

The use, trade and harvest of livestock sera

Summary of the report

By C.E.A. Jochems

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Fetal bovine serum (FBS) is the most widely used serum in the culturing of cells, tissues and organs in vitro, in industry, medicine, and science. It can be used for nearly every cell type. Countries which harbour facilities involved in fetal blood harvest for (commercial) FBS production include: Canada, the USA, Honduras, Venezuela, Brazil, Uruguay, Argentina, Chile, South Africa, France, Sweden, Hungary, Estland, Lithuania, Letland, the Czech Republic, Slovakia, Australia, New Zealand, probably Mexico, probably Paraguay, would include Russia, possibly Spain, possibly Namibia - Botswana - Zimbabwe.

Bovine fetuses used for FBS harvest come available from extensively kept meat cattle (herds are always sent to slaughter in their entirety, whether or not cows are pregnant is not determined), from pregnant cattle sent to slaughter for reasons of unavoidable culling (e.g. due to accident resulting in cripleness), and possibly from cattle which are deliberately made pregnant for the production of FBS. The latter would take / have taken place in Hungary, the Baltic States, and possibly in the Czech Republic and Slovakia. In all other countries - except Honduras - fetuses are derived from pregnant meat cattle. In Honduras, fetuses would only be derived from pregnant cull cows. In the USA fetuses are derived both from pregnant meat cattle and cull cows. Countries which do explicitly not harbour facilities in which fetal blood is harvested for (commercial) FBS production include: Iceland, Norway, Finland, Denmark, the Republic of Ireland, the United Kingdom, The Netherlands, Germany, Austria, Switzerland, Portugal, Italy, Greece, Slovenia, Croatia. Countries not mentioned above have not been investigated. The mondial supply of raw FBS would be approximately 500,000 litre's per annum.

When during evisceration of the mother bovine as part of the regular slaughter procedure, a fetus is discovered, it may be used for FBS harvest. The blood from bovine fetuses which are used for FBS production is usually obtained by means of a cardiac puncture (all countries mentioned above, except Uruguay); alternatively, it may be harvested by means of umbilical vein puncture (Uruguay, Australia), or puncture of the jugular vein (Brazil). A cardiac puncture is the method of preference for septical reasons. The fetal heart must still be beating on order to harvest blood for FBS production purposes by means of cardiac or umbilical cord puncture, in order to pump the blood outside the body.

The time that elapses between death of the mother bovine on the slaughter line, and the performance of a cardiac or umbilical cord puncture is stated to be ± 5 minutes (Chile, serum harvesting company; Brazil, serum harvesting company; USA, former USDA inspector) and $\pm 25-30$ minutes (Australia, serum harvesting companies and relevant authority; New Zealand, relevant authority; South Africa, harvesting company; Sweden, relevant authority). Note that authorities get their information from the companies involved in harvesting. The term of 25-30 minutes may be doubted however, as this statement was usually accompanied by the information that the fetal heart would not function at the time of cardiac puncture and the fetus would be dead. It was argued that the fetus dies at approximately the same time as does the mother. This does not seem probable, as fetuses and neonates of mammals are remarkably resistant to lack of oxygen supply.

A bovine fetus never receives anaesthesia prior to a bleeding procedure. Mammal fetuses can feel pain, depending on the maturity of the nervous system. Bovine fetuses used for FBS harvest are usually at least 6 months of gestational age, though fetuses may be used as soon as 3 months gestation. Pain may be felt at the cortical level, and in the absence of a functional cortex, in the thalamus. Moreover, the pain threshold increases gradually during

life, i.e. fetuses are more vulnerable to pain than are neonates, which are more vulnerable to pain than adults. The assessment of the extent of discomfort a bovine fetus endures as a result of a bleeding procedure is hampered by the lack of oxygen in the fetus at the moment of bleeding. Lack of oxygen (anoxia), probably interferes with pain sensation. Moreover, cerebral anoxia is a common means of inducing unconsciousness in animals post-partum. The resistance of a mammal fetus to lack of oxygen increases with decreasing gestational age. As there are too many variables which influence the fetal physiologic state (e.g. maternal pre-slaughter stress, effects of hypoxia like redistribution of blood flows to the brain (brain stem), heart (myocardium), and adrenals (catecholamine production), maturity at the moment of bleeding) it is not possible to explicitly quantify the amount of discomfort in the fetus associated with a bleeding procedure. Altogether, considering the high severity in adults of exsanguination in itself, and a cardiac puncture in itself, it is stated that it cannot be excluded that a bovine fetus of the appropriate gestational age ((3-4 months), used for FBS harvest by means of cardiac or umbilical cord puncture, experiences low, moderate, or (very) severe pain or suffering from the bleeding procedure. Therefore, it may be suggested to destruct the fetal brain prior to the performance of a cardiac or umbilical cord puncture by means of a penetrative captive bolt, what can be considered a form of euthanasia.

However, a bovine fetus is currently never exposed to any technique rendering it insensible to noxious stimuli prior to bleeding. It remains to be seen if this will happen in the short future. Thus, an ethical problem exists which is related to the use of FBS. The fact that the fetus may endure pain or suffering from a bleeding technique affects the niche which in vitro techniques currently occupy as an alternative in animal experimentation. Additionally, many cells, tissues or organs cultured in vitro for research or production purposes are derived from animals which were killed for the purpose of obtaining these materials. Animals which are killed for the purpose of obtaining their cells, tissues or organs are considered experimental animals according to animal experimentation legislation in many countries.

The ethical problem related to FBS is not the only concern related to its use for the culturing of cells, tissues or organs in vitro. Worries over its costs, availability, quality (contamination, support of cell growth), imprecise molecular composition (batch-to-batch variation) and ethical quality stimulate the search for methods to culture cells without FBS. A final concern might involve the malpractices reported in FBS trade. The consumer may be saddled with a product which is not of the geographical origin he desired (e.g. there seems to be more 'New Zealand' labelled FBS available than is harvested there). Other (incidental?) malpractices include the diluting of New Zealand FBS with FBS from a cheaper geographical origin, and supplying FBS from countries which do not have facilities in which FBS is harvested (including Finland, the UK, the Republic of Ireland, The Netherlands, Denmark, Switzerland, and part of the French-originating FBS). The true geographical origins of these sera have a less favourable bovine disease status than e.g. Finland. The disease status of the geographical origin determines the price of the serum for the consumer. Selling a product as being of a geographical origin it is not of is, an offence of Dutch Law.

Cells, tissues or organs can be cultured in vitro in the absence of FBS. However, the cell type(s) concerned determine the optimum serum (substitute) and concentration. Substitutes for FBS include synthetic media (cell type specific), and reduced-serum media (broader applicability than synthetic media). Fetal horse and fetal pig serum cannot be considered FBS alternatives on ethical grounds, as they are also usually harvested by cardiac puncture. Otherwise, cells can be cultured in the presence of culture medium containing sera from new-born calves (NCS), donor livestock, and sera obtained at slaughter from non-donor animals. Finally, cells can be cultured properly in the presence of culture medium containing a specific fraction of bovine colostrum. The altered compositions of FBS substitutes may influence cell characteristics, and suggests that certain in vitro experiments would have to be re-done after having switched to an FBS substitute. From an ethical point of view, the use of NCS is not recommendable as a substitute for FBS. New Zealand NCS is ethically disputable because of the adverse side effects for both calf and mother animal related to induction of

parturition. Mishandling of new-born calves has been reported from Mexico, Hungary and Brazil. Concerns over this issue remain. Therewith, the use of NCS as a substitute for FBS does not seem recommendable, unless beyond doubt from a geographical origin where proper new-born calf treatment would be assured (e.g. Canada, or Australia). The Severity Index values for the procedures of blood harvest are the lowest for sera obtained from donor animals, sera from non-donor livestock obtained at slaughter (not induced calves), and single blood harvest of new-borns (not induced calves). Note that post natal vertebrates used for blood harvesting usually come under animal experimentation legislation.

Vertebrate fetuses used for experiments c.q. procedures are only subject to relevant protective legislative measures in New Zealand (the 2nd and 3rd trimester of gestation) the United Kingdom (the 2nd half of gestation), and Australia (not defined). South Africa does not yet have protective legislative measures for the protection of animals used for scientific procedures, but a specially designed guideline has been adopted by many institutes. This code also protects vertebrate fetuses (not defined). In those countries, FBS harvest by cardiac puncture or umbilical cord puncture would be considered a procedure. It may be worth noting that authorities and the serum industry of those countries which do protect mammal fetuses in their legislation on the use of animals for scientific procedures, all stated that the fetus is dead c.q. that the fetal heart is not functioning anymore at the time of cardiac puncture.

Altogether, the use of livestock sera does not free the consumer of ethical considerations. The weighing of an in vitro experiment requiring blood serum might be suggested (e.g. human interest vs. animal discomfort from bleeding).