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Review

Sustainability of Pork Production with Immunocastration in Europe

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Abstract: Immunocastration, a technique to replace surgical castration of piglets, consists of two consecutive vaccinations to induce antibodies which transiently suppress testicular functions and avoid boar taint. It is a method to ensure both a high product quality and a high level of animal welfare. The impact of immunocastration on the three pillars of sustainability has been studied extensively. While all aspects of sustainability have been studied separately, however, a contemporary global overview of different aspects is missing. In immunocastrates, performance results are better than in barrows, but worse than in boars. The environmental impact of pork production with immunocastrates is lower than with barrows, but higher than with boars. The level of aggression is considerably lower in immunocastrates compared to boars. Societal concerns are mainly related to food safety, and are not supported by scientific evidence. After second vaccination, immunocastrates switch from a boar- to a barrow-like status. Therefore, the timing of second vaccination is a fine-tuning tool to balance advantages of boars with environmental and economic benefits against increased risk of welfare problems and boar taint. Nevertheless, both synergic and conflicting relationships between the pillars of sustainability must be communicated along the value chain to produce tailored pork products.

Keywords: sustainability; immunocastration; carbon footprint; animal welfare; food safety; pork production; boars; surgical castration

1. Introduction: The Castration Dilemma in Pork Production

In Europe, many citizens are concerned about the impact of intensive production conditions of farm animals on animal welfare and the environment [1–3]. A critical evaluation of the aspects which cause public disapproval is necessary and sustainable improvements have to be introduced, where negative conditions can be avoided. A main problem is that conflicting aims may occur which must be balanced with different market needs as well as stakeholder requirements [4]. Such a situation currently applies in Europe in the debate about castration of male piglets [5–7]. Surgical castration is painful and hurts the animals' integrity, it is therefore a major welfare issue [6]. For centuries, male piglets designated for pork production have been surgically castrated in Europe to improve behavior and product quality [5,8–10]. The fattening of boars has advantages such as requiring fewer resources to produce the same amount of meat due to more efficient feed conversion ratio, reduced nitrogen excretion, and a higher protein accretion compared to barrows and gilts. However, disadvantages in pork production with boars remain, including boar taint and welfare problems due to increased aggression and mounting behavior. Those may limit the acceptance of pork production with boars by farmers, the meat industry and consumers [9,11–13]. In boars, a sex-specific off-odor of the carcass may develop in some growing boars during puberty, which can be mainly ascribed to two substances, androstenone and skatole. Androstenone is a male pheromone which is formed in the Leydig cells of the testes and has a urine-like smell [12,13]. Skatole is a metabolite of the amino acid tryptophan with a fecal odor and is synthesized in the colon by microbial degradation [14]. Boars may accumulate more skatole than barrows or gilts in adipose tissue because the hepatic degradation of skatole is reduced, due to lower activities of CYP2E1 and CYP2A enzymes if concentrations of androstenone or testosterone are high [15]. A cross-national European study by Walstra and co-authors [16] showed that while 29% of the carcasses reveal high androstenone concentrations, only 11% show elevated skatole concentrations and that slaughter weight and genotype modify this percentage considerably (high androstenone level: range 18–42%, high skatole level: range 5–23%). Androstenone and skatole are perceived differently by consumers depending on individual sensitivity. Whereas most consumers are sensitive to skatole [17], Lunde and co-authors [18] described a specific anosmia for androstenone, which explains the variable percentage of consumers perceiving androstenone. Both compounds share the disadvantage that consumers who are sensitive to the substances rate them as very unpleasant and may therefore reject pork from boars more often [19,20]. In addition, aggressive and sexual behavior of boars may lead to animal welfare problems such as leg weakness or penile injuries [11,21].

Growth is the result of a predominance of anabolic over catabolic metabolic processes. In pigs, it is orchestrated by the activity of sex-independent anabolic hormones such as growth hormone and IGF-I, and of catabolic hormones such as glucocorticoids. Gonadal hormones in boars already interact during the fattening period, with the endocrine regulation of growth by decreasing catabolic processes (e.g., androgens) or increasing anabolic processes (e.g., estrogens via stimulatory action on IGF-I secretion). This leads to more efficient growth, increased nitrogen retention and higher protein accretion rate when compared to barrows [22]. Both androgens and estrogens also decrease the voluntary feed intake and improve the feed conversion ratio, explaining the known differences between barrows, gilts, and boars [12]. Taken together, all those factors lead to higher muscle and lower fat deposition. Thus, boars have a higher lean meat content than barrows [23]. Moreover, boars have a higher concentration of polyunsaturated fatty acids (PUFA) in adipose tissue, which may be healthier for human consumption but is regarded as a problem for processed meat products [24,25]. Therefore, boars are more efficient in the fattening period but create problems in terms of product quality and animal welfare [9,11,21,26,27].

Surgical castration is effective in preventing those problems, but also removes the anabolic advantage of boars [12]. In most European countries, surgical castration of male piglets without anesthesia or analgesia is still permitted within the first seven days of life [28]. Usually, farmers castrate male piglets without any pain-relieving methods [29–31]. Already in October 2010, representatives of major stakeholders committed themselves to a roadmap to voluntarily end surgical castration of male pigs in Europe by 1 January 2018 [32]. Despite this commitment, about 63% of all male piglets in Europe were still surgically castrated in 2017, most of them without any pain relieving methods or anesthesia even though alternatives exist [30]. Today, these figures have not changed considerably in Europe.

Immunocastration is an active immunization against GnRH [33] and could be a sustainable alternative to solve the above-mentioned problems of pork production with boars and surgical castrates, and thus could make European pork production more competitive. In contrast to other parts of the world such as Australia and Brazil [10], immunocastration in Europe is not frequently used, with a low percentage of 2.8% in 2017 [30]. Little practical experience of stakeholders and no targeted communication about the consequences of immunocastration [34] of European pig genotypes for management, feed requirements, and product quality exist in the market. These knowledge gaps may explain why a method that might have economic, ecological, and societal advantages still has no market relevance at the moment. Market acceptance could be increased, if the sustainability of immunocastration is scientifically demonstrated. In order to evaluate immunocastration from a sustainability point of view, this review examines factors which are part of the three pillars of sustainability (society, economy, and environment) and how their interactions can lead to both synergic and conflicting relationships within the three pillars.

2. The Principle of Immunocastration

Immunocastration is an active immunization against GnRH, a key hormone of the endocrine cascade regulating reproductive functions. In consequence, the pig's immune system starts the production of antibodies against the hypothalamic hormone GnRH and postpones the pubertal development by suppressing the hypothalamic pituitary gonadal axis [33]. The treatment consists of at least two injections of the vaccine Improvac® during the fattening period. The manufacturer recommends vaccinations at an age of about 12 weeks and again at 4–6 weeks before slaughter. Within a time interval of at least 4 weeks between the first and second vaccination [10]. After the first application of Improvac®, some GnRH antibodies are already formed but their concentration is not sufficient to limit gonadal axis activity [35]. Within one week after the second vaccination, the production of GnRH antibodies increases markedly and suppresses testicular steroid synthesis and in consequence spermatogenesis [36,37]. The drop in testosterone and estradiol concentrations occurs within a week, followed by a reduction in IGF-I secretion [36]. Due to the lack of testosterone in the hormonal feedback system, both immunocastration and surgical castration initially increase the release of GnRH by the hypothalamus but lead to a reduced GnRH synthesis in the hypothalamus further on [38]. In Europe, only one product (Improvac®) is available to date for immunocastration of male pigs. The vaccine is manufactured by Zoetis (formerly Pfizer Ltd., formerly CSL Limited, Parkville, Victoria, Australia) and has been approved by the European Commission in May 2009 for use in pigs within the European Union [39]. Due to the strong interlinked regulation of boar taint compounds and testicular hormones, immunocastration always affects their formation in a similar way [40]. Thus, the only way to maintain the anabolic advantage of boars is the appropriate timing of the antibody formation leading to a tailored cessation of the testicular steroid synthesis. This avoids the accumulation of boar taint till slaughter, although the anabolic effects of testicular hormones are still maintained during the main part of the fattening period [10]. At the same time, male aggressive and sexual behavior can also be reduced as described in Section 3.3. Active immunization against GnRH was already discussed in the 1970s as a potential means by which the reproductive system of mammals might be shut down for various practical and clinical reasons [33]. In 1998, a patent (International application number: PCT/AU1998/000532) has been submitted and was published under the international publication number WO 1999/002180 (21 January 1999; Pfizer Inc. New York, NY, USA). As GnRH itself has no immunogenic effect and does not stimulate antibody production, a proprietary strategy must be used to deceive the immune system and recognize GnRH as an antigen [33]. This strategy includes the use of GnRH or a modified GnRH (truncated or repeated, with or without amino acid substitution) as antigenic target linked to a carrier substance [41]. Antigens which are conjugated through its C terminus seem to produce a higher specific antibody response than constructs in which GnRH is conjugated through its N terminus [42]. In case of Improvac®, the antigenic part of the construct is the C-terminal fragment of GnRH (AS 2–10) conjugated to a diphtheria toxoid and adsorbed to DEAE-dextran (Patent US 8741.303 B2; 3 June 2014; McNamara).

3. Potential of Immunocastration for Sustainable Pork Production

3.1. On-Farm Application of Immunocastration

Even if the first vaccination could be applied at 8–9 weeks of age [10], such an early vaccination may not be recommended if piglets are sold and not raised on the same farm where they have been born, as the vaccination cannot be controlled afterwards and a 100% vaccination rate is required to avoid behavioral and quality problems. As a consequence, the first vaccination is usually carried out early in the fattening period at an age of about 12 weeks. The endocrine changes induced by the second vaccination lead to a switch from boar-specific feed intake, metabolism, and behavior to that of barrows with a further delay of about one week as described in Sections 3.3, 3.6 and 3.7 below. The recommended time between the second vaccination and slaughter is about 4 to 5 weeks to allow the release of already accumulated androstenone and skatole from adipose tissue. Even if long-term studies revealed a resumption of testicular function after 10 to 24 weeks [43,44], a third vaccination is only suggested if animals are slaughtered at a higher age [45].

Several studies have been conducted to evaluate the effect of a variation in the timing of the second vaccination. As further described below, the decision has to be balanced between the conflicting aims of desirable boar-like growth efficiency, lean meat content, and the superiority of barrows in behavior, as well as the quality of adipose tissue and meat. Such differences are obvious in the meta-analysis of Nautrup and co-authors [46] who compared immunocastrates vaccinated for the second time more and less than 4.5 weeks before slaughter. The animals vaccinated later were more boar-like in their growth and carcass characteristics than the immunocastrates vaccinated more than 4.5 weeks before slaughter. Whereas, in some studies, the vaccination protocol of first vaccination/second vaccination at 10/14 and 16/20 weeks of age or 11/21 and 11/18 weeks of age did not lead to significant differences in growth performance and carcass composition [47,48], differences in dressing percentage [47], carcass yield [49], and welfare problems [50] were reported. The early vaccination protocol, however, was not recommended with regard to boar taint [50].

3.2. *Reliability of Immunocastration*

An important criterion for being successful in the market is the reliability and efficacy of the method. Several reviews have described the phenomenon of non-responders [8,10,51]. As with all vaccines, a small percentage of animals will not or will just poorly respond to the vaccine for both disease vaccines and Improvac® vaccination protocols with a two-fold application of the vaccine increase the effectiveness and may provide almost 100% efficacy [52]. It is assumed that on average 0–3% of the Improvac®-vaccinated animals were non-responders [10]. The rate and definition of non-responders, however, varies between studies and depends on the criteria investigated. Thus, non-responders were defined as animals with enlarged testes (similar to the testes size of boars) or with boar taint (above the threshold of 0.5–1 ppm androstenone), despite two assumed vaccinations. Reasons given for non-responding include that these animals might have been accidentally missed during vaccination or might have had a suppressed immune system due to health problems or stress at the time of vaccination. It has to be kept in mind that only healthy animals are suitable for vaccinations. In a study by Sødring and Naadland [53], about 1% of all immunocastrates slaughtered in Norway in 2017 were tested for boar taint as the success of vaccination seemed doubtful due to the size of their testes. 29% of these suspicious animals had androstenone values above 1 ppm and were classified as non-responders. A recent study by Kress and co-authors [35] hypothesized that a stressful unstable social environment could reduce the chance of adequate immunization. Even under intensive housing conditions and additional stress before and after the vaccinations, however, all immunocastrates showed a sufficient immune reaction with high GnRH antibody titers and low testicular steroid production. Similarly, the meta-analyses by Batorek-Lukač and co-authors [23] and Nautrup and co-authors [46] show that immunocastration prevents boar taint effectively and is a reliable method. It seems that if the vaccine is handled and stored correctly, and if the manufacturer's vaccination recommendations are met, almost 100% of the vaccinated animals produce sufficient antibodies and react accordingly [35]. This, however, does not rule out that occasionally insufficient immunizations occur under practical conditions, e.g., if animals are vaccinated only once by accident. As such animals have no higher risk for high boar taint levels than boars, it remains a corporate risk decision of the slaughter house, whether or not to test for boar taint at the slaughter line. With an assumed proportion of 3% non-responders [10] and a tainted carcasses rate of 30% among boars [16], the risk of tainted carcasses in immunocastrates is 0.9%. Assuming a reproducibility of the currently used human nose test at slaughter line to detect boar taint of 23% [54], the risk of marketing tainted carcasses of immunocastrates is far below the currently marketed carcasses of boars with off-odor.

3.3. Consequences of Immunocastration for Animal Welfare, Behavior, and Health in Pork Production

A major benefit of immunocastration is an increase in **animal welfare** by preventing painful surgical castration and the risk of wound infection in piglets. The study by Morales and co-authors [55] shows that the piglet mortality during the first week post-partum is higher in surgically castrated piglets than in intact piglets (6.3% vs. 3.6%). Especially piglets with a low or medium live weight at birth have a significantly higher mortality rate than uncastrated piglets (low:12.2% vs. 6.2%; $p < 0.05$, medium 5.5% vs. 2.7%; $p < 0.05$).

Even with immunocastration, pigs have to be treated by humans. However, immunocastration is carried out later in life during the fattening stage and farmers are given a longer time span to apply the vaccination [56]. Mimicking the injection procedure of Improvac®, McGlone, and co-authors [57] investigated the effects of intramuscular or subcutaneous injection of 1 mL of saline on pain and stress in finishing pigs. In general, no significant changes in activity behavior (such as lying, eating, walking, drinking) and physiology (cortisol concentrations) were noted 1 h after the injections. Thus, injection per se does not affect welfare, although the injection of Improvac® may cause a skin reaction in a small number of cases. While there were no visible site reactions at slaughter, some reactions could be detected by palpation in 6.25% of immunocastrates [58]. Compared to surgical castration, such rather local reactions may trigger minor discomfort in immunocastrates. Moreover, such adverse reactions can be avoided if the vaccine is applied according to the manufacturer's recommendations (subcutaneous injections at the base of the ear) by trained persons. As with all vaccinations, a severe allergic reaction may happen on extremely rare occasions (1.31 per million vaccine doses) within a few minutes of vaccination [59]. Immunocastration is also effective in cryptorchids and avoids the more sophisticated surgical procedure or the even higher risk of boar taint, if the animals are untreated [60].

If the second vaccination is fully effective, immunocastrates show differences in **social behavior**, e.g., less aggression and mounting than boars, and are very similar to barrows demonstrated that the effect of immunocastration on behavior can prevail for a long time [61–65]. Even 16 or 22 weeks after the second vaccination, significant behavioral differences in social, manipulating, and aggressive behavior exist between immunocastrates and boars. On the other hand, the change in behavior appears relatively soon after second vaccination as described above (see Section 3.1) Thus, pigs that received their second vaccination only 1 week before behavioral observation did not differ from those who received Improvac® injection 3 weeks before observation [66]. It can therefore be concluded that the beneficial effects of immunocastration on behavior cover a relatively long time span from (at least) 1 week after second injection well until slaughter. Guay and co-authors [67] investigated the effect of immunocastration on human-pig interactions and handling during transport. There were only a few differences, e.g., more chewing and rubbing on the test person's pants and boots in immunocastrates compared to barrows. Other measures, such as the total time of approaching people did not differ between the two groups. Most studies on immunocastration have been conducted under experimentally controlled conditions, but some studies were also performed on commercial farms. The results obtained under field conditions resemble the experimental farm findings in showing that fighting and mounting is substantially reduced in immunocastrates compared to boars [62,68].

Such aggressive and sexual behavior is relevant for animal welfare, as it may also lead to **health** problems (e.g., scratches and wounding) in boars. In addition, mounting activity has led to lameness and skeletal problems for mounting and mounted animals in 15% of all boars [27]. In the study of Einarsson [58], scratches and lesions in the head region (assessed at slaughter) were highest in boars, much reduced in immunocastrates, and absent in barrows. Schmidt and co-authors [69] reported higher skin lesion scores in the shoulder region (caused by mounting behavior) in immunocastrates before second vaccination compared to barrows, which disappeared after second vaccination. Recent findings show that penile injuries are a major welfare problem in boars [21]. Before boars enter puberty, the penis frenulum prevents the penis from extruding. As soon as the boars enter puberty, they can completely extrude the penis. If a particular boar shows mounting behavior and extrudes its penis, it can trigger other pen mates to bite its penis. This phenomenon occurs both in domestic and wild boars and causes obvious animal welfare problems [21,26]. Immunocastration can reduce the incidence of penile injuries and the risk of severe injuries but does not completely prevent this problem. The vaccination protocol also affects the percentage of immunocastrates with penile injuries: the percentage is low (16.7%) if animals are vaccinated early, and increases up to 41.7% if animals are vaccinated late [50]. A recent study by Kress and co-authors [35] suggests a reduction in aggressive behavior and in penile injuries in immunocastrates compared to boars regardless of their housing environment (stressful, conventional, outdoor access). Another question which requires a lot more research is the application of immunocastration to mature boars. The findings of Bilskis and co-authors [70] reveal that testosterone and libido (characterized by pre-mating behavior) of mature boars (>2 years) can be reduced by immunocastration.

In a study by Cronin and co-authors [61], **feeding behavior** was also determined. At an age of 21 weeks, boars spent much less time in the feeders than immunocastrates and barrows. Weiler and co-authors [71] investigated this effect in more detail. Feed intake of boars was lower than in barrows and immunocastrates due to a reduction of number and duration of meals consumed per day. Immunocastration affected feed intake behavior with meal size increasing by 25%. Considerable increases in feeding behavior at least one week after second vaccination were also observed by Schmidt and co-authors [69] and Van den Broeke and co-authors [72]. Restrictive feeding of immunocastrates after second vaccination can lead to more aggressive behavior and higher incidences of skin lesions, comparable to the level among boars [73]. It is therefore recommended not to feed immunocastrates restrictively during the late finishing period.

3.4. Consequences of Immunocastration for Growth Performance, Carcass, and Meat Quality

Immunocastrates change their anabolic potential from that of boars to that of barrows after the second vaccination [10,33,36,74]. Before second vaccination, immunocastrates have a lower average daily gain and a more favorable feed conversion ratio than barrows, up to the second vaccination [23]. As a consequence, the higher boar-specific anabolic potential and the reduced feed intake can be exploited until the second vaccination as reviewed in detail by several authors, e.g., [23,46,75]. After the second vaccination, feed intake of immunocastrates increases significantly [23,71,72] but compared to barrows, they grow still more efficiently [23]. A recent meta-analysis by Nautrup and co-authors [46] including 78 studies showed that, over the entire fattening period, immunocastrates have higher average daily gains than boars and barrows, whereas their feed conversion ratio is intermediate between barrows and boars.

In most of the studies with a fixed duration of fattening, hot carcass weights also differ. Hot carcass weights of immunocastrates are lower than those of barrows, but higher than those of boars [46]. In terms of dressing percentage, boars are inferior to barrows mainly due to higher weights of the genital tract. The dressing percentage of immunocastrates is even poorer due to a higher volume of the gastrointestinal tract [75]. In terms of lean meat content of the carcass, boars are superior to immunocastrates, which have a higher backfat thickness. Compared to barrows, however, the carcasses of immunocastrates are leaner [23]. Regarding the valuable parts of the carcass, immunocastrates have heavier shoulders and hams than barrows, but lighter bellies. Compared to boars, the carcass traits of immunocastrates are quite similar, but the bellies are heavier [23,46]. In total, the carcass yields of immunocastrates are more favorable than those of boars as well as barrows.

The meat quality of immunocastrates is similar to that of barrows. Both have higher levels of intramuscular fat and lower shear force values than boars [23]. Furthermore, the accumulation of boar taint in adipose tissue is significantly reduced by immunocastration [23,46]. The fatty acids composition of immunocastrates is also comparable to that of barrows and has less PUFAs than boars, which is particularly important in the production of dry-cured products [10]. The meta study of Nautrup co-authors [46] and the review of Čandek-Potokar and co-authors [10] both confirm these findings and suggest that the timing of the second vaccination allows for a product quality tailored to the demands of different pork markets.

3.5. Suitability of Immunocastration for Alternative and High Quality Production Systems

Immunocastration is mainly used in the production of male animals for standard conventional pork products [56]. Nonetheless, the methodology can be used for alternative production systems. In the production of traditional high quality pork products such as dry-cured hams and shoulders, animals are slaughtered at higher live weights [10,45]. In Iberian high quality production systems, boars and gilts are castrated surgically either to prevent boar taint or undesirable performance losses in female animals during estrus [76], or in extensive free-ranging housing systems in order to prevent unwanted pregnancies during fattening [77,78]. However, castration of females jeopardizes animal welfare and increases production costs and infection risks [76,79]. For traditional products, immunocastration is a good alternative to surgical castration or fattening of entire boars or gilts, as neither performance nor product quality are negatively influenced [45,77,80–82]. In a study by Pinna and co-authors [45] with heavy pigs (165 kg live weight) produced for Parma ham, three vaccinations were recommended to prevent boar taint reliably.

Immunocastration could also have positive effects on organic pig production: In a study by Grela and co-authors [83] boars, immunocastrates, barrows, and gilts were fattened under organic conditions. Growth performance as well as feed conversion ratio and lean meat content were more efficient in immunocastrates and boars than in barrows or gilts. Immunocastration was evaluated most favorably both from production and meat quality perspectives. Immunocastration can be considered as a suitable method for organic pig farming. As mentioned above, organic production systems should also take into account that, for longer fattening periods, animals should be vaccinated a third time in order to reliably prevent boar taint. Looking at the Council Regulation on organic production and labelling of organic products [84] at the European level it remains unclear how immunocastration is classified. According to the European veterinarian code, Improvac® is classified in a subgroup of hormone-like substances [85] and according to the EU Council Regulation mentioned above, no hormone-like substances may be used in organic pork production (EC no. 834/2007). From a scientific point of view, immunocastration is not a hormone application at all, so the EU leaves the decision of whether immunocastration is permitted on a national level or not to the EU-members.

In a study by Bilskis and co-authors [70] the efficacy of immunocastration was tested in cull boars from artificial insemination (AI) programs. It showed that even in mature boars (>2 years), testosterone levels decreased significantly after the third vaccination to a level found in young immunocastrates. In a further study with AI boars by Oliviero and co-authors [86], it was also shown that a single dose of Improvac® has no negative effect on the fertility of young AI boars. Immunocastration thus allows to use boars for AI services and to prevent boar taint in case of culling by a second vaccination. Such boars can be sold and used for meat products similarly to sows. Immunocastration provides possibilities for alternative production systems to maintain added value by higher animal welfare standards while at the same time delivering high quality products, thus bringing together the two formerly conflicting aims.

3.6. Consequences of Immunocastration for Feeding Requirements

Before the second vaccination, a sufficient amino acid provision is required to support the high protein deposition levels in boars. Thereafter, animals change their metabolism within two weeks [87,88] as described in Section 3.1. In contrast to the increased fat deposition after second vaccination [23,89], the protein deposition seems to remain nearly constant [90]. However, because of the increased feed intake after the second vaccination as described in Section 3.3, the feed intake can be limited or the amount of protein per kg of feed, to limit the increase in nitrogen emission. Quantitative restriction of feed intake has been shown to limit protein deposition in immunocastrates [91] but triggers behavioral problems as described in Section 3.3. Utilization of dietary fibers to dilute protein and energy, on the other hand, does not satisfactorily decrease the intake of protein and amino acid in immunocastrates [92]. Alternatively, protein and amino acid to energy ratios can be decreased rapidly from the second vaccination onwards in order to limit the excess in protein and amino acid intake. Studies have therefore proposed to decrease the dietary lysine to energy ratio by 20–35% [89,93], but this second option largely depends on the level of feed intake [91]. Moreover, the way animals use dietary energy affects the efficiency of energy utilization as described below in Section 3.7. Labussière and co-authors [94] showed that five weeks after the second vaccination, immunocastrates exhibit a lower basal heat production (783 vs. 856 kJ/kg BW $^{0.60/\text{day}}$) than boars but an increased heat increment (25.6 vs. 21.6% of ME) when animals were fed the same diet. The difference in basal metabolism can be directly linked to the level of testosterone and anabolic hormones. The difference in energetic efficiency is indicative of the utilization of dietary protein as an energy source for ATP provision and lipid deposition [90], which is less efficient than the utilization of carbohydrates and lipids for such purposes [95]. Most of the time, feeding recommendations are nevertheless supported by measurements in animals in a steady state, e.g., before the second vaccination, or when the transition phase has finished. It has also been shown that modified feeding behavior following the second vaccination [71] is associated with modified glucose metabolism [96,97], which may affect energy efficiency. Because discrepancies between animals in their transition from boar to barrow status may occur, the kinetics in metabolism changes should be considered carefully because of the large variations in speed of feed intake increase between animals or groups of animals [71].

3.7. Consequences of Immunocastration for the Environmental Burden

While pork is of high nutritive value, the pig's omnivorous nature and the way it is fed nowadays negatively affects the perception of pork because of environmental concerns. Major points that influence this perception include the consumption of edible proteins for humans, the global warming potential of meat production, and the excretion of nutrients (most important nitrogen and phosphorus) leading to water eutrophication and soil acidification [98]. Diet composition is an important factor here. Today, pigs are most often fed cereals, legumes, and by-products from the cereal and oil food industry [99]. With the selection towards higher efficiencies, the environmental burden per kg of pork has diminished [100]. Key driver is feed conversion ratio. A study by Reckmann and Krieter [101] showed that feed conversion ratio was the performance parameter in finishing that had the largest impact on global warming, eutrophication, and acidification potential. In the same study, increased lean meat percentage was also linked with decreased environmental impact, although partially because of the link with improved feed conversion ratio. The functional unit of expressing the environmental impact—per pig place, per kg of pig, per kg of carcass, or per kg of meat and the time period included (life cycle assessment or fattening period)—may also affect the interpretation [98,100,102]. In boars, with no pharmaceutical products used for castration, while the feed conversion ratio is low, lean meat percentage is high and carcass yield better than in immunocastrates [23,75,103]. Expressed per kg of pig, carcass or meat, this type of male pig raising is therefore expected to be most environmentally friendly. Hence, boars are compared to different scenarios for pork production the most environmental friendly one [99]. Still, the estimated impact may differ between farms and management strategies and the assumptions made. In a study by Bandekar and co-authors [102], it was concluded that boars had a slightly higher global warming potential than the baseline scenario with barrows. However, they compared slaughtering male pigs at a low slaughter weight (91 kg) with keeping barrows until 125 kg and using ractopamine in barrows. So their model assumed only small differences in feed efficiency despite the lower slaughter weight in boars. This result may not be valid in Europe, where ractopamine is not used and where boars and barrows are slaughtered at a similar weight, but with a larger difference in feed efficiency than assumed by Bandekar and co-authors [102].

An improved environmental impact may be expected with immunocastrates versus barrows, at least per kg of pig due to differences in performance [75]. Indeed, the carbon footprint of a pigs' feed intake was significantly higher in barrows compared to boars and immunocastrates, with intermediate results for gilts [104]. Nitrogen efficiency was also higher in immunocastrates than in barrows and slightly lower than in boars [105]. Immunocastration is therefore considered to lessen the environmental impact of pork compared to barrow production [102,106,107]. Comparing barrows receiving ractopamine throughout finishing with immunocastrates receiving ractopamine after second vaccination, Bandekar and co-authors [102] estimated a reduction of 2.39%, 2.57%, and 2.96% in global warming potential, energy use and water use per kg pig, respectively. As the dressing percentage in immunocastrates is somewhat lower than in boars and barrows [23,75,103], the difference between barrows and immunocastrates in environmental impact per kg of carcass may be less pronounced. On the other hand, the lean meat percentage is higher in boars and immunocastrates than in barrows. Thus, also per kg of meat, immunocastrates can be expected to have a lower impact than barrows. This was confirmed by the study of De Moraes and co-authors [107], who calculated a 3.7% improvement of global warming potential per kg live weight and of 5.0% per kg of meat in immunocastrates versus barrows.

Apart from the differences in performance and hence the amount of feed consumed, the environmental cost of the product for vaccinating pigs also needs to be taken into account. In a study carried out by the manufacturer of Improvac® and an independent consulting firm [107], the calculated contribution of the product manufacturing accounted for 0.01% of the global warming potential, compared to 36% assigned to the feed consumed and 30% to the slurry management. In barrows, there is increasing pressure for using analgesics and anesthetics during castration. Isoflurane, currently used in some European countries for castration under anesthesia, is a potent greenhouse gas. Environmental burden by the use of isoflurane or others anesthetic drugs has to be considered in the assessment of environmental sustainably [108].

One shortcoming in most studies comparing different types of male pig production is that they often do not correct for altered nutrient requirements and thus for possibly different diets in these different production systems. Compared to boars, barrows have lower amino acid requirements. Hence, barrow diets may contain less soybean meal than boar diets. While their feed conversion ratio is worse, the environmental impact per kg of feed consumed by barrows may be lower than in boars. A classic reductionist approach may overestimate the difference in environmental impact. Similarly, the finishing diet of immunocastrates may be optimized to minimize their environmental impact. It needs to be taken into account that male pigs are only half of the pigs born on a farm. On individual farm level, the effect may depend on whether male and female pigs are raised and fed together or separate as described above (Section 3.6). While ceasing the castration of piglets may improve the environmental sustainability of pork production, this will only happen with optimal management and especially feeding. Key principles such as precision feeding, the use of enzymes such as phytase to increase nutrient digestibility, and the application of free amino acids to reduce total crude protein content may have a more pronounced effect than that achieved by just the castration decision. Further insights in the sustainable feeding of pigs, in particular immunocastrates, are therefore crucial.

3.8. Consequences of Immunocastration for Economy

Immunocastration is highly controversial in international pork markets and globally rarely used in practice. There are however some international differences, while some countries reject the method completely [10,30], in other countries such as Brazil and Australia, immunocastration is already widely used with more than 50% of all male pigs vaccinated [10,34,109]. Based on a press release by Zoetis in June 2018, more than 2.5 million doses of the vaccine Improvac® are sold each month worldwide [110]. This means that with an average of two vaccinations per animal, about 15 million immunocastrates are produced annually. In 2018, 1.27 billion pigs were slaughtered globally [111]. Assuming that half of the slaughtered pigs are male, 634.6 million of male pigs were slaughtered in 2018. The global proportion of immunocastrates is then about 2.36%. Within three years, both the absolute number and the proportion of immunocastrates have doubled worldwide between 2015 and 2018 [8,110,111].

The cost per dose of Improvac® range between 1.4 € and 1.5 € [112]. With two vaccinations plus labor costs (45–50 s for both vaccinations per pig), the additional expenses amount to 3–4 € per pig [113,114]. Decreasing costs are likely, as depending on the size of the farm-larger purchasing volumes may lead to discounts which create economies of scale. Additionally, it is possible that generic pharmaceuticals or other vaccines may increase the cost competition of suppliers, further reducing vaccination costs per animal. At present, only one product for pigs is available on the European market (Improvac®), and the manufacturer has a monopoly in this segment. A review of Vondeling and co-authors [115] shows that pharmaceutical prices fall by 6.6–66% after patents expire. A recent study by Verhaagh and Deblitz [114] even estimated price reduction at 55%, based on historical discounts after patent expiration. This could further increase the economic profitability of immunocastration. Along the pork supply chain, additional costs may arise from factors such as specialization of production systems, special sorting of immunocastrated animals or carcasses, removing the testes, boar taint detection, or rejected carcasses due to boar taint. As described above (Section 3.2), the risk of immunocastrates for displaying boar taint is very low. This explains why many economic studies do not consider the cost of boar taint detection at slaughter line in their research [113,116]. In addition, the economic efficiency of pork production systems with immunocastrates is influenced by the pricing scheme that is applied. An analysis by Niemi and co-authors [116] shows that additional costs of 1 € per metric ton of pork arise if immunocastrates are sold according to the boar pricing scheme. If the production systems adapt and immunocastrates are sold similar to barrows, a value added of € 21 per metric ton pork arises. Irrespective of these aspects, the studies by de Roest and co-authors [113] and Verhaagh and Deblitz [114] show increased production costs of immunocastrates on farm level due to vaccination costs, labor costs, and feed costs. On average, these additional production costs are compensated by higher revenues due to higher performance resulting in more pigs produced per place and year. As a consequence, immunocastrates represent a viable alternative for European pig producers.

Even though immunocastration could be very beneficial in terms of animal welfare, product quality, environment, and production efficiency, market shares of immunocastrated male pigs are very low in Europe as shown in Table 1. Despite the fact that European stakeholders aimed to end surgical castration by 2018 [32], there is still no common political strategy recognized within the pork chain. European pork markets are too diverse [30] and in addition to pork production with boars (see Table 1), each nation develops more or less efficient implementation strategies (see Table 2).

Table 1. Population shares of male pigs raised as boars, immunocastrates or barrows in Europe (2017), ranked according to size of pig population [30].

Country	Boars (%)	Immunocastrates (%)	Barrows (%)	Pig Population (×1000)
Germany	20	<1	80	28,046
Spain	80	5	15	25,495
Denmark	<2	0	>97	12,402
Netherlands	65	0	35	12,013
France	22	<0.1	78	11,835
Italy	2	5	93	8561
Belgium	8	15	80	6351
Romania	0	5	95	5180
UK	98	<1	2	4383
Hungary	1	0	99	2935
Austria	5	0	95	2846
Portugal	85	2.5	12.5	2014
Norway	<1	6	94	1644
Switzerland	5	2.5	92.5	1573
Czech	5	5	90	1548
Ireland	100	0	0	1468
Sweden	1	9	90	1354
Finland	4	0	96	1258
Slovakia	0	10	90	637
Latvia	0	0	100	368
Estonia	0	0	100	359
Slovenia	1	0	99	288
Macedonia	0	0	100	200
Luxembourg	1	0	99	90
Iceland	0	0	99	36
Total	**34**	**2.8**	**63**	**132,884**

Table 2. National strategies to substitute surgical castration without pain reliving methods, according to the year of implementation [10,29,30,117].

Country	Year	Alternatives Implemented
Norway	2002	Local anesthesia (lidocaine) with analgesia (meloxicam)
Netherlands	2009	Surgical castration under anesthesia (CO_2) for export market
Germany	2009	End of surgical castration without anesthesia postponed until 2020. Meanwhile analgesia (meloxicam); anesthesia (esp. isoflurane) required only in some organic programs; immunocastration in some high-quality meat programs
Switzerland	2010	Anesthesia (isoflurane)
Denmark	2011/2019	Analgesia (meloxicam); from 2019 on, plus local anesthesia (procaine)
Belgium	2011	Surgical castration with analgesia (meloxicam) for export market; immunocastration domestic retail market
France	2013	Analgesia (meloxicam)
Sweden	2016	Local anesthesia (lidocaine) with analgesia (meloxicam); one smaller retailer prefers immunocastration
Austria	2017	Analgesia (meloxicam)

3.9. Societal Concerns and Immunocastration

Stakeholders' acceptance is crucial for a sustainable use of immunocastration in European pork markets. The perception of the procedure is very heterogeneous and varies between countries. Nations with a high proportion of boars in pork production do not discuss alternatives intensively. Countries where pork production is traditionally based on barrows and gilts have more difficulties abandoning surgical castration without anesthesia or analgesia, as pork production with boars is rejected and immunocastration hardly accepted [34]. Despite intensive animal welfare debates on surgical piglet castration, the study by Tuyttens and co-authors [118] show that pig producers prefer to continue surgical castration, as this seems to be the most efficient and reliable way to produce a high product quality. The studies by Tuyttens and co-authors [118] and Schübeler and Koch [119] point out that farmers are rather neutral about immunocastration and that their knowledge about the method is even lower than about other alternatives to piglet castration.

In a study by Aluwé and co-authors [120], farmers were asked for their attitude towards immunocastration before and after practical experience with this technique. It turned out that experience with immunocastration even had a negative effect on the attitude of farmers. Their main concerns were consumer acceptance, reliable prevention of boar taint, economic efficiency, and the risk of accidental self-injection. However, it cannot be excluded that the farmers gave a lower score because of high expectations prior to the trial. Similar results were obtained in the studies by Tuyttens and co-authors [118] and Schübeler and Koch [119]. A review by Mancini and co-authors [34] showed that the majority of consumers are unaware that male piglets are castrated surgically without anesthesia or analgesia. Furthermore, only a few consumers knew of immunocastration. Among consumers, attributes such as animal welfare, price, product quality and food safety are recognized. When making purchase decisions at the counter, these attributes are weighed and result in the acceptance or rejection of pork from immunocastrates. In terms of animal welfare and product quality, consumers rate immunocastration more positively than pork production with boars or barrows, but are more skeptical about food safety and prices. Thus, the results of consumer studies are unequivocal. A recent study by Di Pasquale and co-authors [121] shows that Italian consumers rate meat from immunocastrates more positively than meat from surgical castrates or entire males, with a low risk perception of immunocastration. This leads to a higher willingness to pay for products from immunocastrated male pigs. The provision of more extensive information on immunocastration had no effect on the decisions of consumers.

Immunocastration can also be an alternative for different production systems as described above. Consumers accept immunocastration for the production of Parma ham if animal welfare, product quality and consumer safety are guaranteed [122]. On the other hand, Heid and Hamm [123] show that German consumers are skeptical about immunocastration in organic pork production because they are worried about residues in meat. Fredriksen and co-authors [124] show that consumer concerns can be minimized by information programs from public authorities. Furthermore, some studies show that information material for target groups increases consumer acceptance of immunocastration—especially if audio-visual techniques are employed [118]. A study by Mörlein and Schübeler [125] investigated which wording should be used by staff at the meat counter to communicate with consumers about immunocastration. It turned out that quality-oriented facts were more important than technical information. For consumers who were more critical and very interested, however, further information material covering technical aspects should also be provided. Moreover, a variety of sensory studies show that pork from immunocastrates is preferred to pork from boars and was rated as similar or even better than pork from barrows [34,46]. A recent study by Čandek-Potokar and co-authors [126] shows that Slovenian consumers prefer pancetta from boars with low boar taint levels to pancetta from immunocastrates or barrows. If boar taint concentrations were high, pancetta from immunocastrates and barrows was considered better.

As mentioned above, one major concern of consumers are possible residues in pork of immunocastrates. As part of the European Medicines Agency [127] approval process for Improvac®, food safety was evaluated and several studies tested hormonal and oral efficacy of the synthetic antigen used in the vaccine. In sheep, the hormonal efficacy was first tested by intravenous application of the compounds used in Improvac®, then of the complete antigen, in order to measure the LH release. The GnRH fragment itself only had a potency of 0.2% on LH-release when compared to injections of the natural GnRH [128], as the first amino acid, which is involved in receptor binding, is missing [129]. The diphtheria toxoid has also been used for other vaccines and has neither toxic nor hormonal activity [127]. Similarly, the injection of the whole antigen revealed no hormonal activity.

The oral effects of the vaccine were tested in pigs and rats. In pigs, the normal dose of 2 mL Improvac® was administered twice, at the age of 13 and 17 weeks. Neither GnRH antibodies were detected in serum nor decreasing testosterone levels. Even a 70-fold dose of Improvac® applied orally to rats did not change the GnRH antibody concentrations [128]. It was therefore concluded that the vaccine is not orally effective [128] and the withdrawal time was set at 0 days before slaughter [39]. The main risk for the operator is a potential self-injection of the vaccine. In the scientific report of the European Medicines Agency [127], the risk of self-injections is estimated at 0.00004%. However, in order to minimize the risk of self-injections, the manufacturer of Improvac® provides a safety device for vaccination [112]. Nevertheless, the consequences of a potential self-injection have to be estimated. As with all mammals, the hormone GnRH is crucial for reproduction and no species differences in GnRH amino acid sequence exist between pigs and humans [130]. Vaccination against GnRH would therefore lead to transient infertility in both females and males. After an accidental self-vaccination, the user must not carry out further vaccinations to avoid high GnRH antibody production. In a study by Simms and co-authors [131] with prostate cancer patients, GnRH vaccination was tested to suppress testosterone-induced tumor growth in 12 patients with advanced prostate cancer. In five patients, a significant decrease in testosterone concentrations was shown. The suppression of testicular function was transient and testosterone returned to normal concentrations after 9 months.

4. Conclusions

Immunocastration is a technique to improve pork quality, animal welfare, economic profitability, and environmental protection, which can contribute to a more sustainable pork production in Europe. Nonetheless, conflicting aims within each pillar of sustainability as well as between the three pillars have to be balanced against each other in the production process (see Figure 1). High product quality with low boar taint levels and higher levels of intramuscular fat work well with production systems which optimize welfare aspects through an early second vaccination. These advantages have to be balanced against the higher anabolic potential of boars which can create economic and environmental benefits. The later the second vaccination is applied, the better its effects for the environment and for farm profitability. As demonstrated by this example, synergic aims exist between the pillar of economy and the pillar of environment. On the other hand, conflicting aims between these two pillars and the pillar of society also exist. Within the value chain, targeted communication about the impact of the timing of the second vaccination is essential in order to make use of this opportunity to produce meat quality tailored to various market segments with different impacts on sustainability.

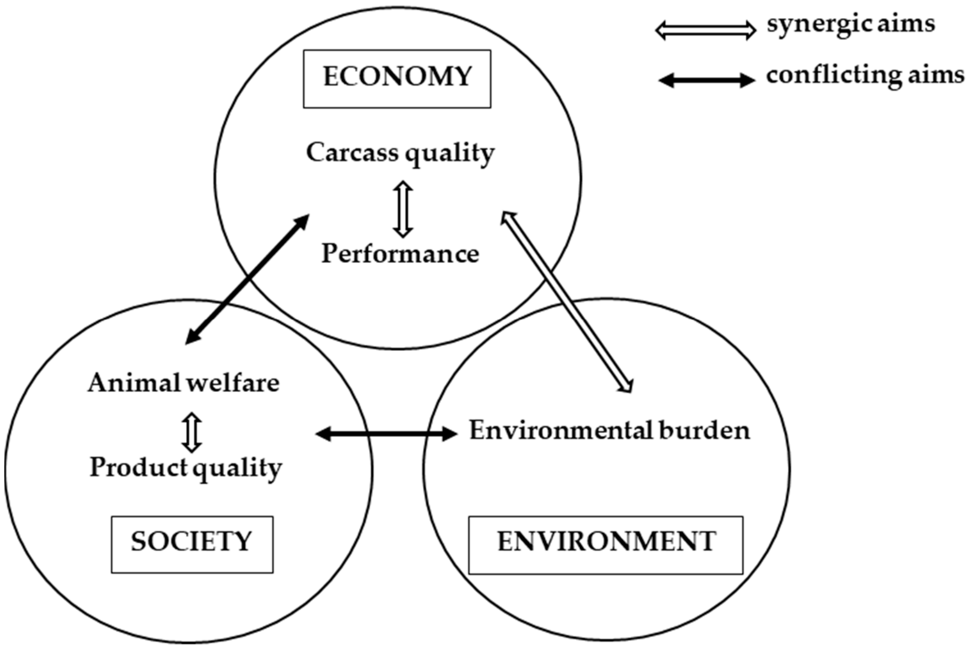

Figure 1. Relationships between the main criteria influenced by immunocastration within the frame of sustainability.

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