake of food or water contaminated with oocysts, it is assumed that a large proportion of affected humans may have become infected by consuming meat or other animal products that contained infective parasitic stages of *T. gondii*.
Human toxoplasmosis includes congenital and postnatally acquired toxoplasmosis. Congenital toxoplasmosis is transmitted from the recently infected mother to the foetus. Placental or foetal infection may cause abortion, the birth of severely affected children (e.g. hydrocephalus, seizures, retardation) or children developing symptoms of toxoplasmosis in later life (e.g. ocular toxoplasmosis). In most cases, postnatally acquired *T. gondii* infections have no severe consequences for infected humans. It is assumed, however, that a large number of ocular uveitis cases in humans are caused by postnatal *T. gondii* infection. Toxoplasmosis in immunocompromised patients (e.g. transplant patients) is of growing importance. This form of toxoplasmosis can result either from a reactivated, persistent infection or from a recently acquired new infection. In some cases, the infection has been transmitted from the infected donor of an organ to the uninfected recipient patient.
Farm animals represent a direct source of infection for humans, but also a possible reservoir for the parasite. Moreover, *T. gondii* may also be pathogenic to livestock, as it is an important abortifacient for small ruminants. Toxoplasmosis is responsible for considerable economic losses in some regions and particular farming systems, e.g. in areas where the small ruminant industry is relevant. Published information on the costs that *T. gondii* infections cause in livestock production is scarce. The most recent peer reviewed reports from Great Britain and Uruguay suggest annual cost of about 5-15 million US $ per country. Thus, due to the zoonotic potential and due to its possible detrimental effect on livestock production it is important to control *T. gondii* infections in livestock.

Risk
Knowledge on potential risk factors for *T. gondii* infections in livestock is a prerequisite to implement effective biosecurity measures on farms to prevent *T. gondii* infections. Risk factors identified by many studies are cat-related, but also others associated with a potential contamination of fodder or water, and with access to a potentially contaminated environment.
In humans, risk factor studies suggest that the consumption of raw or undercooked meat is a major source of *T. gondii* infections in Europe. The environmentally resistant *T. gondii* oocysts, shed by domestic cats, also contribute to an unknown extent to human infections. As cats are definitive hosts of *T. gondii,* oocysts shed by cats may cause infection, e.g. directly during cleaning the cat litter box, by soil contamination, via eating unwashed vegetables or fruits as well as drinking or swallowing oocyst contaminated surface water. Elevated risks of infection were also associated with locally produced cured, dried or smoked meat, raw oysters, clams or mussels, working with meat and drinking goat milk, but the relative importance of these individual risk factors needs to be determined.

Diagnostics
Serological diagnostics plays a key role in diagnosis of both, toxoplasmosis in animals and humans. Commercial serological tests, based on both, native or recombinant proteins, are available for humans and many animal species. For some animal species, in particular cattle, equids and to some extent also pigs, the existing serological tests seem to be not reliable in identifying animals with a viable *T. gondii* infection, i.e. animals that could, if used for meat

production, transmit the infection to consumers if this meat is consumed insufficiently treated (e.g. cooked). Gaps exist in serological assays that could be easily applied in multiplexed assays, i.e. assays able to assess antibody responses to several infectious agents at the same time. Such assays could significantly improve and accelerate slaughterhouse surveys and examinations. Gaps exist in terms of tests for specific applications, such as tests able to reliably differentiate the acute from a chronic infection or differentiating between infections caused by different stages of the parasite (e.g. tissue cysts vs. oocysts driven infections).
To determine the presence of the parasite, e.g. in case of clinical toxoplasmosis, DNA detection methods are readily available but - especially in the veterinary sector - only a few are commercially available. DNA detection assays are not able to differentiate between viable and non-viable parasites. A diagnostic gap is the reliable and sensitive detection of viable parasites in meat and no easy solution is in sight.
A further gap are tools to specifically bind parasitic molecules, to concentrate these molecules/parasites and to increase the diagnostic sensitivity by a pre-analytic concentration step, such as tools for immune-magnetic separation.

Vaccines
For humans no vaccination has been developed yet. There is only one vaccine available in the veterinary sector for use in sheep. It is a live vaccine, commercially and seasonally available in a few regions of the world (including France, Ireland, New Zealand, Norway, Spain and UK). It has a short shelf life of a few days and needs refrigerated delivery. Furthermore, this vaccine poses a risk to pregnant animals; this excludes it from application in pregnant sheep or sheep close to mating. It is potentially infective for users and should not to be handled by pregnant women.
Thus, more user-friendly and safer vaccines against toxoplasmosis are needed, predominantly in livestock species, in which toxoplasmosis is of economic importance. Optimally, such vaccines are subunit or DNA vaccines. Vaccines to increase food safety by preventing food animals to establish tissue cysts following vaccination seems to be an additional application. Further, a transmission blocking vaccine for young cats could considerably reduce the oocyst contamination in the environment and could probably be commercialised with other well accepted cat vaccines.

Pharmaceuticals
In the veterinary sector, except the companion animal sector, only symptomatic treatment is available, aiming at reducing clinical signs during acute infection (e.g. fever). In the human sector, mainly Macrolide antibiotics (Spiramycin) or Folate inhibitors (Sulfamethazine Pyrimethamine sulphate) are applied, especially during pregnancy to avoid transplacental transmission of *T. gondii* and congenital toxoplasmosis. Further substance groups may act against the parasite including Polyether ionophore antibiotics, Quinolones and Triazinones. However, overall there seems to be a low commercial potential, due to difficulties in applicability, potential residue problems, and high developing costs until a registration is achieved. But since drugs against toxoplasmosis in livestock may also provide novel options for the development of effective pharmaceuticals for the human sector there are opportunities for new drug developments.

Knowledge
There was a tremendous increase in the cell-biological knowledge on the intermediate host stages of *T. gondii* as an intracellular pathogen, especially on its interaction with the host's immune system. However, basic knowledge is lacking largely in case of other parasite stages, including the oocysts excreted by definitive hosts or the parasitic stages developing in the gut of felids, i.e. stages preceding the oocysts development. However, these stages are of outmost importance if blocking vaccines for young cats are going to be developed.

Conclusions
Toxoplasmosis represents an important infectious, zoonotic disease in humans, causing also huge economic losses in livestock, especially in small ruminants. New developments in the field of diagnostics and vaccines represent promising options to reduce *T. gondii* infections in animals and humans.