A comparison between Infectious Bronchitis (IB) live-attenuated vaccine strains Ma5 and H120

MSD Animal Health

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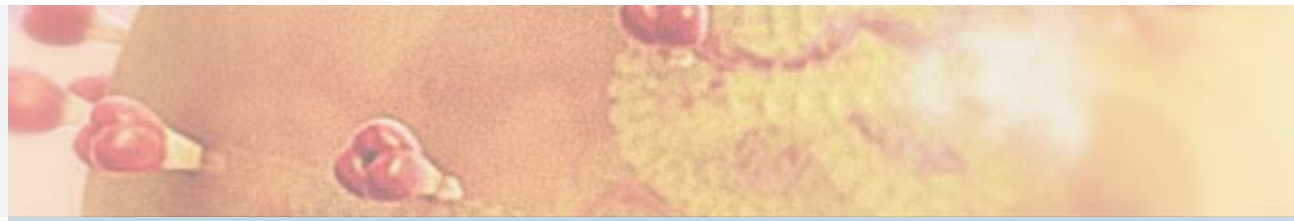

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Abbreviations

IB	Infectious Bronchitis
Mass	Massachusetts
MDA	Maternally derived antibodies
ND	Newcastle Disease
qRT-PCR	Quantitative RT-PCR
S	Surface protein

Summary

- Ma5 and H120 are live attenuated IBV vaccine strains of the Massachusetts serotype for use in broilers, layers and breeders
- Both Ma5 and H120 can be used safely from 1 day of age onwards
- Ma5 is proven to be more immunogenic than H120 (faster onset of immunity, better protection)
- Ma5 can be used as a single component vaccine or as a combined product with ND vaccine Nobilis® ND Clone 30 without interference problems
- Ma5 represents an important Protectotype™, resulting in good levels of protection against many of the existing IB variants
- The use Nobilis® IB Ma5 results in increased flock performance and profitability

Introduction

Infectious bronchitis (IB) vaccines H120 and Ma5 are two live-attenuated vaccines of the Massachusetts (Mass) serotype that continue to be used worldwide as part of vaccination programs to control diseases caused by IB virus in chickens of all ages and type. This paper will describe the origins of these two vaccine strains and consider some of their similarities and differences.

Before considering each of these vaccines, it is important to mention what are the characteristics of the ideal live attenuated IB vaccine. It should induce a high, long lasting immunity without causing any disease or adverse reaction in chickens with either high or low levels of maternally derived immunity. It must be stable so that it does not increase in virulence during passage in the chicken. Ideally it must be capable of being administered at the same time as live attenuated vaccines against other poultry diseases. In stimulating immunity, it is essential that it replicates in the respiratory tract, yet must do so without causing more than minimal damage to the ciliated epithelial lining of the trachea. From what has been said, it will be realised that this ideal will never be completely achieved, but none the less, must be aimed for.

History of the two vaccine strains

H120

One of the first IB vaccines to be produced, it was developed in The Netherlands in the early 1960s from the "H" strain of IB virus, so called because of the initial letter of the farmer (Huyben) from whose chickens the original isolate was obtained. The isolate, characterised as IB and shown to be of the Massachusetts serotype, was attenuated by serial passage in embryonated eggs. The vaccine called H52 was developed from material given 52 passages in embryonated eggs, whilst the H120 vaccine was developed from material that had received 120 passages. Further details of the origin and development of this strain can be found in the Review by Bijlenga *et al.* (2004).

The H strain was one of the earliest live attenuated IB viruses to be produced and the H120 vaccine is possibly still the most widely used live attenuated IB vaccine globally today; not only as a primary vaccine in broilers, but also for the initial vaccination and boosting of future breeders and future layers. However, concerns have been raised regarding its ability to provide adequate protection against IB challenges in both broilers and breeder/layers in all situations. The main problem perceived was the frequent need to revaccinate, since the currently available vaccines did not provide a long term and uniform level of protection, especially when given at day-old. This is an increasing problem as an increasing number of new IB variants are identified worldwide. Another difficulty, is knowing when to apply the vaccine in the face of different levels of maternally derived antibodies (MDA). Furthermore, problems of interference associated with the need in many countries to vaccinate against Newcastle Disease (ND) at the same time as IB, led to the need for an IB vaccine which could be used together with ND vaccines. To meet these concerns, the Nobilis® IB Ma5 vaccine was developed.

Ma5

Up to this time, all live attenuated IB vaccines had been produced by attenuating the virus by serial passage usually, as with H120, in embryonated eggs. This means that any vaccine sample will always contain a number of sub populations of the virus, which may have different characteristics. Ma5 is different as it was plaque purified. This means that only one specific virus particle was selected and perpetuated. This results in a homogeneous virus population with identical properties, thereby reducing the biological variation within the vaccine virus population and guaranteeing a predictable behaviour in the field.

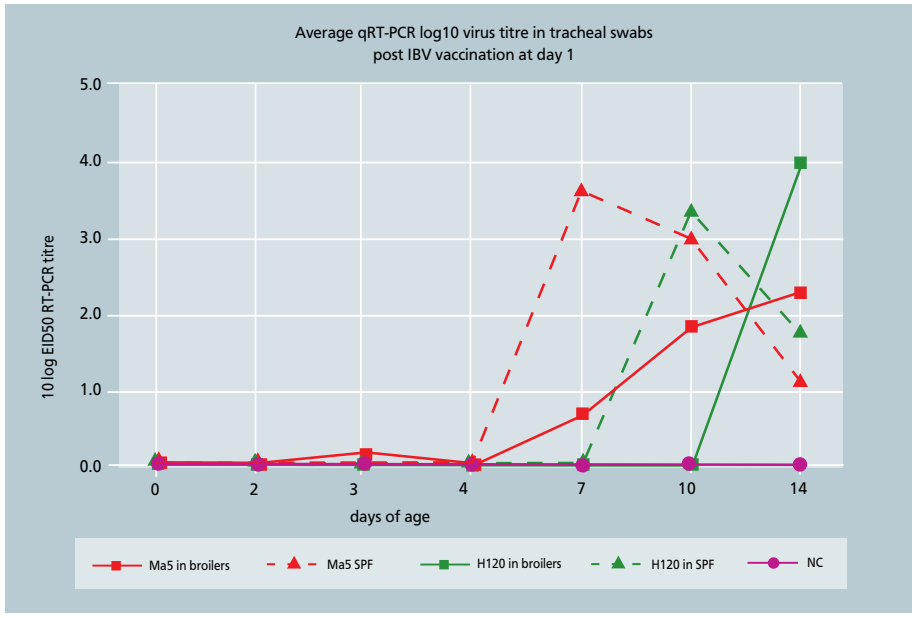
In order to develop Nobilis®IB Ma5, an attenuated Holland strain of the Mass serotype was adapted to grow in chicken embryo kidney cell cultures, grown in petri dishes so that individual plaques, or virus particles, could be selected and their properties determined. Many vaccine candidates were selected and tested to determine their immunogenicity and pathogenicity for the chicken. After extensive testing, one candidate shown to have the desired characteristics was selected for vaccine development. The vaccine developed from this specific strain was designated **Nobilis®IB Ma5**. At an earlier stage of development the IB Ma5 strain was shown to have the unusual ability for an IBV of being able to spontaneously haemagglutinate chicken red blood cells (U S Patent No 4751079); a feature which had been shown to be associated with greater immunogenicity.

The special characteristics of the Ma5 vaccine include:

- Homologous virus population for predictable behaviour and genetic stability
- The fact that it is a better inducer of immunity than is H120
- Its ability to break through high levels of MDA, meaning that it is highly effective even when administered at day-old, yet is also safe when given to chickens with low levels of MDA
- Can be combined with other vaccines such as ND vaccine Nobilis®ND Clone 30 without problems of interference; this results in good IB as well as good ND protection

A study performed at GD Deventer, The Netherlands by Dr J. de Wit clearly showed that when the two vaccines were compared, Ma5 performed better than H120 in both SPF chickens as well as in broilers in the face of MDA In this study, quantitative RT-PCR technology (qRT-PCR) was used to compare the replication of both H120 and Ma5 vaccines following administration by spray to either 1-day-old SPF chickens or to commercial 1-day-old broilers with high level of MDA to IB. This work showed that the peak of replication of the Ma5 vaccine occurred approximately 3 days earlier than that of H120 in SPF birds and 6 days earlier in commercial birds (Figure 1). This is important because the longer delay before H120 replicates to a sufficiently high titre to induce protective immunity, means a greater risk of field infection occurring before the chickens are adequately protected. Also, the longer delay in the replication of the H120 vaccine would increase the risk of interference with later vaccinations compared to Ma5, meaning reduced efficacy against field challenge or increased vaccination reactions.

Figure 1 *Average qRT-PCR virus titre (10log EID_{50}) in tracheal swabs of commercial broilers and SPF chickens vaccinated with H120 or Ma5 at day-old.*



Relationship between H120 and Ma5

Both viruses are of the Massachusetts serotype, and their close relationship to each other is confirmed both antigenically and by studying the genome of the two viruses.

Antigenic relationship

By performing cross neutralisation tests it has been shown that the two viruses have a very close antigenic relationship (Table 1).

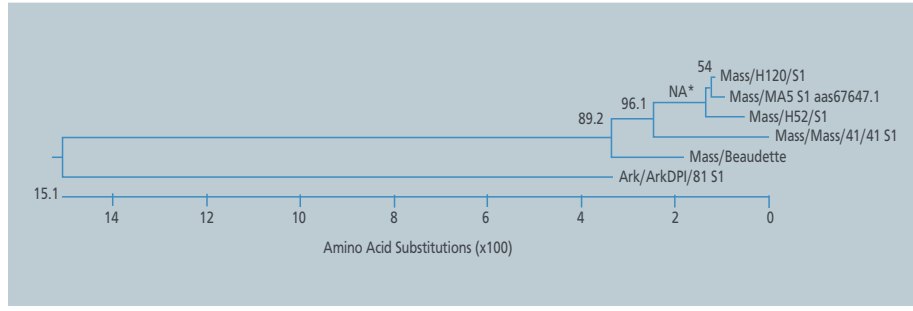
Table 1 *Cross neutralisation between the H120 and Ma5 strains of IB.*

Vaccine strain	Reciprocal cross neutralisation titre (log2) using specific antiserum to different IB strains	
	H120	Ma5
H120	7.0	7.0
Ma5	7.0	7.0

Genotypic relationship

Based on the results of nucleotide sequencing of the entire S1 part of the spike of the IB genome, the close relationship between H120, Ma5 and M41 (all of the Massachusetts serotype) has been demonstrated (Dolz, *et al.*, 2008; Jackwood, personal communication) [Figure 2]). Although an analysis of hypervariable sequences of the S1 gene (Bochkov, *et al.* 2006) showed that these 3 viruses could be grouped in similar, but different clusters, they do none the less show this close genetic relationship.

Figure 2 *Phylogenetic tree showing relationship between different strain of the Mass serotype; Arkansas is included for comparison.(Jackwood, personal communication).*



Conclusion

The close relationship of both the Ma5 and H120 vaccine strains of the Massachusetts serotype has been confirmed both antigenically and by studying the genome of the two viruses. Although sequence studies have shown that they are of the Massachusetts serotype, they can still be readily differentiated by phylogenetic analysis.

Safety of H120 and Ma5 vaccines

Safety of a live IB vaccine is crucial, especially when administered to very young birds. The current IB field pressure in most parts of the world underlines the importance of early vaccination. This means that in most cases vaccines are applied to birds at the first day of age, upon hatching. For this reason, the vaccine used at such a young age must be safe for chickens with either low or high levels of MDA.

The safety aspects of H120 and Ma5 are illustrated in the following experiments. The safety aspects evaluated are: the effect of the vaccine strains on the ciliated epithelium of the trachea and its genetic stability (no reversion of virulence). It is also important to evaluate the possible effect of a live vaccine virus on the reproductive organs of future layers and breeders.

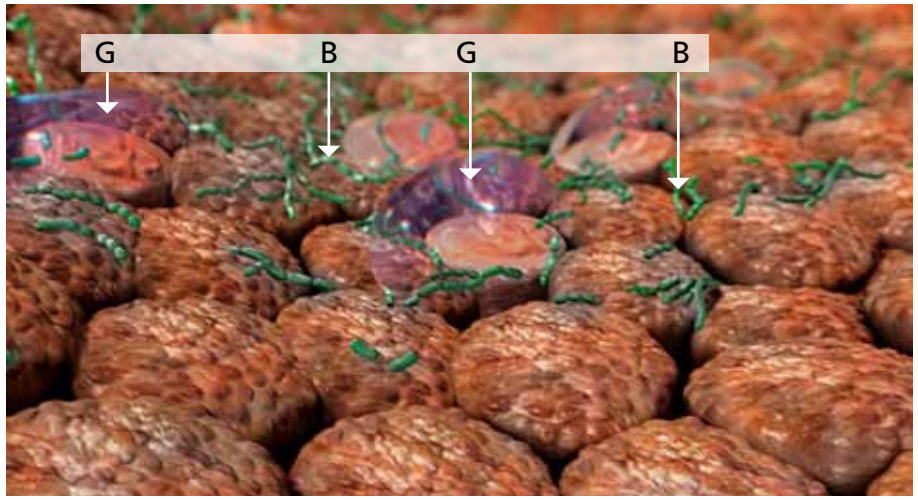
The ciliostasis test

This test is used in many of the experiments described subsequently and therefore it will be explained here, with examples. (see also Cook *et al.*, 1999).

The ciliostasis test is a tool to measure the effect of a virus on the tracheal mucosa. The tracheal mucosa represents a mechanical barrier against foreign particles in the respiratory tract (so called "muco-ciliary apparatus"). This barrier consists of motile hair-like structures called cilia and secretory cells (Goblet cells)- see Figure 3. They trap and eliminate foreign particles such as dust and bacteria. In the ciliostasis test tracheal rings taken from different parts of the trachea of vaccinated and/or challenged birds are prepared and observed under low power microscopy. The rings are scored from 0 to 100% according to the level of ciliary movement; protected birds show average scores of >50% of motile cilia; unprotected birds can show partially to completely deciliated tracheal surfaces (see Figure 4).
This is a useful test for both IB and ND because each virus causes transient immobility of the cilia lining the trachea.

Figure 3 *Normal surface of the trachea covered by cilia, among which mucous producing Goblet cells (not shown) are found.*

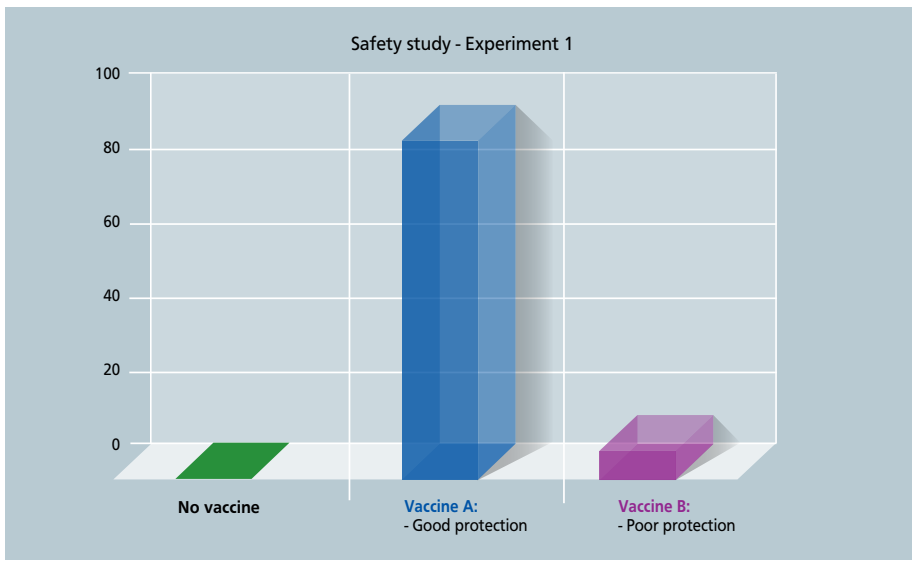
Figure 4 *After an IB infection the cilia on the cell's surface are destroyed. The mucous producing Goblet cells can easily be recognized. The bare tracheal surface is open to secondary (bacterial) infections.*



B: Bacteria G: Goblet cell

Example of results obtained using the ciliostasis test:

Figure 5 *Percentage protection against IB challenge in vaccinated birds measured by the ciliostasis test.*



Experiment 1

The safety of the 2 vaccines was compared in day-old SPF chickens. Initially clinical signs and ability to detect the virus in the trachea at 4 days post inoculation were determined. The results (Table 2) show that H120, well proven to be a very safe vaccine, caused more respiratory signs and could be recovered from more of the chickens that could Ma5, thereby confirming the safety of the Ma5 vaccine.

Table 2 *Clinical signs and virus reisolation of IB H120 and Ma5 vaccines 4 days after inoculation.*

Vaccine strain	% of chickens with clinical signs	% of chickens from which virus was recovered
H120	26	40
Ma5	0	10

Experiment 2

The next method used to determine safety was by assessment of the ciliary activity of the ciliated epithelium of the trachea as described above by using the "ciliostasis test". The results (Table 3) show that Ma5 caused no more ciliostasis than did H120. The scoring system used in the comparison was:

0 = 100% ciliary activity; mean score for 5 rings examined.
4.0 = No ciliary activity; total damage to the ciliated epithelium of the trachea.

Table 3 *Safety of Ma5 and H120 vaccines for day-old SPF chickens.*

Vaccine strain	Mean ciliostasis score (days post vaccination)	
	4	10
H120	0	1.8
Ma5	1.1	0.9
Unvaccinated control	0	0

Conclusion

The results show that both strains replicate in the tracheal mucosa but that Ma5 caused no more ciliostasis (damage) than did H120.

Conclusion

Again, based on histological assessment, the two vaccines were shown to cause minimal tracheal alterations.

Experiment 4

Genetic stability is important for a live IB vaccine. Lack of genetic stability can result in an increase in the pathogenicity of a vaccine virus in the field after dissemination from bird to bird. The stability of the Ma5 vaccine was clearly demonstrated when vaccine virus given 5 back passages in chickens was compared with the starting material by inoculating them both into 1-day-old SPF chickens. The results (summarised in Table 5). show that, as is well known for the H120 vaccine, the back passaged Ma5 vaccine caused no more damage to the tracheal epithelium than did the vaccine virus that had not been serially passaged in chickens. The scoring system used in the comparison was:

0 = 100% ciliary activity; mean score for 5 rings examined.
4.0 = No ciliary activity; total damage to the ciliated epithelium of the trachea.

Experiment 3

In another experiment, sections of tracheas were taken and examined histologically at 3 and 7 days after vaccination of day-old SPF chickens. Tracheal lesions were scored as follows:

Score 0 - no lesions observed
Score 1 +/- occasional lesions observed
Score 2 + mild lesions observed
Score 3 ++ moderate lesions observed
Score 4 +++ severe lesions observed

Table 4 *Histopathological examination of tracheas of SPF chickens following inoculation at day-old with H120 or Ma5 vaccines.*

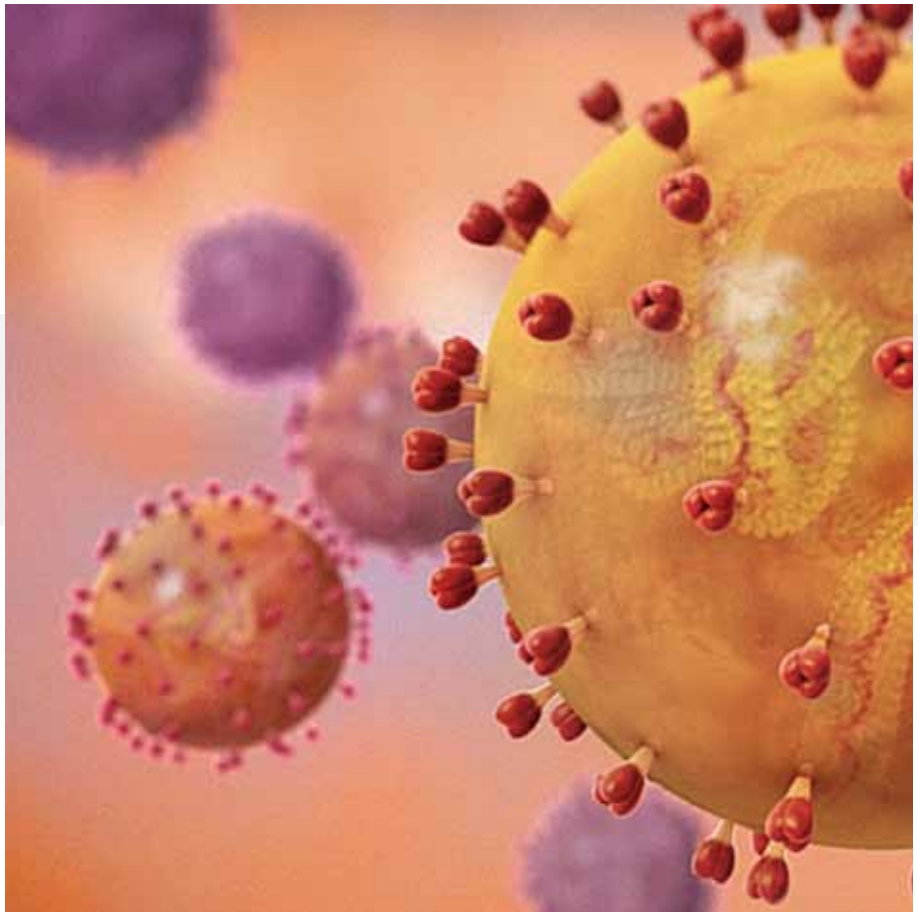
Vaccine strain	Cumulative tracheal lesion score / group (days post vaccination)	
	3	7
H120	9	3
Ma5	7	4
Unvaccinated control	0	0

Table 5 *Safety of the Ma5 vaccine and back passaged virus for day-old chickens.*

Ma5 virus at	Mean ciliostasis score (days post inoculation)		
	5	13	21
Vaccine level	1.8	2.3	0
After 5 bird passages	2.4	1.9	0
Control	0	0	0

Conclusion

The back passaged Ma5 vaccine caused no more changes to the tracheal epithelium than did the vaccine virus that had not been serially passaged in chickens, thereby confirming the safety and stability of the vaccine.



Safety for future laying birds

Both H120 and Ma5 vaccines are commonly given to future breeders and layers at as young as one day of age, therefore it is important to ensure that they have no adverse effect on the female reproductive tract and therefore on future egg laying performance.

In a large scale study, groups of chickens were vaccinated at day of age and followed until they came into lay. The parameters studied are indicated in Table 6. Mortality throughout was very low and well within normally expected levels. Neither vaccine adversely affected the age at which egg laying commenced, indicating their safety, when administered at 1-day-old, for future laying hens.

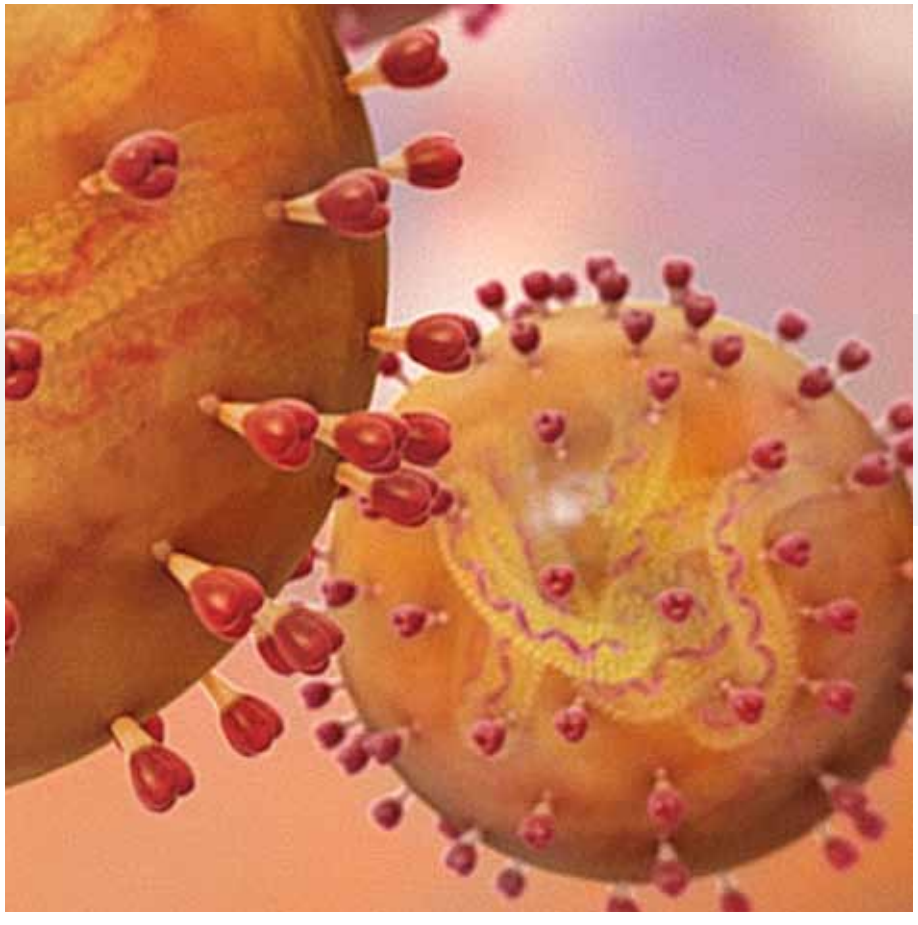
Table 6 *Comparison of safety of H120 and Ma5 vaccines for future breeders.*

Vaccine	Number in group	Number died from 1-day-old to point of lay	% mortality to point of lay	Number died in lay	Mean age in days at start of lay (SD)
Ma5	150	16	10.7	2	163.5 (9.4)
H120	136	23	15.3	1	167.9 (8.9)

Summary safety studies

The Ma5 vaccine resulted in:

- Less chickens with clinical signs after vaccination
- Less virus reisolation after vaccination
- Less tracheal changes in vaccinated chickens
- No adverse effect on the reproductive tract of future laying birds



Efficacy studies in the Laboratory

Efficacy of H120 and Ma5 vaccines - homologous challenge.

The efficacy of the two vaccines was compared in SPF chickens following vaccination at day-old and challenge with the homologous, virulent IBV M41 strain 5 weeks later. The level of protection provided by the two vaccines was compared at 4 days post challenge using several parameters: clinical signs, virus recovery from the trachea and damage to the ciliated epithelium of the trachea (ciliostasis test - see above and Cook *et al.,* 1999).

Table 7 *Comparative efficacy of H120 and Ma5 vaccines given at 1 day of age against homologous challenge 5 weeks post vaccination.*

Vaccine strain	% Protection 4 days post challenge when assessed by		
	Clinical signs	Virus isolation	Ciliostasis test
H120	73	60	80
Ma5	100	90	100
None	8	0	0

Conclusion

The results show that, whilst the H120 vaccine provided good protection, the Ma5 vaccine was more efficacious.

Cross protection against IB variants - Protectotype™

New IBV serotypes continue to emerge. These new serotypes can emerge as a result of only a few amino acid changes in the S1 part of the spike genome of the virus (see Figures 6A, 6B and 6C). With the continuing emergence of new serotypes of IBV it seemed prudent to evaluate the level of cross protection obtained by the use of currently available IB vaccines. Vaccination / challenge experiments including currently available IB vaccines (such as Nobilis® IB Ma5) enable us to evaluate the level of cross protection that the currently available vaccination protocols can provide. In this way, field viruses can be grouped into a Protectotype™ rather than into serotypes, based on the response of the chickens after challenge. This is more relevant from a practical point of view. Importantly, this work has shown that it is undesirable and not always necessary to consider developing new live IB vaccines for each new serotype.

The H120 vaccine has been found to induce some protection of the respiratory tract against heterologous challenge with strains of the Belgian B1648 and French 84084 and 84221 serotypes (Cook *et al.,* 1999), although protection was improved if the chickens were revaccinated 2 weeks later with a vaccine developed from the heterologous serotype 4-91 (Parsons *et al.,* 1992). However, there are many reports indicating that H120 does not protect adequately against heterologous challenge and (as stated above) the need for an IB vaccine which provided protection against the increasing number of different IB variants was one of the incentives for the development of Ma5.

Our experimental model is based on the use of different live IB vaccines and protection is measured by means of the ciliostasis test. In our protectotype model the vaccines Nobilis® IB Ma5 (Massachusetts) and Nobilis® IB 4-91 are used.

Figure 6A *The surface (S) protein of IBV appears as a "Corona" on the virus membrane.*

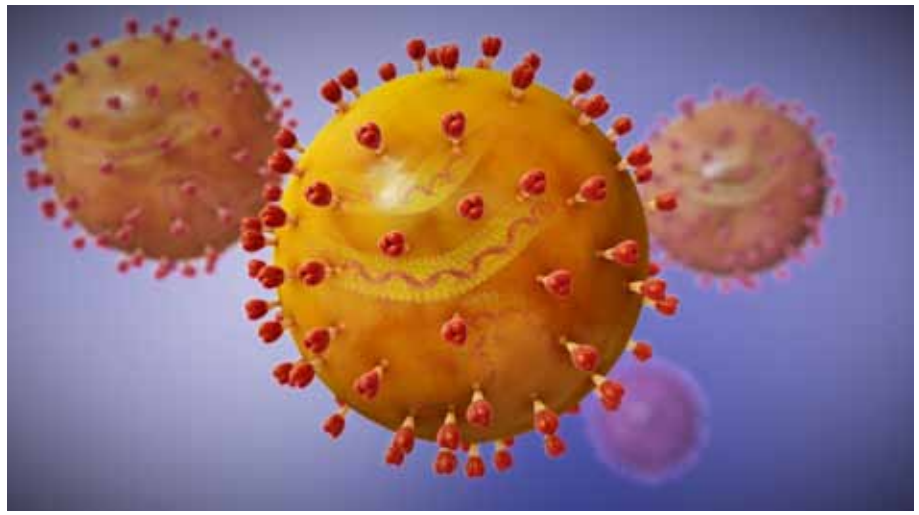
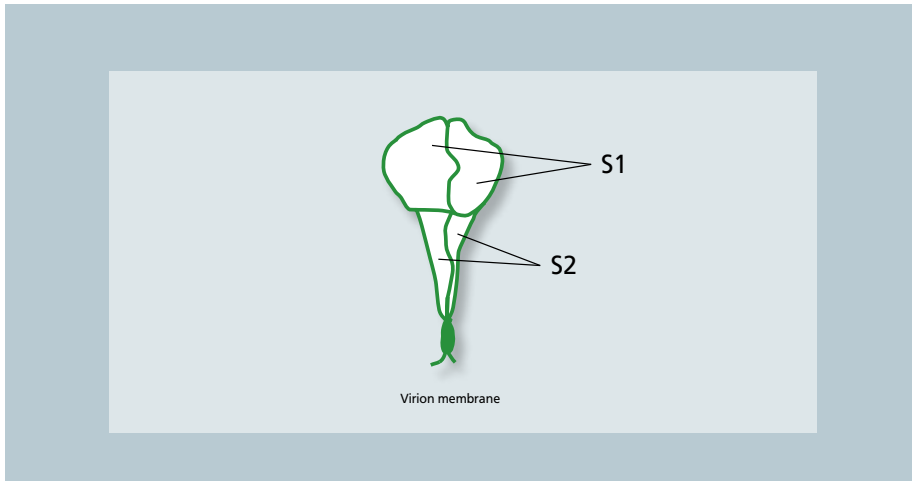


Figure 6B *Model of the structure of the "S" protein on the surface of the IB virus (Cavanagh 1983)*



With the recent interest in, and concern about, IB variants worldwide, a number of studies have been performed to show that in the case of challenge with some heterologous IB variants, the Ma5 vaccine can provide reasonable protection when used alone, although in many cases its use in a vaccination program including also the 4-91 vaccine provided better protection. Some examples are shown in Table 8; for more information see Cook *et al.* (1999).

Figure 6C *Representation of differences in the "S" protein of several IBV strains which result in different serotypes of the virus*

Table 8 *Heterologous protection using IB Ma5 vaccine alone or followed by 4-91 vaccine 2 weeks later.*

Novel IB variant	Protection score[1] following vaccination with		Assessment of results
	Ma5 (day old)	Ma5 (day old) + 4-91 (2 weeks)	
A	84	91	Ma5 vaccine used alone protected well
B	88	88	
C	82	87	
D	53	90	Improved protection using 2 different IB vaccines
E	47	89	

[1] protection score = $\left[1 - \frac{\text{mean ciliostasis score for vaccinated/challenged group}}{\text{mean ciliostasis score for corresponding challenge controls}}\right] \times 100$

The higher the score, the better the protection

Compatibility

Vaccination with live vaccines at an early age is important to prevent birds from developing diseases. However, the short live span of broiler chickens makes it difficult to plan a proper vaccination program against relevant diseases within a given timeframe. The increasing number of live-attenuated vaccines which are given to young chickens results in problems of interference between them and/or reduced efficacy of one or other of the vaccines. This is a major concern when IB and ND vaccines are administered at the same time, or with only a short interval between them. It is well recognised for example, that the IB H120 vaccine cannot be used effectively at the same time as ND vaccines, such as LaSota, because of reduced protection against each disease and because of the possibility of increased vaccination reactions.

It is therefore convenient and desirable to use combined vaccine when possible, provided the components are compatible. Compatibility between vaccine viruses is therefore of the utmost importance in order to overcome interference problems. As stated above, interference may result from the combination of live vaccines against IB and ND. It may result in lack of protection and severe post-vaccination reaction. Interference depends on many factors, in particular the viral concentration, the invasiveness and the immunogenicity of the vaccine strains involved. However, the problem could be overcome to a large extent if an effective bivalent (IB/ND) vaccine could be developed without there being any interference in the efficacy of the two components. Such a product is the Nobilis® Ma5+ Clone 30 vaccine.

Compatibility of IB Ma5 and ND Clone 30 vaccines when formulated as a single product

Efficacy

The results in Table 9 show a comparison in broilers, housed under experimental conditions, of the efficacy of an IB Ma5+ND Clone 30 combined vaccine and an IB H120+ND Clone 30 combined vaccine in protecting against challenge with either IB (M41 strain) or ND (Herts strain). Groups of day-old broilers that had been vaccinated by eye drop were challenged with IB, and groups vaccinated by coarse spray were challenged with ND 5 weeks later. Protection was assessed 4 days post challenge. Following IB challenge, the birds vaccinated with Ma5+Clone 30 were completely protected, whilst in the group vaccinated with H120+Clone 30, protection was only partial, meaning that Nobilis®ND Clone 30 interfered with the efficacy of the H120 vaccine in the combination. Following ND challenge, some mortality occurred in the H120+Clone 30 vaccinated group, meaning that the H120 vaccine caused partial interference with the efficacy of the Clone 30 component in the combination; the group vaccinated with Ma5+Clone 30 showed an excellent level of protection against the ND challenge, proving that there was no interference between the strains in that vaccine combination.

Table 9 *Efficacy of combined live attenuated IB/ND vaccines.*

Vaccine strains	Route of vaccination	Assessment of protection 4 days post challenge with		
		IB challenge M41 strain		ND challenge Herts strain
		% clinical signs	% tracheal damage[2]	% mortality
H120/Clone 30	eye drop	30	42	ND
H120/Clone 30	coarse spray	ND[1]	ND	17
Ma5/Clone 30	eye drop	0	0	ND
Ma5/Clone 30	coarse spray	ND	ND	0
Unvaccinated controls	-	80	100	100

[1] Not done [2] Measured by the ciliostasis test

These data taken together show that Ma5 in combination with ND Clone 30 is a superior vaccine to that in which the IB component is H120.

Field studies

Having established the good results for safety and efficacy of the Ma5 vaccine strain under laboratory conditions, several field studies were carried out to evaluate the effect of vaccination with Nobilis®IB Ma5 under field conditions. These studies involved the collection and evaluation of production parameters in broilers, including in some cases laboratory challenge studies in birds collected from the field.

Safety and efficacy of the combined Nobilis® Ma5+Clone 30 vaccine under field conditions

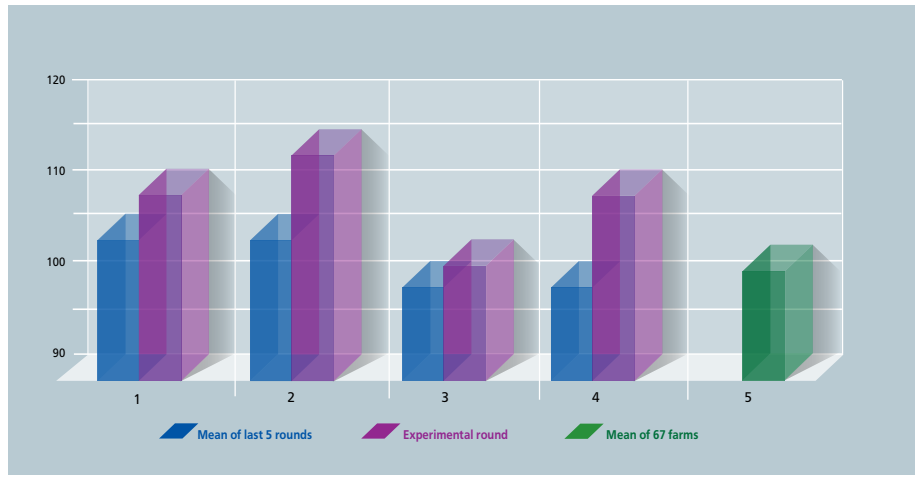
A series of more than 20 field trials were performed in commercial broiler flocks of different size and breed in The Netherlands by van Dijk. Vaccination with the combined Ma5+Clone 30 vaccine was done by coarse spray at either day-old (in the hatchery) or on the farm at 7 days. A number of different parameters were measured and in some cases it was possible to compare performance with that of previous flocks on the same site where IB and ND vaccines had been given separately. Based on assessment of vaccine reactions, serological response, mortality, growth rate, feed conversion and production index, all experimental flocks showed improved performance and in the case of mortality and production index, the improvement was statistically significant. For full details of the results see van Dijk, (1991).

Comparison of H120 and Ma5 vaccines under field conditions

Further field trials were conducted to compare the performance (based on mortality levels and production indices) of flocks vaccinated with Ma5 with that of previous rounds on the same sites in which H120 was the IB vaccine used. Some of the trial sites had a history of respiratory problems; others did not.

Based on a comparison of mortality and Production Index, flocks vaccinated with Ma5 (both on farms with a history of respiratory problems as well as on "normal" farms) performed better when compared to previous rounds on the same sites where H120 vaccine had been used (Figure 10).

Figure 10 *Comparison of the percentage improvement in the production index for farms vaccinated with Ma5 (purple) compared to performance of previous rounds on the same sites (blue).*



In the comparison the average of other 67 farms (green) raised during the same period.

Controlled laboratory challenge of birds vaccinated with IB Ma5 under field conditions

Because a challenge can not be guaranteed under field conditions, from some of the field trials, birds were taken to the laboratory to be challenged under controlled conditions. The results (Table 10) show that in all trials, and following vaccination at different ages, protection against homologous experimental challenge was good. The total number of birds challenged was 150 and overall, protection was 85%.

Table 10 *Laboratory challenge (M41 strain) of birds vaccinated in the field.*

Field study number	Age in days when vaccinated	Challenge at days post field vaccination/age		% Protection[1] at 4 days post challenge
1	1	28	28	79
		42	42	83
2	1	28	28	87
		42	42	87
3	10	18	28	73
		32	42	87
4	10	18	28	80
		32	42	80
5	17	11	28	100
		25	42	93

[1] Based on assessment of tracheal ciliary activity (ciliostasis test)

The results show that the Ma5-vaccinated birds were well protected at both challenge times.

Conclusion

Taken together, the results of the field trials indicated that the use of Ma5 resulted in improved performance of the vaccinated flocks and that it provided solid protection to the vaccined birds.

Summary efficacy studies

The Ma5 vaccine resulted in:

- Good protection against homologous and heterologous IB challenge
- Improved performance of vaccinated flocks

Guidelines for Vaccination

Nobilis®IB vaccine Ma5 can be administered as a single component vaccine or as the combined vaccine Nobilis® Ma5 + Clone 30 by coarse spray, eyedrop or in the drinking water. When used in combination with ND Clone 30, protection will be obtained against both IB and ND challenges.

Administration by coarse spray or by eye drop will give the best response. These should be the methods of choice, especially when vaccinating young birds. Nobilis®IB vaccine Ma5 will induce an adequate level of immunity that will last for at least 42 days and protect against challenge by field viruses which are considered to belong to the same Protectotype™.

A vaccination program depends largely upon the local situation. A vaccination protocol that includes Nobilis IB 4-91 will increase the breadth of protection against most of the variants strains circulating in the field.

The following program can be used as a guideline:

Table 11 *Guideline for a vaccination program.*

Broilers

Age	Vaccine	Administration
1 day	Ma5 (+ND Clone 30)	Coarse spray; eye drop
14 days	4-91	Coarse spray; eye drop

Layers and breeders

Age	Vaccine	Administration
1 day	Ma5 (+ND Clone 30)	Coarse spray; eye drop
2-3 weeks	4-91	Coarse spray; eye drop
6-8 weeks	Ma5 (+ND Clone 30)	Coarse spray; eye drop; drinking water
8-12 weeks	4-91	Coarse spray; eye drop; drinking water

The vaccination program for layers and breeders should be completed with the use of preferably, a multivalent inactivated vaccine at point of lay such as Nobilis®IB multi to provide protection during the whole laying period.

For further information: www.infectious-bronchitis.com

Table 12 *Comparison of properties of Nobilis® IB Ma5 and H120.*

Feature compared	H120	Ma5
Serotype	Massachusetts	Massachusetts
Parent strain	Dutch field strain	Mild Mass H
Method of attenuation	Serial passage in embryos	Plaque picking in cell culture, then embryo passage
Spontaneous haemagglutination	No	Yes
Safety	Well demonstrated	Well demonstrated
Efficacy-homologous challenge	Well demonstrated	Well demonstrated
Efficacy- heterologous challenge	Few data; variable	Well demonstrated
Compatible with ND vaccine	No	Yes
Immunogenicity	Good	Very good
Results under field conditions	Good	Very good

Conclusions

This paper describes the similarities and differences between two live-attenuated vaccines of the Massachusetts serotype of IB, Nobilis® IB Ma5 and the H120 vaccine strain (Table 12). Although both of the Massachusetts serotype, the vaccines can be differentiated from a genotypic point of view. Nobilis® IB Ma5 proved to be as safe as H120 for birds of all ages and to induce better protection in vaccinated birds independent of their MDA status, either as a single component vaccine or in combination with Nobilis® ND Clone 30. Altogether, the use of Nobilis® IB Ma5 resulted in increased flock performance and profitability in comparison to flocks vaccinated with H120.

Why is Nobilis® IB Ma5 your best choice for IB prevention?

- **Nobilis® IB Ma5 can be used from 1 day of age onwards in broilers, layers and breeders**
- **Nobilis® IB Ma5 is safe in birds with low or high levels of maternally derived antibodies**
- **Nobilis® IB Ma5 has proved to be more immunogenic than IB H120**
- **Nobilis® IB Ma5 represents an important Protectotype™ with wide coverage against many IB variants**
- **Nobilis® IB Ma5 can be used as a single component vaccine or as a combined product with ND vaccine Nobilis® ND Clone 30 without interference problems**
- **Nobilis® IB Ma5 results in increased flock performance and profitability**

Nobilis® IB Ma5 is a winner!

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notes

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