Article published online: 2024-04-10

Editorial Commentary

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J Clin Interv Radiol ISVIR 2024;8:68–70.

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The recently published editorial has nicely captured the reality of the off-label use of numerous drugs and devices in day-to-day clinical practice.[1] It brings to light the dilemmas that the off-label use of products can present.

When venturing beyond the boundaries contained within the instructions for use (IFU), we walk a tightrope between achieving the desired treatment outcome and maintaining the patient's safety. Instead of wrestling with the question of whether we should treat on-label or off-label, maybe we should examine why we are offered these two choices in the first place. If a product clearly has a beneficial treatment effect and clinicians have observed that its safety profile is acceptable, then why doesn't it gain an on-label indication? In other words, is the regulatory path too rigorous to encompass and adapt to the reality of day-to-day clinical practice?

We can consider this question using the authors' example of Histoacryl (B. Braun, Melsungen, Germany) and its decade-long off-label use as an embolic agent. Since the Food and Drug Administration's (FDA's) stamp of approval is the benchmark used throughout the world, let us look at the process the FDA would require for Histoacryl to receive an on-label indication as an embolic agent.

In order to gain approval for a new indication, a product like Histoacryl would have to go through the supplemental new drug application (sNDA) process. Compared to gaining original approval for the drug, there is not a reduced burden of proof in order to receive approval for a new indication. The FDA has been working to streamline the review process and to expedite approvals. Full approval for an sNDA may now be granted using an intermediate endpoint on a case-by-case basis. This change has been made in order to weigh the urgency of an unmet clinical need and a product's utility in meeting that need. The main barrier lies in obtaining the necessary data in order to submit the sNDA application. These data may need to come through trial work, which we know is costly and takes time. It would stand to reason that the company producing the drug would lead the charge to organize and finance any requirements for the sNDA process as they would have the most to gain financially. Is it actually the case that it would be worthwhile to go through this potentially lengthy and expensive process, though? The reality is that the benefits of seeking approval for a new indication do not usually outweigh the drawbacks.

When a product has been found to be safe and effective, clinicians will use it without the on-label indication. Histoacryl is a prime example of this common practice. Despite the lack of formal approval for a new indication, the company is not missing out on the sale. Both the companies and physicians know that it is highly unlikely that winding the clock back to perform randomized trials would be successful. If the product fills a much-needed clinical gap and physicians have anecdotally determined that it is safe and effective, then equipoise has essentially been lost and physicians would be unwilling to randomize patients. So, if we are stuck with our present reality in which both the on-label and off-label worlds coexist, how do we allay our fears about ensuring that the drugs and devices we use are truly safe? After all, regulatory processes exist for a reason, as they force us to collect and analyze our data to prove efficacy and safety. Additionally, we also know that there have been many examples in medical history in which our anecdotal perception of safety has been proven to be incorrect when put to the test through a trial.

The answer to our concerns lies in data. It is my firm belief that keeping track of our data is a powerful and essential tool for the confirmation of hypotheses. As clinicians, we owe it to our patients to be more diligent about collecting our data. If

DOI https://doi.org/10.1055/s-0043-1777848.
ISSN 2457-0214.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

obtaining this information through a prospective randomized trial is out of reach, then the solution could be data collection using real-world registries. The Vascular Quality Initiative (VQI) registry publishes a broad spectrum of topics germane to vascular disease and is an example of the power of real-world data collection. With 14 registries under the VQI umbrella, over 4,000 physicians from several countries have contributed data from over 800,000 procedures. This collaboration has resulted in a treasure trove of valuable information for publication to address wide-ranging topics concerning vascular health such as Racial Disparities in Treatment Indications and Outcomes for Limb Ischemia[2] and machine learning to predict outcomes following endovascular abdominal aortic aneurysm repair.[3]

Although it requires additional time and discipline to participate in a real-world registry like VQI, the abundance of valuable data it contains shows that over time, it pays tremendous medical dividends by answering our questions about the efficacy and safety of our treatment therapies. This important information could also be a solution to achieving an on-label indication for a product.

Funding
None.

Conflict of Interest
None declared.

References

1 Garg S, Nidugala K, Shyamkumar N, Kalva S. Off-label use of devices and drugs in interventional radiology. J Clin Interv Radiol ISVIR 2023;07:139–140
2 Semaan DB, Abdul-Malak OM, Avgerinos ED, et al. Racial disparities in treatment indications and outcomes for limb ischemia. Ann Vasc Surg 2023;96:89–97
3 Li B, Aljabri B, Verma R, et al. Machine learning to predict outcomes following endovascular abdominal aortic aneurysm repair. Br J Surg 2023;110:1840–1849

