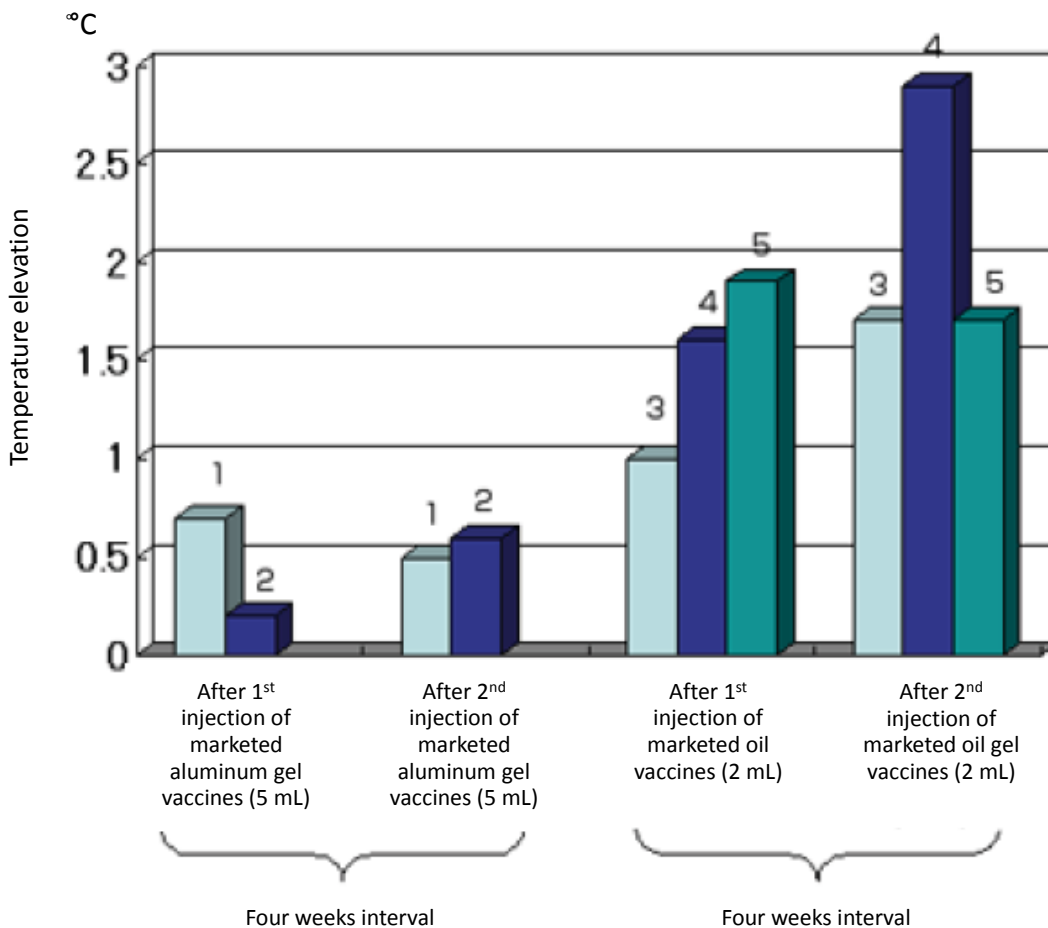


What Is Pig-friendliness Expected for Vaccines?

Regarding vaccines, we would like to address 2 points of pig-friendliness expected especially for inactivated vaccines. The 1st point is pig-friendliness of adjuvants added to enhance the effect of vaccines. The 2nd point is pig-friendliness of antigens, which are active ingredients of vaccines. In terms of friendliness of adjuvants, for example, fever which develops after injection of oil adjuvant vaccines, indicates the intensity of the stimulus (Figure 1).

Figure 1 Increase in pig temperature after injection of oil vaccines (Laboratory study)



5 pigs aged two months were tested.



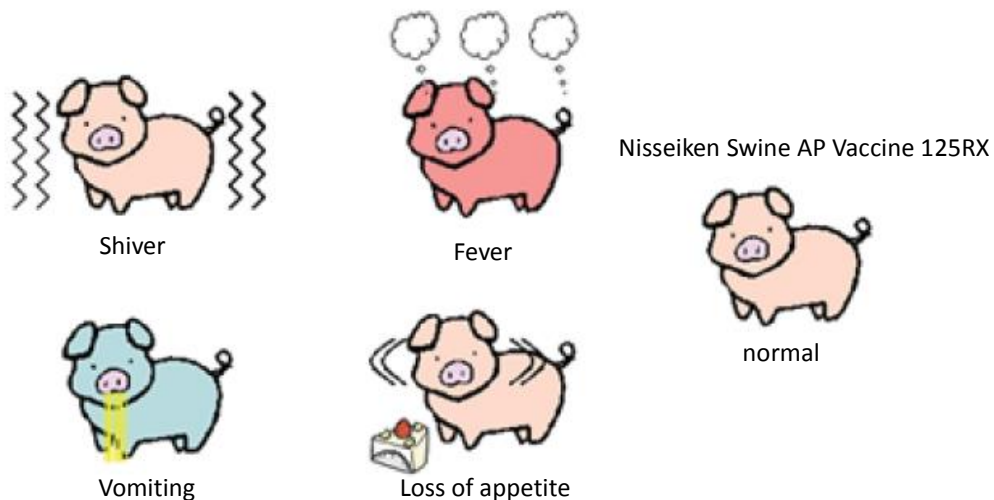
(Figure 2)

In addition, oil adjuvant vaccines are associated with scars of tissue response due to injectants as well as residual injectants which remain in muscles for a long time (Figure 2). The rest period described in the instructions for use of oil adjuvant vaccines is the period required for this residue to disappear. It seems that the degree of response to the stimulus of injectants differs markedly among pig groups. Some pig groups show an intense response to commercially available oil adjuvant vaccines. Therefore, it is important to select a vaccine which is suitable for your pig group. Even if you have had no problems so far, when you have changed your pig groups or your pig suppliers, you need to observe your pigs while paying attention to this point.

For aluminum gel adjuvants, on the other hand, such anxieties are not necessary.

For active ingredients, the 2nd point of pig-friendliness, attention should be paid to problems caused by excessive amount of endotoxins, a component which certain types of bacteria have and which constitutes bacterial bodies, contained in vaccines. *Actinobacillus pleuropneumoniae* (AP) vaccine is a good example of such problems. Have you ever got worried by symptoms of pigs such as loss of spirit, loss of appetite, shaking, and vomiting which developed immediately after injection of an AP vaccine? (Figure 3)

Figure 3 Adverse events developed in pigs after injection of Apx vaccine including App endotoxins



It seems that the degree of response to endotoxins also differs markedly among pig groups; some pig groups show almost no response notable, and other pig groups show a strong response which may inhibit productivity. In any case, it is better to select a vaccine with less stress for pigs. Among many types of endotoxins, endotoxins of AP have an extremely high toxicity for pigs. Liquid medium, in which growth of a large amount of AP occurs when AP vaccines are manufactured, contains a large amount of this endotoxin. Traditional vaccines consisting only of AP bacterial bodies were brought to a safe level by using washed bacterial bodies for vaccine. However, this procedure alone was no longer sufficient for the 2nd-generation AP vaccines whose effect is enhanced by adding cytotoxins produced by AP as new antigens. It has become an important technical challenge how to minimize endotoxins which may be mixed into cytotoxins purified from cell culture supernatants. Nisseiken has overcome this challenge by making *Escherichia coli* without endotoxins of AP produce non-toxic cytotoxins of AP, by applying the latest technology. As a result, Nisseiken has succeeded in developing vaccines with dramatically high in safety (Table 1). Nisseiken is committed to the development of products with high safety with the aim of developing pig-friendly vaccines.

Table 1 Comparative safety study of three types of marketed AP Vaccine – Adverse events after injection-

Vaccine	Pig No.	1 st injection					2 nd injection				
		Fever	Shiver	Depression	Tachypnea	Vomiting	Fever	Shiver	Depression	Tachypnea	Vomiting
AP125RX	1	-	-	-	-	-	-	-	-	-	-
	2	-	-	-	-	-	-	-	-	-	-
	3	-	-	-	-	-	-	-	-	-	-
A	4	+	+	-	-	-	+	+	-	-	-
	5	+	+	-	+	-	+	-	-	-	-
	6	+	+	-	-	-	+	+	-	-	-
B	7	+	+	++	-	-	-	+	+++	-	-
	8	+	+	++	-	-	-	-	+	-	+
	9	-	++	+++	+	-	-	++	+	-	-

Pigs: SPF pigs aged about forty days

Vaccine: AP125RX (Nisseiken Swine AP Vaccine 125RX), A, B
Each vaccine was injected following its dosage and administration.

Symptoms: Fever - : Equal to or lower than 41.4°C, + : 41.5°C
Shiver - : No, + : Lasting less than 60 minutes, ++ : Lasting at least 60 minutes
Depression - : No, + : Lasting less than two hours, ++ : Lasting 2-6 hours, +++ : Lasting at least six hours
Vomiting - : No, + : Yes