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Structured process for evaluating new products for production systems: Animal science perspective

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Introduction

This paper provides a format for evaluating prospective new products in animal production systems. Proper experimental design and analysis is important to prevent making a poor decision. This process begins with a Screening format. In some ways, this process is analogous to 'screens', conducted by Pharmaceutical companies, on a variety of candidate compounds to be developed for a specific malady. In our case, there are more products proposed by Service providers than are feasible to rigorously test. Animal production companies, and their science advisors, must use a structured process to (1) screen or select worthy products to (2) evaluate for efficacy. Data from the latter are used to (3) estimate value for the system. This process is not complete, however, until one knows the extent to which the new product performs in the system. In large systems, segments (or regions) may differ in their ability to implement. There may be regional differences in health of the 'pig flow' and this may affect response to the product. The template that Hanor has devised, as a guide through the decision-making process, is presented. Due credit is given to Kendall (2005) for his excellent work.

Prospective products screen

The screening process in our decision making template is guided by 4 considerations:

- Is there a specific need for this product in our production system?
- Is there a plausible biological explanation for this product's efficacy?
- Is there 'proof of concept' data

Are there specific conditions necessary for product response?

These 'hurdles' make it clear that commercial companies must do a certain amount of homework, prior to presenting their product to decision-makers (DVM, MS-Ph D animal scientists, experienced Production leaders) for consideration. It is important to know the approximate cost from initial data so that we can determine if this product is appropriate. However, it is acceptable if the cost per pig treated is not 'nailed down' in the early phase of product life. This is especially true under 'dire' circumstances (e.g., PCVAD), when collaborative efforts are needed to accelerate a prospective product decision in order to resolve a pressing problem. We enter this situation as a willing participant in the 'proof of concept' or initial data phase, but proper experimental design and analysis is adhered to. This exception to the screening process is rare, but warranted by the situation's urgency.

Does the product address a specific need?

This goes without saying, except that the time available for Production Technical personnel to test and implement new products is in short-supply. For this reason, priorities are established by the Production team. Products that address a lower priority are normally excluded on this criterion alone.

Plausible biological explanation

Vendors must be able to provide a plausible explanation why their product improves performance. If the product protects the animal against disease then how is that accomplished? There must be science-based rationale (e.g., in vivo challenge, proof of concept in a naturally challenged herd) that is able to withstand 'mild' critique. However, it is acceptable if a thorough understanding of the mechanism or mode of action is not known. Demonstrating that a technology provides a repeatable performance response, with sufficient return over investment (ROI) is immediately more important. Mode of action information can be assembled over time, because this research generally requires significant financial resources and time.

Proof of concept data

Proof of concept or initial data is needed to confirm product efficacy and to establish potential value. This data may come from a variety of acceptable sources such as University trials (small scale but detailed) if they are conducted by credible researchers, or from experiments conducted in Commercial research facilities. Methods must be detailed so that the apparent competence of the experiment can be judged. Experimental design and statistical analysis must be shown. A low Type I error rate of 5-6% is preferred, because it minimizes the risk of declaring a difference in performance, when none exists. The secrecy associated with some systems, requiring that the data be cited as 'mid-west producer' is understood but nonetheless unacceptable. The report cannot be independently verified.

Sow studies are the most difficult to do correctly because (1) there are so many variables to control when conducting the test, and (2) the numbers required to overcome variation characteristic of variables such as litter-size is large. Some responses are possible (e.g. +1.5 p/L) but not probable and must be viewed with caution. Another problem is with European-based studies and growing pigs. Diet differences are normally significant and this can influence the response. For example, nursery pigs that are fed diets without plasma and (or) antibiotics are more likely to exhibit a growth response to an essential oil product (OEO). These diet omissions make it more likely that pathogens will cause immune stress (enteric or systemic), so that OEO is more likely to produce a growth response through pathogenic control.

Specific conditions necessary for response

A classic consideration in product response is whether it works under conditions of high or low health status or both (but with different responsiveness). This is a moot point for vaccines. In their case, efficacy and then dose related effectiveness must be determined as the 'specific conditions'. Non-traditional feed additives are emerging for treatment of systemic (e.g., dried plasma or colostrum for PCVAD) and enteric pathogens (e.g., OEO for ileitis and hemorrhagic bowel) have important questions beyond efficacy. The 'timing' of treatment application is also vital because effectiveness and cost competitiveness with pharmaceutical alternatives is at stake. Does the amount to be used in the feed change with season (e.g., summer heat stress reduces feed intake) or if it is added to the water, does it react with pharmaceutical's that may be provided?

What about the 'me too' data

'Me Too' products are an important part of the product landscape, but they are immediately disqualified if the company has not done their homework. An example is the 'essential oil' products that are emerging from a variety of commercial sources. The proposal that each is equally effective in controlling hemorrhagic bowel in growing pigs or coccidiosis in the sow herd, despite having some differences in chemical composition or purity is unacceptable. 'Me Too' products, that are inferior, can reflect poorly on genuinely good products and cause confusion about a product class. In some cases, the product may simply appear too late to be considered because of more important system priorities. They tend to drive down cost through increased competition, but more data is required by the provider to offset our lack of incentive.

Prospective product testing

Products that pass the 'Screening' stage must now be tested within the Production system to determine effectiveness. Each system develops their own method of evaluating new products. An increasing number of systems have or consult with trained animal scientists, who understand experimental design and data analysis. Hanor and several other groups have a Pyramid style format for research, beginning with a Discovery center (allows for detailed evaluations with 4-8 treatments) at the pinnacle and proceeding immediately to Field test barns, Field test sites and finally to Regional tests.

Five axioms lay the foundation for product testing:

- Proper experimental design
- Suitable replication to overcome normal variation
- Reliable data collection
- Data collected must be comprehensive enough to answer the questions
- Analytical capability (statistical, financial)

Experimental design

The research method can be successively applied in the commercial setting but improper experimental design is a big problem. Experiments need to be simple and sources of variation managed. This requires proper experimental design to control factors (that produce variation) that are outside the control of the researcher, and those not associated with the Product being tested. Adequate replication gives power to the test. There are 'global' sources of variation, whose effects can be minimized by design but interpretation often has to be made with them in mind. These (major) sources include: Season (time), pig flow (health status) and site (management confounded with pigs derived from different sow farms). If the test is simple and properly designed so that a conclusion, positive or negative, can be reached then the trial was successful.

Trials that are conducted at Hanor research farms typically involve 2-4 treatments for comparison. Number of treatments is dictated by the number of replications required for each criterion. All treatments must be represented in a block (site, barn, sex etc). Research farms (finish, sow) are part of our production system, but they are equipment for detailed testing. We find the excellent and practical reference by animal scientist, T. R. Morris (1999), to be very useful in designing experiments, computing the number of replicates (barns, pens, sows) needed per treatment and so forth.

Some examples of poor experimental design include: (1) Treatments that are not equally represented across Finish sites (e.g., 3 treatments per 8 barn site); (2) Three treatments randomly placed over 2 sites (16 barns total) but with each gender housed in separate barns. (3) Sow Litter-size research is the most difficult to do correctly, because there are so many variables to control. For example, sire can have an impact on LS born (age, line, individual variation within line) and can be controlled by using pooled semen. Another example of poor experimental design involved the evaluation of different proportions of two

feed additives that were intended to improve Lactation feed intake. Four treatments were applied to 16 farrowing rooms, but a treatment was applied to 4 successive rooms before allocating the next treatment. The main problem was that treatments were separated in time and because of climate changes, summer room temperature varied by 15-18 F. Limiting the total number of treatments to two would limit the number of questions that could be addressed but the conclusion is more reliable.

Number of replicates requires an understanding of variation

Prior to conducting a trial, a statistical power test has to be computed for each criterion to ensure adequate replication. The advantage of conducting research within a Production system is the ability to generate an enormous number of replications. Relatively large amounts of variation can be 'overwhelmed' by a large number of experimental units (pens, barns, farrow rooms).

Comprehensive data - To answer important questions

The type of data to collect depends on what questions you want to answer. However, sometimes the questions that are most important to ask are limited by the data that one is willing to collect. If the questions are right but the measures are 'too simple' then the wrong conclusion can be drawn. This is illustrated nicely using nursery nutrition research, since dietary components (and the feed budget) have an impact on piglet health. Simple measures such as ADG and FCR are normally affected, but they are not very powerful. Mortality (DL) may be affected, but this criterion is sometimes of little value, unless the number of replications is greater than that which is normally required to assess ADG and FCR effects.

If the question is to address how the additive affects weaned pig growth and health, then additional variables must be taken. This was illustrated in a study that involved two dietary components, separately or in combination (plasma, oats) (Musser, 2004). In this trial, the number of pigs pulled and injected with an antibiotic (due to apparent illness) was reduced significantly with plasma, oats and especially the combination. Treatment also affected the number of smaller pigs at the end of the nursery period. If the conclusion were based on ADG, FCR and Feed cost per lb gain, the value of extra diet cost was negligible. When the cost of antibiotic treatment was added to the evaluation, the more expensive diets (plasma, oats) had the best ROI. The greater proportion of small pigs from diets without plasma, oats (or both) suggest a further penalty in market carcass weight. Another excellent illustration of this concept was published by Pearce et al. (2002).

Competent helping hands

One cannot under-estimate the time and energy required to undertake a Product test or to implement a successful Product into the system. There are several groups who have provided 'additional hands' and highly skilled minds to help conduct large scale Product tests that could not otherwise have been completed (e.g., APC Inc, Bryan Allen, Drs. J. Crenshaw and J. Campbell).

Exceptions to neatly designed trials

Special situations exist where Site has to be the experimental unit because certain characteristics of disease transmission. Certain trials may require a farm level comparison that utilizes process control charts to assess whether there has been a shift in performance that corresponds to product initiation and withdrawal (switch-back protocol). The latter procedure was used by Campbell et al. (2006), who studied the ability of animal plasma to modulate the response of a sow farm to PRRS activity. An excellent example of how Site (sow farms) was effectively used as the experimental unit was published by Hagen et al., (2000). The choice of which procedure to use will be driven to a large extent to cost of the test material.

Decision to implement a new product and verifying efficacy on a large scale

The value of a Product is determined by computing the ROI from internal test data. The decision to implement a Product depends on its' value in relation to ease of implementation. Implementation and subsequent verification are beyond the scope of this paper so readers are referred to **Figure 1**, which briefly summarizes the process that was developed for Hanor. The New Product is implemented in the Production segment (or region) that is best able to deliver on the protocol or that satisfies any special conditions for efficacy. Data must be collected from the system to verify that the anticipated response is delivered on before the 'approved' Product is incorporated into the Production quiver.

Summary

A structured process is needed to facilitate sound decision-making when considering the plethora of New Products that are emerging. The process that has been developed for The Hanor Company is summarized in **Figure 1**. Each organization must prioritize needs for the Production system and focus on them. Prospective Products must align with these priorities or be 'Screened' out from further consideration. Product's that emerge from the Screening process and that are then 'proven' to have value must move past one more obstacle – verification that it works in the field. The axiom that the Product must 'always work or it doesn't work at all' is lethal. The differentiating factor for each system is implementation so this is the first place to start. The major challenge for the vendor is - understanding conditions under which the Product is most efficacious.

Figure 1: Summary of the key steps in a structured process to selecting and implementing new products in a production system

Prospective Product Screening Process

- Is there a specific need for the Product in the Production system?
- Is there a plausible biological explanation for the Products' efficacy?
- Is there 'proof of concept' or initial data to support the claim?
- Are there specific conditions necessary for Product response?

'*Me Too'* Products are not excused from verifying efficacy, independently

Prospective Product Testing – 5 Axioms of the Structured Process

- Appropriate Experimental Design to control random variation (includes experimental unit choice)
- Suitable replication to overcome random variation
- Reliable data collection process
- Data must be comprehensive enough to answer the questions posed
- Competent analytical capability (Statistical and Financial)

Exceptions to '*discrete*' treatments exist and sometimes require a Farm level experiment that involves 'Process Charting' that is more typical of a manufacturing process. Objective is to determine whether there is a shift in performance that corresponds to Product initiation and withdrawal.

Decision to Implement a New Product

- Product value to the Production system determined with Internal data and Financial approach
- Product value is determined by Return over Investment (preferred to reduced cost)
- Decision to Implement Product depends on (1) Financial value and (2) Ease of implementation

Track System Performance to Verify that Value is Delivered On

- Implement Product in the Segment of Production that is most able to deliver on the protocol or that which meets specific conditions necessary for the Product to perform
- Capture Production data to verify the expected response
- What If the Evaluation does not yield the anticipated response? Review Implementation
- Start with Implementation since it is the most distinguishing feature between Systems
- Perhaps other factors need to be understood before the Product can be used

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