

## Avoiding the Gas-Guzzler: Eight Steps to More Productive Observational Studies

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The automobile industry is in a precarious state. With factories designed to churn out light trucks, SUVs and other gas-guzzlers, the industry has been ill-prepared for the shift toward energy-efficient vehicles. Whether its denial or archaic thinking or lack of responsiveness or inflexible factory design it's pretty clear that Detroit (and even Tokyo) has encountered a perfect storm certainly exacerbated by a global economic meltdown, but one nonetheless largely on their own making.

Is this an allegory for the pharmaceutical industry? Perhaps. I'll limit the metaphor, however, to the subject of research studies, and specifically to observational, non-interventional studies. Suffice it to say that our industry needs to retool in order to cost-effectively respond to the need for these unique types of studies. Analogous to producing an SUV when a Smart Car is what's really needed, while observational studies may be able to utilize certain standard parts from the research process assembly line, a fundamentally different perspective is required overall to respond to what the consumer really wants.

They go by different names: "real world" research; non-interventional study; observational initiative; "late stage" research programs; epidemiological survey; post-marketing surveillance; patient registry; post-approval, non-interventional, observational, real world outcome trial. The common theme is to measure without interfering with what's being measured; in other words, to observe and, of course, to learn something along the way.

However, the specific words and phrases employed to describe a study, while not unimportant, tend to cloud study's underlying intent. The strategic purpose – the business rationale – behind the study all too often gets lost in the dust when getting a research program started.

**This is far more critical than many industry professionals realize, as it's the study's strategic purpose that drives how the study should be "operationalized," and as such, directly impacts not only its budget, but also its outcome.** This is most acute in the case of post-approval, observational studies, for which the industry often employs practices and

perspectives designed for pre-approval, interventional research and, in so doing, ends up with a gas-guzzling study.

So in shopping for the energy-efficient vehicle that is an observational study, the first step is to:

- 1. Re-think What Transportation is Needed!** – The observational study is a means to an end; a mechanism for getting you to your destination. The other words, an observational study can be a response to a number of business issues, ranging from a mandate for safety data to the need to document a product's 'real world' economic value or, as is the case increasingly, somewhere in between. The *goal* is to demonstrate safety and/or economic value, typically in a post-approval setting; the *vehicle* is the observational study. IT is critical to consider this context as it will inform how the study is designed and undertaken – what specific type of care you need to get you where you're going. Don't assume the car you've always bought is the right way to go this time!
- 2. Gain Consensus** – Most researchers and project managers dive right into the design and operational aspects of the study before the strategy objectives have been fully articulated and, importantly, agreed upon. As an observational study can have multiple stakeholders representing varying perspectives, consensus is essential as to what is to be achieved and whether a modest tweak can support additional objectives. OK, it's not necessarily easy when you want a Ferrari, your spouse wants a Hummer, and the kids want a Mini Cooper. But understanding and discussing how everyone will be using the vehicle is essential. At the end of the day, no one may be perfectly satisfied: that, however, is a good indication that consensus has been achieved!



3. **Remember your Destination** – Fundamental to the successful observational study is knowing where you want to go. In other words, envisioning your destination – defining success – is critical. And not just ‘success’ in terms of the study, but more broadly defined, in terms of the observational study’s underlying business purpose, as this will help inform an inventorying of the supporting activities necessary to ensure that, when the study is completed, the strategic goal can actually be achieved. For example, maintaining frequent interactions with regulators or health authorities may be critical in ultimately achieving success for the strategic objectives the observational study seeks to fuel.
4. **Consider Driving Conditions** – OK, now we’re in agreement as to where we’re heading and that an observational study is the vehicle in which we’ll be driving. Here’s the thing: this car performs and is used differently than a truck! An observational study can’t be undertaken as a randomized, clinical trial if we really want to document the real world. That means we’re going to have to accept a standard of evidence that differs from the RCT. And that means that we’re going to be able to use a different operational approach (and maybe save some gas)!

Here’s a quick example: Consider that RCTs are commonly monitored by an external contract research organization (CRO) to maximize data quality and to ensure that the study is being undertaken as per protocol and that other study procedures are being followed. By contrast, rarely will you see an observational study program that includes drug accountability procedures or even protocol adherence assessments, as drug is rarely supplied and as there’s really no protocol to adhere to. Hence, for these reasons alone, the nature and extent of the study monitoring procedures must be considered for the observational study.

What’s more, to fulfill the goal of, for example, a study that seeks to document product use in community based physician practices, site recruiting activities need to be refined. Whereas in a RCT, a premium would be placed on sites

experienced in clinical research, that may not be the critical factor in an observational study. Training activities, however, may need to be readdressed. In addition, in an observational study with typically liberal inclusion criteria, patient identification and accrual need to be orchestrated in a unique manner.

**Fundamentally, every operational aspect of an observational study should be challenged to determine whether there is another way.** Dad’s old Buick just isn’t going to cut it.

5. **Consider Resource Requirements** – Sorry, I’ve momentarily run out of automobile metaphors. The point here, however, is that the customized operational requirement supporting the observational study should now lead to a re-evaluation of the resources required to run the study and the available internal and external assets. Rule of Thumb: An observational study can cost one-fifth that of a similarly sized RCT: your mileage may vary!

An observational study may even be able to be run internationally with little external support, whereas this would be an unlikely consideration for a RCT. At the very least, traditional study resources must be challenged and very important, evaluated using a non-traditional template. Shop for the car with *your* needs – not those of the dealer – in mind!

In addition, consider that the care may run on alternative fuel. A more efficient approach to data collection, for example, may accentuate the operational efficiency of the observational study. In other words, internet-based electronic data collection (EDC), designed specifically for observational research, can generally improve the overall efficiency of the study, often eliminating the need for traditional data management activities. Indeed, an effective EDC approach may substantially lighten the requirements for external study support!

6. **Does it Include a GPS?** – Now that we’re pretty sure what kind of vehicle we want, we can get a bit more specific on our needs. Now is the time to frame the study itself, actually be working in



reverse. If we envision the destination, we can ensure ourselves that we've got all the supporting equipment in place to get us there. What issue will the study explore? (Note that I didn't say "what question will the study answer," as this may be an unrealistic goal for the observational study). What analyses will be required to support the exploration? What data will be required to support the analyses? What statistical techniques should be used to make sense of the data? How will data be obtained? How will patients be recruited? And on and on back to the fundamental operational components that need to be specified as precisely as possible.

By the way, now's a good time to make sure the chair of an external Advisory Board is along for the test ride ...

7. **You Better Shop Around** – There will be a need for RCTs, just like there will always be a market for pickup trucks. But your observational study needs a zippy little energy-efficient compact car, so start shopping. Here's where things get interesting: do you want to try the dealer specializing in compact gas-friendly cars, or should you go with the name brand company that is testing the energy-efficient waters? There's no right answer, but if you develop a customized template for evaluating the vendors, it'll help.

So now's the time to develop the detailed Request for Proposal to enable you to make an apples-to-apples comparison. Does the specialized vendor have the bandwidth to support your clinical study? Does the global CRO have the nuanced understanding of observational research to provide a more energy-efficient solution? Can I get it in metallic blue?

The better you've thought through your operational needs, and the more precisely you've articulated them in the RFP, the easier your selection process will be. If the RFP leaves too much to interpretation, unless the vendor truly understands observational research, you'll be likely to get a proposal for a vehicle far

heavier and clunkier than you need. It's not their fault: that's what they're selling and they'd rather error in the direction of too much versus too little!

8. **Is My Mileage Really That Great?** – True story: I bought a hybrid vehicle last year and the miles-per-gallon performance has been disappointing. So you just never know! But maybe I'm not using it the right way. The point is that, now that you've driven it off the showroom floor, you may need to operate the energy-efficient vehicle differently than you're used to. And that you need to remember what it is you're driving, lest you be tempted to drag race with the teenagers down the block. You bought the car – you're undertaking the observational study – for all the right reasons, but you've got to keep those reasons in mind so that your expectations remain appropriately tempered. It's critical to maintain vigilance over the study so that its underlying strategic vision is faithfully reflected in all program activities and materials.

The conditions under which products are approved for market use are generally not the conditions under which the product will actually be used! Observational research can be the most appropriate vehicle for exploring and documenting how a product performs in the real world. Indeed, pre-approval research can be compared with automobiles on the company test-track, whereas post-approval, observational studies gauge a car's performance in traffic conditions! And in actual traffic today, a vehicle with decidedly different specifications may be better able to navigate the hazards that are unique to post-approval road conditions.

The underlying business drives (no pun intended this time) both the rationale for the operational structure of observational research. An observational study is generally right on target for examining real world product safety, cost-effectiveness, quality-of-life, and/or clinical effectiveness, but as it is a vehicle with important limitations, it must be operated within a different, specialized context. There's no need to load up on gas-guzzling, luxury features when energy-efficient, basic transportation is all that's really needed.

Enjoy the ride!